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FOREWORD

Since time in memoriam, horses have been renowned for their athletic prowess and work capacity, and documenting and understanding the physiologic basis for these abilities has occupied many industrial-age equine scientists for more than a century. An integrative approach is essential to the elucidation of the mechanisms by which horses work, compete, or perform the various recreational activities that contemporary society asks of them. The performance or 'output' of an equine athlete is determined by many complicated interdependent biological processes. Understanding how these processes function and relate to each other is mandatory if the horse is to be effectively trained and managed during its working or competitive life. Such understanding is also pivotal to the clinical application of basic physiologic and pathologic principles, and is therefore necessary to ensure the successful diagnosis and management of exercise-related diseases in horses.

Modern day equine exercise science is generally regarded to have been born in 1967 with the publication of Sune Persson's doctoral thesis.[1] This was the first work that documented data generated from horses exercising on a high-speed treadmill. The subsequent widespread availability of such treadmills has had a great deal to do with defining the current state of knowledge with respect to basic and applied equine exercise physiology. The inception of the quadrennial International Conference on Equine Exercise Physiology (ICEEP) in 1982 has also provided a regular forum at which investigators can describe new fundamental and clinical findings pertaining to exercise in horses of all ages. Despite the great strides in equine exercise science that have been made in the last 35 years, it is important to recognize the contributions of the pioneers who helped develop many of the techniques upon which current scientific methodologies are based. These people also made fundamental observations that are still pivotal to much of the work that is being conducted today. Nathan Zuntz was a Berliner professor of animal science who, with a number of colleagues, notably Drs. Curt Lehmann and Oscar Hagemann, investigated the metabolism of horses during rest and work. These studies are truly extraordinary by today's standards. Zuntz and Lehmann built the first Laufband, or treadmill, and used a facemask and tracheotomies to measure oxygen consumption and carbon dioxide production in two horses at speeds up to 3.5 m/s.[2] Zuntz and Hagemann further refined these results by measuring oxygen consumption, carbon dioxide production, arteriovenous oxygen content difference, aortic blood pressure, tidal volume, heart rate and respiratory frequency in horses that were walking, trotting and walking backwards freely, and while pulling loads of 66–78 kg uphill, downhill and on the horizontal![3] These data were impressively similar to those that are determined under similar exercise conditions today.

The ability of the horse to increase its blood volume during exercise and the associated rise in hematocrit are two hallmarks of equine exercise or work, particularly in warmblooded horses. Scheunert, Krzywanek and Müller were the first to observe that hematocrit of horses could increase by up to 50 percent during exercise, and that the magnitude of this increase was related to workload.[4,5] Their observations were published in 1926. They also noted similar events in dogs and observed that splenectomy eliminated this exercise-related hemoconcentration. The contractile nature of the equine spleen was subsequently confirmed by Steger in 1938.[6] These phenomena are still the basis of various studies designed to evaluate different aspects of metabolism and the dehydration status of horses under different exercise conditions.

As well as the above cited work, interested readers are also referred to the work of two other teams of people in particular. First, Samuel Brody and colleagues conducted a seminal series of studies at the University of Missouri with the aid of a treadmill that they built. They focused on equine energetics, the efficiency of metabolism, nutrition, work and growth in the second quarter of the 20th century and published their findings in a collection of 66 Missouri Agricultural Experiment Station Research Bulletins. Among other things, Brody et al. showed that the caloric cost of movement per unit live weight, per unit horizontal distance covered, is not affected by the size of the animal and is independent of speed. He also demonstrated that minute ventilation is exponentially related to the energetic cost of work or exercise.

The Russian scientists Karlsen and Nadaljak published a series of papers from 1960–1965 that were, unfortunately, difficult to obtain. Karlsen, with Brejtsen, provided the first 'modern' documentation of the synchrony of breathing and stride frequencies[7] and, with Nadaljak, displayed great ingenuity in conducting the first field study of horses exercising at high speed.[8] Together these investigators recorded an oxygen consumption of 62.8 L/min in a Standardbred galloping on a track at 11.1 m/s.

I mention these things because, in the words of the famous Australian neurologist, Sir Sydney Sutherland (1910–93), it is important to 'honor those who go first even if those who come later go further'. In the 66 chapters in this book, the reader will find the latest information regarding the physiologic responses and adaptations of the various equine body systems to exercise and training. This information is also linked to exercise-related clinical problems of the same body systems. The chapters have been written by a number of contemporary experts in these fields. There are also sections on breed-specific activities and other 'applied' aspects of equine sports medicine. This book represents an ambitious and valuable contribution to the body of equine exercise-related physiologic and clinical literature. With it the reader has the opportunity to follow a subject from its basic principles to its current state of knowledge in both the physiologic and clinical or applied sense. Producing such a volume is a major undertaking and the principal editors and contributors are to be congratulated on their efforts. However, our knowledge base is incomplete; i.e., it is not perfect. When considered in terms of progress made over the last 120 years, one might even suggest that there have been few major

breakthroughs and that, rather, new information has come to light in an almost begrudging but inevitable fashion. In reality this is the essence of the scientific process and it is the principal reason that this book should prove to be so useful. It is also the main reason that such books need to be regularly revised and it is hoped that this will not be the only edition of this very complete and valuable text.

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References

1. Persson S. On blood volume and working capacity in horses. Acta Vet Scand Suppl 1967; 19: 1–189.
2. Zuntz N, Lehmann C. Untersuchungen über den Stoffwechsel des Pferdes bei Ruhe und Arbeit. Landwirtsschaftliche Jahrbücher 1889; 18: 1–156.
3. Zuntz N, Hagemann O. Untersuchungen über den Stoffwechsel des Pferdes bei Ruhe und Arbeit. Landwirtsschaftliche Jahrbücher 1898; 27: 1–438.
4. Scheunert A, Krzywanek FW. Fluctuations in the amount of blood corpuscles. Pflügers Arch 1926; 213: 198–205.
5. Scheunert A, Müller C. Effect of activity on the blood of horses. Pflügers Arch 1926; 212: 468–476.
6. Steger vonG. Zur Biologie der Milz der Haussäugetiere. Deutsche Tierärztl Wchnschr 1938; 46: 609–614.
7. Karlsen G, Brejtse N. Synchronizitat der Rhythmen von Atmung und Bewegung – Grundlage fur die Entwicklung eines schnellen Trabes (in Russian). Konevodstvo i Konesport 1965; 35: 22–24.
8. Karlsen GG, Nadaljak EA. Interchange of gaseous energy and respiration of trotters at work. Konevodstvo i Konesport 1964; 34: 27–31.

PREFACE

The diagnosis and treatment of disorders of the equine athlete is a specialty requiring not only the ability to recognize and treat clinical abnormalities, but also an understanding of the physiologic demands of exercise and requirements of competition and training. The science of equine exercise physiology has progressed to the stage that it now provides a sound, scientific basis for much of equine sports medicine. The current level of knowledge, while still incomplete and imperfect, of the physiologic processes underlying the acute responses to exercise and the mechanisms and effects of exercise conditioning, provides a sound, fundamental understanding of the workings of the equine athlete. Contemporary equine exercise physiology is comprised of not only the physiologic responses to exercise and training, but also nutrition, biomechanics, behavior and pharmacology. This fundamental knowledge informs our decisions regarding appropriate training, nutrition, care and treatment of the equine athlete.

We recognized that equine exercise physiology and equine sports medicine had advanced to the stage where there was a need for a comprehensive and integrated source of information for practitioners, students of veterinary medicine, graduate students in equine exercise physiology, residents in training and well-informed lay horsemen and women. This book attempts to meet that need. As with the first attempt at any major project, this book is imperfect and will not be all things to all readers. However, we hope that we have filled, at least partially, the requirement for a comprehensive source that integrates the basic and clinical sciences of the equine athlete.

Our belief in the importance of integrating both the basic and clinical sciences dictated the structure of this book. Each of the major body systems is described beginning with detailed coverage of the physiologic responses to acute exercise and to conditioning. This is then followed by one or more chapters describing the important clinical abnormalities of equine athletes. Our belief is that knowledge of the fundamentals of exercise science is essential for an understanding of the clinical abnormalities of the equine athlete. However, for those readers with little interest in the clinical abnormalities of athletic horses, the basic science chapters can be read alone and will provide a sound understanding of the physiology of equine athletic performance. Chapters in the last section of the book dealing with parasite control, veterinary aspects of training the various breeds of horse, aged athletes, and more, provide a pragmatic, utilitarian approach to the athletic horse.

Finally, we thank the colleagues and students with whom we have had the pleasure of working and who provided much of the knowledge contained within this book. Our profound gratitude is extended to the authors of sections of this book with an appreciation of the effort that was required to compile new comprehensive material on their designated topic. We hope that they, and the readers, are pleased with the final product.

Kenneth W. Hinchcliff
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2004

CHAPTER 1

Integrative physiology of exercise

Kenneth W. Hinchcliff and Raymond J. Geor

The horse as an athlete

Comparative physiology

The horse is an extraordinary athlete, a characteristic that is the result of evolution of horses as grazing animals on the ancient prairies of North America. Survival in these open lands was enhanced by speed, to escape predators, and endurance, required to travel long distances in search of feed and water. These attributes are shared by pronghorn antelopes, another species that evolved on the prairies. The equid characteristics of speed and endurance were subsequently modified or enhanced by selective breeding by humans.

Horses were domesticated on more than one occasion, based on analysis of mitochondrial DNA from a wide variety of current domestic breeds and Przewalski's horses.[1,2] Domesticated horses were then selected and bred for certain traits, depending on the intended use. Large, heavy breeds of horses were bred for draft work, such as pulling plows, sleds or carts, or military work, such as the chargers that carried heavily armored knights into the battles of the Middle Ages. Lighter horses were bred for speed and endurance and were used for transportation, herding and sport. Horses have been bred or adapted to a large variety of uses. Thoroughbred race horses run at high speed (18 m/s, 64 km/h) over distances of 800 to 5000 meters, Standardbred horses trot or pace at high speed for distances up to 3600 m, Quarter Horses sprint for 400 m or less at speed as high as 88 km/h (see Chapter 32), sometimes around figure of eight courses delineated by barrels (barrel racing), and Arabians trot for up to 160 km in a single day during endurance events (and over longer distances during multi-day races). In contrast, draft horses pull huge weights (1000 kg or more) short distances in pulling competitions, Warmbloods perform elegant, but demanding, dressage routines, and ponies pull lightly laden jinkers or buggies.

Regardless of their size, provenance or intended use, all horses have in common an ability to perform physical activities, including running or jumping, at a level that surpasses that of most other animals of similar body size. The concept of body size is important as many physiologic variables, and especially the maximum values of these variables, do not scale directly with bodyweight but often more closely scale to an exponent of bodyweight.[3] Commonly, exponents range between 0.68 and 0.75. This exponent is derived empirically from the measurement of variables such as maximum running speed or maximum rate of oxygen consumption ($\dot{V}O_{2max}$). Typically, when expressed as a one-to-one function of bodyweight (i.e. per kg) values for many variables are much higher for smaller mammals. The necessity to scale variables allometrically has fascinating physiologic implications and interpretations.[3] However, direct comparison among species is to some extent specious from the point of view of depicting differences in physical capacity, given that the absolute values of these variables vary to such a large extent. Nonetheless, such comparisons are frequently made, if only to reinforce the magnitude of the maximal absolute values of these variables in the exercising horse (Table 1.1).

The athletic capacity of horses is attributable to a number of physiologic adaptations. In some cases these adaptations are not affected by training, for example lung size, whereas others change in response to training, for example blood volume (see Chapters 28 and 38). The superior athletic ability of horses is attributable to their high maximal aerobic capacity, large intramuscular stores of energy substrates and in particular glycogen, high mitochondrial volume in muscle, the ability to increase oxygen-carrying capacity of blood at the onset of exercise through splenic contraction, efficiency of gait, and efficient thermoregulation.

The maximal aerobic capacity ($\dot{V}O_{2max}$) of horses is approximately 2.6 times that of similarly sized cattle.[8] The larger aerobic capacity in horses is permitted by a larger

Table 1.1 Selected physiologic variables of athletic and non-athletic species[4–7]

Species	Bodyweight (kg)	Speed[a] (km/h)	Duration of exercise	$\dot{V}O_{2max}$ (mL O_2/kg/min)	HR[a] (beats/min)	Energy expenditure per day (kcal)
Thoroughbred race horse	450	64 (max)	2 min	180–200	240 (max)	30 000
Endurance race horse	400	15	12 h	180		38 000[b]
Steer	470			80		
Goat	32			80		
Greyhound	34	64 (max)	60 s	Not reported	300[a]	2160
Sled dog	25	20	10 days	170	300	11 000[b]
Human (Olympic class)	70	36 (max)	9.4 s	85	220	7000[c]
Pronghorn antelope	32	65	10 min	300		

[a] During customary athletic activity.
[b] Day of racing.
[c] Tour de France cyclists.
HR, heart rate; max, maximum value.

maximum cardiac output and stroke volume and higher hemoglobin concentration.[8] Maximum heart rate is not different between horses and cattle. In addition to the cardiovascular differences between cattle and horses, horses also have lungs that are twice as large as those of cattle with gas exchange surfaces 1.6 times those of cattle.[9] Thus, horses have structural adaptations that enhance oxygenation of blood in the lungs, oxygen transport capacity of blood and the ability to deliver oxygen to tissues. The oxygen transport chain, from air to muscle, of horses is suited to transportation of the large volumes of oxygen required to support the high metabolic rate of strenuously exercising horses.

Substrate is required to support these high metabolic rates during exercise. Substrate to support exercise is either carbohydrate or fatty acids. Oxidation of fatty acids is limited and reaches maximal values in other species at a work intensity of approximately 40–60% of $\dot{V}O_{2max}$.[10,11] It is likely that a similar phenomenon occurs in horses. Additional work above this exercise intensity is fueled solely by oxidation of carbohydrates, predominantly glycogen.[12] Horses have high intramuscular concentrations of glycogen, as do other athletic species such as dogs.[13] Muscle concentrations of glycogen in horses are approximately 140 mmol/kg of muscle (wet weight) compared with 80–100 mmol/kg in humans.[14] High intramuscular concentrations of substrate are important for fueling muscle contractions during exercise. The flux of glucose from blood into muscle and subsequently to the mitochondria provides only a small amount (< 10%) of the energy used during intense exercise,[15] probably because of limits to the rate of transportation of these compounds during exercise.[13] The presence of large amounts of readily available substrate in close proximity to mitochondria is therefore essential for horses to undertake strenuous exercise.

Mitochondria provide the energy for muscle contraction. The greater the quantity of mitochondria per unit of muscle weight, the greater is the oxidative capacity of muscle. Muscle of horses contains approximately twice the concentration of mitochondria as does muscle of cattle, a similarly sized animal but with a much lower aerobic capacity.[16] This greater aerobic capacity in muscle, when supported by adequate substrate availability and oxygen delivery, permits a higher whole animal maximal aerobic capacity.

Oxygen transport from the lungs to exercising muscle is achieved by the circulation. In addition to cardiac output, oxygen delivery is limited by the oxygen-carrying capacity of blood. Horses achieve rapid increases in the oxygen-carrying capacity of blood by increasing hemoglobin concentration through splenic contraction. Splenic contraction in anticipation of exercise and during exercise increases the circulating red cell mass without concomitant increases in plasma volume.[17] The resulting increase in hemoglobin concentration increases the oxygen-carrying capacity of arterial blood by up to 50% during intense exercise. The beneficial effect of this autoinfusion of red cells at the start of exercise is apparent in horses from which the spleen has been removed.[18–20] Splenectomized horses have lower hematocrits during exercise, altered systemic hemodynamics including lower right atrial and pulmonary artery pressures, and reduced capacity to perform strenuous exercise.

Energetically efficient gait is challenging for large animals because of the slow rate of contraction and low power output of their muscles.[21] However, the gait of horses is energetically efficient,[22] with the muscular work of galloping being halved by elastic storage of energy in muscle and tendon units.[23] For the forelimb, this use of stored energy and the subsequent catapult action mean that the biceps and brachiocephalicus muscles are less than one-hundredth the size that they would need to be were there no use of stored energy.[21]

In summary, a large number of physiologic and anatomic features act in concert to endow the horse with extraordinary athletic capacity. Optimal athletic performance is dependent

upon optimal integrated functioning of these physiologic and anatomic features.

Integrative physiology of exercise

The detailed responses of each body system to acute exercise and to repeated exercise (conditioning or training) are described in chapters throughout this book. These responses, although described in isolation for each body system, do not occur in isolation, but rather occur as a component of a complex and integrated response to exercise, the ultimate goal of which is to provide substrate for muscle contraction while maintaining homeostasis.

Exercise results in coordinated changes in almost all body systems. Fundamentally, exercise is associated with an increase in power output achieved by contraction of muscles. Contraction of muscles consumes adenosine triphosphate (ATP) and triggers an increase in metabolic rate to replace expended ATP. Increases in metabolic rate are dependent upon an adequate supply of substrate and, ultimately, oxygen. Energy production can be achieved for brief periods of time by anaerobic metabolism, but ultimately all energy production is linked to substrate oxidation and an adequate supply of oxygen.

Production of ATP during exercise is proximately dependent on supplies of substrate for oxidation and of oxygen. A schematic of factors influencing the supply of these fuels to muscle is depicted in Fig. 1.1. The important concept is that there are a number of steps in the process or transport chain by which each of these products is delivered to the muscle cell. Because these processes are sequential and often non-duplicative, a limitation in one process or function will limit the rate of the whole system. In some cases these rate-limiting steps may be modified by training, in which instance the rate of oxygen or substrate delivery will be increased, or may not be altered by training. The consequences of these differences are discussed below under 'Factors limiting performance'.

At the onset of exercise there is a coordinated response by a large number of body systems to increase fuel availability, maintain acid–base balance within acceptable limits, and limit body temperature. These responses include a large increase in flux of substrate, the nature of which depends on the intensity and duration of exercise. Increasing exercise

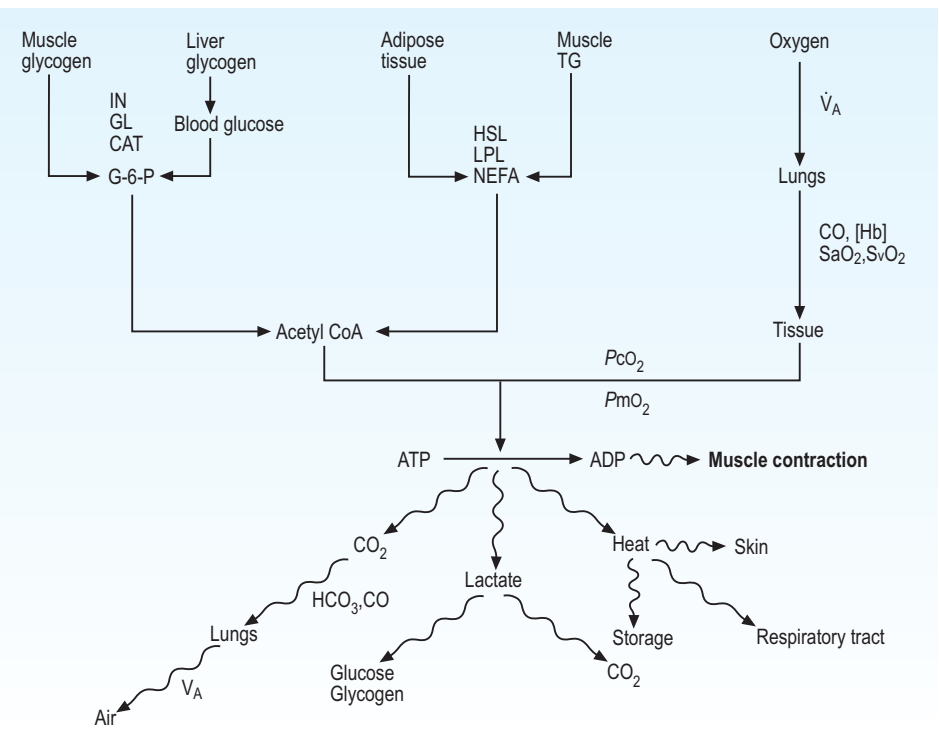


Fig. 1.1
Schematic of substrate and oxygen flux demonstrating the integrated and sequential nature of many processes. Substrate supply to produce ATP that powers muscle contraction is through both lipid and carbohydrate. Carbohydrate is provided from muscle glycogen by phosphorylase or from glucose in blood. Important controlling hormones are glucagon, insulin and the catecholamines, in addition to control by local physicochemical factors. Lipid substrate is provided from both intramuscular and adipose tissues, with the former being more important during exercise. Ultimately carbon molecules are delivered to the mitochondria wherein they are oxidized to produce carbon dioxide, heat and work. Oxygen delivery to the mitochondria is dependent upon a chain of events leading from the atmospheric air to the mitochondria. Muscle contraction is associated with production of work, carbon dioxide, heat and lactate (under conditions of anaerobic metabolism). ADP, adenosine diphosphate; ATP, adenosine triphosphate; CAT, catecholamines; CO, cardiac output; CoA, coenzyme A; CO_2, carbon dioxide; G-6-P, glucose-6-phosphate; GL, glucagon; [Hb], hemoglobin concentration; HCO_3, bicarbonate; HSL, hormone-sensitive lipase; IN, insulin; LPL, lipoprotein lipase; NEFA, non-esterified fatty acid; PcO_2, capillary oxygen tension; PmO_2, mitochondrial tension; SaO_2, arterial oxygen saturation; SvO_2, venous oxygen saturation; TG, triglyceride; V_A, alveolar ventilation.

intensity results in a greater proportion of total energy production being derived from carbohydrates in muscle (glycogen) and blood (glucose, either absorbed from the gastrointestinal tract or produced by the liver) than from fat (see Chapter 37). The supply of these substrates is controlled by the hormonal responses to exercise, which include a reduction in blood insulin concentration and increases in blood catecholamine, cortisol and glucagon concentrations (see Chapter 35). The net result is increased delivery of glucose to muscle from the blood as a result of increased hepatic glycogenolysis and gluconeogenesis. However, blood-borne glucose provides only a small proportion (< 10%) of carbohydrate used during intense exercise, the remainder coming from intramuscular stores of glycogen.

Oxidation of substrate during exercise is dependent upon a nearly constant supply of oxygen. Oxygen delivery to the muscle is dependent upon optimal functioning of the respiratory and cardiovascular systems, which are described in detail in this text (see Chapters 28 and 32). Increased oxygen delivery to muscle is achieved through increases in minute ventilation, alveolar ventilation, oxygen-carrying capacity of blood (secondary to splenic contraction), and cardiac output. Increases in values of these variables with exercise are roughly dependent on the relative intensity of exercise.

Aerobic metabolism and anaerobic glycolysis result in the production of waste products principal among which are carbon dioxide and lactate. Carbon dioxide is produced by the aerobic metabolism of carbohydrate or fat. Produced in the mitochondria of metabolically active cells, it diffuses into the blood wherein it is transported either as dissolved carbon dioxide or as bicarbonate (see Chapter 39). Transportation of the large amounts of carbon dioxide produced during exercise results in marked increases in venous partial pressure of carbon dioxide and venous blood bicarbonate concentrations.

Lactate, and associated H^+, is produced during anaerobic metabolism. A 3-carbon monocarboxylate compound, lactate moves out of muscles and into other tissues by diffusion and by active transport by monocarboxylate transporters. Lactate is metabolized to carbon dioxide and water in well-oxygenated metabolically active tissues, or is recycled to glucose and glycogen in the liver, kidney and inactive muscle cells (see Chapter 37). The hydrogen ions produced during anaerobic metabolism are buffered by intracellular buffers, including proteins, and by extracellular buffers, the most quantitatively important of which is bicarbonate. Despite this buffering, intense exercise induces a pronounced acidosis and acidemia with decreases in arterial and mixed venous pH and base excess, decreases in arterial bicarbonate concentration and marked increases in carbon dioxide tension in venous blood. The acidosis associated with maximal exercise is severe and tolerable only for short periods of time. Resolution of the respiratory acidosis occurs within seconds to minutes of the cessation of exercise, whereas metabolic acidosis is slower to resolve, taking 30–60 minutes.

Muscle contraction produces heat which if not effectively dissipated results in hyperthermia (see Chapter 41). The heat generated by an exercising horse is sufficient to raise its body temperature by 3–5°C. If exercise is prolonged and not accompanied by effective heat dissipation, the rectal temperature may exceed 42°C, a temperature associated with markedly increased risk of heat shock and illness. Heat generated in muscle is transported by the blood to the skin and respiratory tract, from where it is lost into the ambient air. Heat dissipation from horses is achieved by evaporation of sweat, evaporation of respiratory tract secretions and convective loss of heat in air moving over the horse's skin and respiratory membranes.

Physiology of training

Training is essential for horses to compete effectively and safely. All equine athletes undergo some type of training regimen to prepare them for the rigors of competition. Training prepares the equine athlete for competition by inducing the physiologic adaptations necessary to perform at a high level with minimal risk of injury, and by providing the appropriate behavioral and psychological factors essential for effective competition. In order to adequately prepare a horse for competition, the horse should regularly perform the type of activity that it will perform in competition at an intensity that will induce the physiologic changes needed to permit optimal performance.

Repetitive exercise induces a multitude of physiologic and anatomic adaptations in horses. The specific responses of each body system are dealt with in detail in the relevant sections of this book. However, there are a number of concepts that are common to many body systems.

The adaptive response

An important concept is that some physiologic processes, functions or anatomic structures are malleable and able to adapt in response to the stresses and strains imposed by repetitive exercise. Collectively, induction of these adaptive responses to exercise is called training or conditioning. Strictly speaking, training refers to changes in behavior induced by certain practices whereas conditioning refers to the physical changes that occur in response to repetitive exercise. However, the terms are often used synonymously.

The adaptive responses induced by repetitive exercise act to reduce the effect of the strain induced by the physiologic stressors associated with exercise. The body acts to minimize the disruption to homeostasis induced by exercise by increasing the capacity of the system to deal with the work imposed by exercise. For example, the stress of increased force production by muscle during exercise stimulates changes in muscle structure and function that act to reduce the stress on individual muscle fibers, while increasing the overall capacity of the muscle. This phenomenon is common to many, but not all, body systems and the cumulative effect is a change in body composition and capacity for physical work.

Mechanisms of training effects

Repetitive exercise (exercise training) results in a multitude of changes in the body at cellular, tissue, organ and whole organism levels. At the most fundamental level, training occurs through increased production of proteins, both structural and functional proteins. Accumulation of metabolites and waste products is believed to induce increased transcription of DNA specific for proteins, including enzymes, that control rate-limiting functions associated with these metabolites. Increased transcription, if associated with increased translation of mRNA to protein and appropriate post-translational events, results in production of more protein. The increased quantity or activity of the enzymes then results in an increase in the maximal rate at which the metabolites can be processed or waste products eliminated. At an organ level these changes result in an increase in function, usually associated with increases in organ size.

Principles of training

For training to be effective in inducing the desired conditioning, there must be a degree of 'over-reaching'. Over-reaching refers to the performance of an activity at a sufficient intensity and duration to induce some strain into the organism. Without this strain, there will be no conditioning effect.

It is also important to recognize that training is task specific. The task for which conditioning is desired must be performed. For example a horse trained to compete in endurance events will be poorly trained for sprint racing. Given the specificity of training, there are three principles of training expressed for human exercise physiology:[24]

1. Repetition
2. Summation
3. Duration.

To induce a training effect, there must be repetition of the training stimulus. The number of repetitions varies with the type and intensity of exercise. Summation refers to the total amount of work performed. To achieve some degree of over-reaching, the total amount of work performed must be sufficient to induce some strain. If tasks are performed without sufficient time for substantial recovery between repetitions, then the total amount of work needed to achieve a training response may be lower than if recovery is allowed to occur.[24] Finally, the training stimulus must be of sufficient duration to induce an effect.

These principles of training must be used in a thoughtful and planned manner in order to induce the maximum training response while reducing the risk of injury. The art of training involves the judicious use of exercise of various intensities and durations in order to induce the optimal adaptations that will permit successful competition while preventing injury or occurrence of overtraining.

Overtraining

Overtraining is a well-recognized syndrome in human athletes in which increases or maintenance of training intensity are associated with decrements in performance.[25,26] Diagnosis of overtraining in humans is complicated by the absence of any one definitive test, although psychological profiles including evaluation of mood are the most specific indicators of overtraining.[25] The situation is even more complicated in horses for which psychological and mood evaluation is not available. Overtraining in horses is characterized by decrements in performance and maximal rate of oxygen consumption.[27,28] Specific aspects of overtraining are addressed in other sections of this book.

Factors limiting performance

Maximal performance involves the coordinated optimal functioning of almost all body systems. In most cases, maximal performance requires that these body systems operate at or close to their maximum capacity. Conceptually, this integrated maximal function may be viewed as a pipeline. The maximum overall flow through the pipe is limited by the narrowest segment of the pipe. This analogy is often employed for oxygen transport during exercise and the system is viewed as one of tuned resistors, with no one individual element limiting the capacity of the system.[29] While this analogy is appropriate for healthy animals, it may not be so for animals with performance-limiting abnormalities, such as lameness or airway obstruction. In this instance, a single abnormality is sufficient to impair performance. Specific aspects of poor performance are dealt with elsewhere in this book.

For healthy horses the actual performance-limiting factor depends on the type of exercise and its duration. Standardbred or Thoroughbred race horses running at top speed are probably limited by oxygen transport. In these animals the malleable components of the oxygen transport chain (red cell mass, mitochondrial volume, muscle capillarity) have adapted to the extent that the capacity of these components approaches or exceeds the capacity of the non-malleable components, such as lung volume or tracheal diameter. A reduction in the capacity of the non-malleable component, for example a reduction in laryngeal diameter secondary to laryngeal hemiplegia, will reduce the capacity of the whole system. This has important consequences for a horse performing at maximal intensity. However, if the capacity of the non-malleable components exceeds that of the malleable components, then a reduction in capacity of the non-malleable component may not reduce performance, for instance in the case of a dressage horse with laryngeal hemiplegia. In this case, the disorder will probably not limit the physiologic capacity of the horse to perform its task (although the associated respiratory noise may detract from the performance).

For other types of performance, other factors are limiting. Three-day event horses may be limited by their capacity to thermoregulate, endurance horses by their capacity to maintain fluid and electrolyte homeostasis, and draft horses by the strength of their muscles. Clearly, the factors limiting exercise capacity of horses vary with the type and duration of

exercise. However, an understanding of what is likely to limit performance for each breed and use of horse is important not only in understanding the physiology of that form of exercise, but also in determining the likely causes of poor performance in animals with clinical disease.

References

1. Vila C, Gotherstrom A, Leonard JA. Widespread origins of domestic horse lineages. Science 2001; 291:474–477.
2. Jansen T, Forster P, Levine MA. Mitochondrial DNA and the origins of the domestic horse. Proc Natl Acad Sci USA 2002; 99:10905–10910.
3. Schmidt-Nielsen K. Scaling: Why is animal size so important? Cambridge: Cambridge University Press; 1984.
4. Reynolds A, Reinhart G, Carey D, et al. Effect of protein intake during training on biochemical and performance variables in sled dogs. Am J Vet Res 1999; 60:795.
5. Lindstedt SL, Hokanson JF, Wells DJ, et al. Running energetics in the pronghorn antelope. Nature 1991; 353:748–750.
6. Hinchcliff K, Reinhart G, Burr J, et al. Metabolizable energy intake and sustained energy expenditure of Alaskan sled dogs during heavy exertion in the cold. Am J Vet Res 1997; 58:1457–1462.
7. Hill R, Bloomberg M, Legrand-Defretin V. Maintenance energy requirements and the effect of diet on performance in racing greyhounds. Am J Vet Res 2000; 61:1566–1573.
8. Jones JH, Longworth KE, Lindholm A, et al. Oxygen transport during exercise in large mammals. I. Adaptive variation in oxygen demand. J Appl Physiol 1989; 67:862–870.
9. Constantinopol M, Jones JH, Weibel ER, et al. Oxygen transport during exercise in large mammals. II. Oxygen uptake by the pulmonary gas exchanger. J Appl Physiol 1989; 67:871–878.
10. Weber JM, Brichon G, Zwingelstein G, et al. Design of the oxygen and substrate pathways. IV. Partitioning energy provision from fatty acids. J Exp Biol 1996; 199:1667–1674.
11. Achten J, Gleeson M, Jeukendrup AE. Determination of the exercise intensity that elicits maximal fat oxidation. Med Sci Sports Exerc 2002; 34:92–97.
12. Weber JM, Roberts TJ, Vock R, et al. Design of the oxygen and substrate pathways. III. Partitioning energy provision from carbohydrates. J Exp Biol 1996; 199:1659–1666.
13. Weibel ER, Taylor CR, Weber JM, et al. Design of the oxygen and substrate pathways. VII. Different structural limits for oxygen and substrate supply to muscle mitochondria. J Exp Biol 1996; 199:1699–1709.
14. Essen-Gustavsson B, McMiken D, Karlstrom K, et al. Muscular adaptations of horses during intense training and detraining. Equine Vet J 1989; 21:27–33.
15. Geor R, Hinchcliff K, Sams R. Glucose infusion attenuates endogenous glucose production and enhances glucose use of horses during exercise. J Appl Physiol 2000; 88:1765–1776.
16. Kayar SR, Hoppeler H, Lindstedt SL, et al. Total muscle mitochondrial volume in relation to aerobic capacity of horses and steers. Pflugers Archiv: Europ J Physiol 1989; 413:343–347.
17. Persson SDG. On blood volume and working capacity of horses. Acta Physiol Scand 1967; Suppl 19:9–189.
18. McKeever KH, Hinchcliff KW, Reed SM, Hamlin RL. Splenectomy alters blood-pressure response to incremental treadmill exercise in horses. Am J Physiol 1993; 265:R409–R413.
19. Persson SG, Ekman L, Lydin G, Tufvesson G. Circulatory effects of splenectomy in the horse. II. Effect on plasma volume and total and circulating red-cell volume. Zentralbl Veterinarmed A 1973; 20:456–468.
20. Persson SG, Lydin G. Circulatory effects of splenectomy in the horse. 3. Effect on pulse-work relationship. Zentralbl Veterinarmed A 1973; 20:521–530.
21. Wilson A, Watson J, Lichtwark G. A catapult action for rapid limb protraction. Nature 2003; 421:35–36.
22. Hoyt D, Taylor CR. Gait and energetics of locomotion in horses. Nature 1981; 292:239–240.
23. Minetti A, Ardigo L, Reinach E, Saibene F. The relationship between mechanical work and energy expenditure of locomotion in horses. J Exp Biol 1999; 202:2329–2338.
24. Viru A, Viru M. Nature of training effects. In: Garrett W, Kirkendall D, eds. Exercise and sport science. Philadelphia: Lippincott, Williams and Wilkins, 2000:67–95.
25. McKenzie DC. Markers of excessive exercise. Can J Appl Physiol 1999; 24:66–73.
26. Petibois C, Cazorla G, Poortmans J-R, Deleris G. Biochemical aspects of overtraining in endurance sports: a review. Sports Med 2002; 32:867–878.
27. Tyler C, Golland LC, Evans DL, et al. Changes in maximum oxygen uptake during prolonged training, overtraining and detraining in horses. J Appl Physiol 1996; 81:2244–2249.
28. Hamlin M, Shearman J, Hopkins W. Changes in physiological parameters in overtrained Standardbred racehorses. Equine Vet J 2002; 34:383–388.
29. Lindstedt SL, Wells DJ, Jones J, et al. Limitations to aerobic performance in animals: interaction of structure and demand. Int J Sports Med 1988; 9:210–217.

CHAPTER 2

Clinical exercise testing: evaluation of the poor performing athlete

Eric K. Birks, Mary M. Durando and Ben B. Martin, Jr

Introduction

The widespread availability of high-speed equine treadmills at universities and major veterinary referral centers has led to the development of a number of programs that utilize a treadmill examination as part of the diagnostic evaluation of poor performance in equine athletes.[1–3] As a number of structural and/or functional abnormalities only manifest during intense exercise, appropriate diagnostic information for many of these potentially performance-decreasing problems are best obtained during controlled exercise afforded by a high-speed treadmill. This chapter will provide a discussion of the more common techniques utilized in the diagnostic workup of horses with athletic performance that is less than expected. A detailed flowchart of a typical performance evaluation protocol is shown in Fig. 2.1.

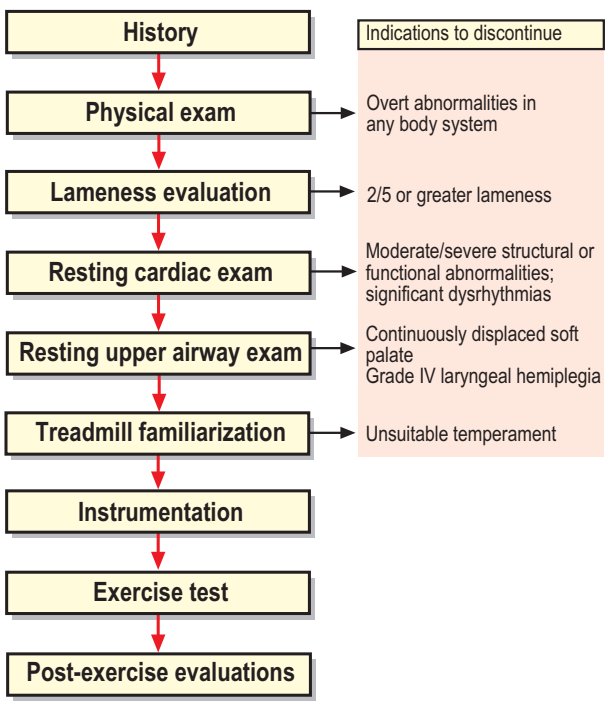


Fig. 2.1
An example of a diagnostic protocol for evaluation of horses with a primary complaint of poor athletic performance.

History

A thorough, accurate history is an essential initial step in attempting to identify the cause(s) of poor athletic performance. This includes not only a detailed description of the presenting complaint, but also the type/duration of any present or previous illnesses, any previous surgeries, present diet (including all supplements), present and past training protocols, and a complete performance record. Obtaining an accurate database requires that the individuals providing the information actually have the necessary specific, first-hand knowledge of the equine patient and any associated problems. Transportation providers, grooms, relatives, even absentee-owners, etc. are often unaware of the pertinent medical information that is required to assess the patient adequately.

For those patients that have been competing, a complete official performance record can often indicate whether an individual's performance has always been less than expected,

or if there has been a recent reduction in performance. Recent changes in competitive performance are often indicative of the onset of specific medical abnormalities, whereas poor performance throughout the individual's career may indicate that the expectations of the owners/trainers exceed the ability of the animal to compete at the desired level of performance.

Physical examination

The fact that a horse arrives at a referral center or university hospital with a primary complaint of 'poor athletic performance' indicates that up to the time of presentation no specific cause for reduced performance had been identified by any of the previous individuals examining the horse. However, this does not mean that a specific abnormality or illness is not present. Therefore, it is essential that a thorough physical examination of all body systems be conducted in order to rule out obvious organic disease or abnormalities. It is tempting to focus upon those systems most obviously involved in exercise (i.e. cardiovascular, respiratory, and musculoskeletal). However, abnormalities in virtually any system can also have an impact upon exercise performance.

Lameness evaluation

Although overt lameness is understood to impact severely on performance, the effects of mild-to-moderate lameness are often overlooked as a potential cause of diminished performance. As treadmill exercise can often mask or confuse all but the most severe lameness, treadmill evaluations are not indicated in lame animals. Additionally, the risk of potentially exacerbating an existing lameness does not usually warrant a high-speed treadmill evaluation. Instead, a thorough lameness examination, including diagnostic regional nerve blocks, radiographs, nuclear scintigraphy, or other imaging modalities, is indicated in these horses. Only if athletic performance continues to be less than expected after resolution of any causes of obvious lameness would a treadmill evaluation be indicated. Other abnormalities found during the physical examination, such as certain cardiac arrhythmias (e.g. atrial fibrillation), or overt lower airway disease, among others, should also be resolved before a treadmill evaluation.

In some cases, resolution of a specific cause of lameness may require significant rehabilitation time. Should multiple body system dysfunctions be suspected in addition to mild/moderate lameness, and if definitive diagnosis requires a dynamic evaluation, then a treadmill examination may still be indicated. This is particularly important if correction/treatment of any of these potentially performance-limiting dysfunctions also requires prolonged recovery time for return of normal function. Certainly, it is undesirable to exacerbate any diagnosed lameness, so the potential risk of further damage to the horse, as well as the safety of the treadmill personnel, must be weighed carefully prior to continuing with a high-speed treadmill examination. A compromise may involve a treadmill evaluation at reduced running speed.

Resting cardiac examination

A thorough examination of the cardiovascular system during resting conditions is critical to identify potential structural/functional abnormalities that may impact exercise performance.[4] This examination must include careful auscultation of the entire thorax to identify possible dysrhythmias, murmurs, or other abnormal heart sounds, along with possible evidence of primary or secondary pulmonary dysfunction. Peripheral pulse quality and venous distension should also be evaluated, as they may be important indicators of cardiovascular dysfunction. Heart rhythm should be evaluated by electrocardiography (ECG) (Fig. 2.2); cardiac structure and function are assessed with echocardiography. The ECG during rest should exhibit a regular sinus rhythm, although occasional second-degree atrioventricular block is considered a normal finding in healthy horses. Occasional premature beats are also acceptable, and not thought to

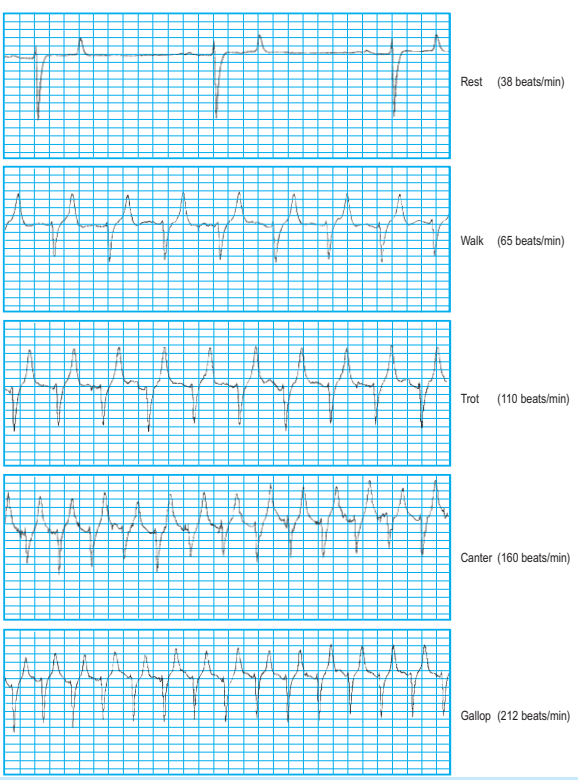


Fig. 2.2
Normal electrocardiograms (ECG) from horses without overt cardiac abnormalities. Heart rate ranges for each of the exercise intensities are given in the text.

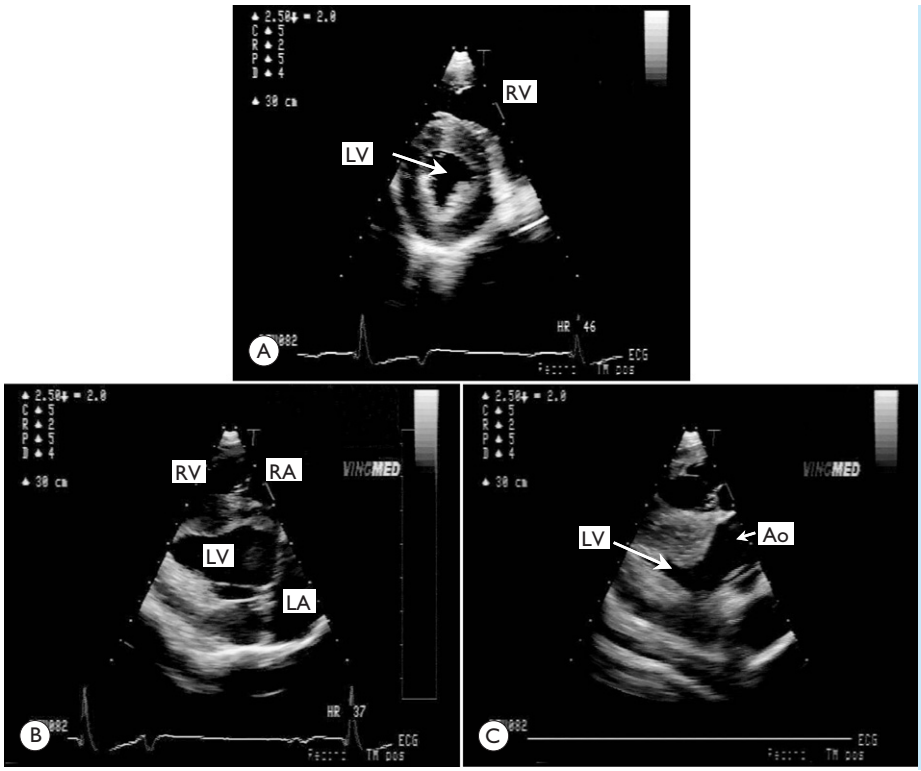


Fig. 2.3
Standard two-dimensional (2-D) echocardiograms from the right side. (A) Right parasternal short-axis view just below the level of the mitral valve. (B) Right parasternal long-axis four-chamber view of the heart. (C) Right parasternal long-axis view of the left ventricular outflow tract. Ao, aorta; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

interfere with performance, as long as they disappear with exercise. A complete echocardiographic evaluation consists of two-dimensional (2-D) images to assess both structure and function (Fig. 2.3), M-mode images for measurements and calculated indices (Fig. 2.4), and Doppler studies to determine regurgitant blood flow. Detailed references have been published describing these echocardiographic techniques.[5–8] On a 2-D image, a normal heart should not have any evidence of chamber enlargement, and should have obvious thickening and inward motion of the ventriclar myocardium during systole. M-mode images from short axis views are used to measure ventricular and aortic dimensions and to calculate indices such as fractional shortening (FS). Fractional shortening provides an indication of cardiac contractility, and is calculated from measurements of the left ventricular internal diameter in systole (LVIDs) and diastole (LVIDd) taken from

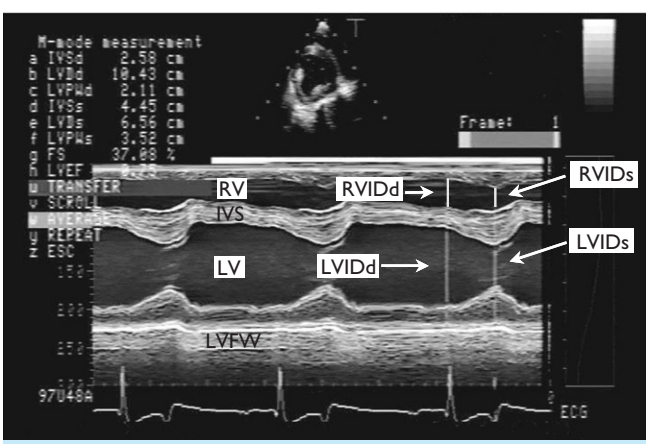


Fig. 2.4
Standard M-mode echocardiogram from a right parasternal short-axis view taken at the level of the chordae tendineae. Fractional shortening is calculated from this view. IVS, intraventricular septum; LVIDd, left ventricular internal diameter at end-diastole; LVIDs, left ventricular internal diameter during systole; LV, left ventricle; LVFW, left ventricular free wall; RV, right ventricle; RVIDd, right ventricular internal diameter at end-diastole; RVIDs, right ventricular internal diameter during systole.

Table 2.1 Values of selected cardiac dimensions at rest

Cardiac dimension	Average (range)
Ao	8.13 (6.9–9.2)
LVIDd	11.92 (9.7–13.1)
LVIDs	7.45 (5.8–8.8)
IVSd	2.85 (2.3–3.44)
IVSs	4.21 (3.16–5.16)
LVFWd	2.32 (1.72–3.40)
LVFWs	3.85 (3.00–4.62)
LAD	12.82 (11.30–14.52)
%FS	37.42 (29.41–44.67)

Ao, aorta; LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; IVSd, intraventricular septum in diastole; IVSs, intraventricular septum in systole; LAD, left atrial diameter; LVFWd, left ventricular free wall in diastole; LVFWs, left ventricular free wall in systole; FS, fractional shortening.
Data adapted from Durando and Young.[4]

M-mode images obtained at the chordal level immediately below the mitral valve, using the following formula:

$$FS = \frac{LVIDd - LVIDs}{LVIDd} \times 100$$

A number of investigators have measured normal heart chamber and wall dimensions.[7] A brief summary of the more commonly determined dimensions is given in Table 2.1.

Overt abnormalities identified at rest are often sufficient indication not to continue with a high-speed treadmill evaluation. These include, but are not limited to, atrial fibrillation, multiple ventricular premature depolarizations (VPDs), paroxysmal ventricular tachycardia, obvious abnormal ventricular wall motion, and/or significant valvular dysfunction. In some situations, a treadmill examination may still be indicated even with evidence of cardiac dysfunction. This is especially true when abnormalities in multiple systems are suspected, but require a dynamic examination for definitive diagnosis. With moderate/severe resting cardiac abnormalities, a high-speed treadmill examination may place the horse and/or personnel at risk. In these cases, a treadmill test may be conducted at reduced speed.

Resting upper respiratory tract evaluation

Endoscopic examination of the upper respiratory tract (URT) from the nostrils to the level of the carina should be conducted not only under passive resting conditions, but also during induced swallowing and with short-term nasal occlusion. Even without a definitive history of prior surgical intervention, a thorough visual examination of the entire URT should be completed, as the present owners/trainers may not be aware of all previous surgeries. Abnormalities in anatomy and/or function can have a significant impact upon ventilation during exercise, thereby contributing to reduced athletic performance. However, many abnormalities detected during an endoscopic examination are incidental findings that generally have little or no impact on exercise performance. Such insignificant findings would include, but are not limited to, hyperplasia of the pharyngeal lymphoid tissues (more common in younger horses), some asynchronous movement of the arytenoids, and mild flaccidity of the pharynx, epiglottis, and/or soft palate.[9,10] Abnormalities that are suggestive of possible ventilation impairment during exercise, and therefore warrant high-speed treadmill examination, would include moderate/severe flaccidity of the epiglottis, soft palate, and/or pharyngeal walls, asynchronous and/or asymmetric movement of the arytenoids, and intermittent displacement of the soft palate. Severe abnormalities observed during the resting examination, such as chronically displaced soft palate, grade IV laryngeal hemiplegia, or arytenoid chondritis, preclude a treadmill evaluation. Although it is often tempting to terminate the diagnostic work-up when mild/moderate upper respiratory tract abnormalities are identified, it must be stressed that a complete evaluation of all body systems should be conducted prior to rendering a definitive diagnosis of the cause of poor performance. Often multiple body systems have significant abnormalities,[1] and, when this is the case, repairing/treating only one of them without regard to other potential problems can lead to unrealistic expectations regarding improvement in athletic performance. The more commonly diagnosed upper respiratory tract abnormal findings are discussed in detail in Chapter 4.

The observation of a normal resting upper respiratory tract (Fig. 2.5), inconclusive evidence of soft palate displacement, or grade II/III laryngeal hemiplegia, are all indications for proceeding to a dynamic evaluation of the upper respiratory tract during a high-speed treadmill exercise evaluation.

Treadmill familiarization

Should the preceding evaluations of the patient reveal no obvious cause for reduced athletic performance or when potential dysfunction can only be diagnosed during exercise, a high-speed treadmill evaluation is indicated. Because the majority of individual horses have not been required to run

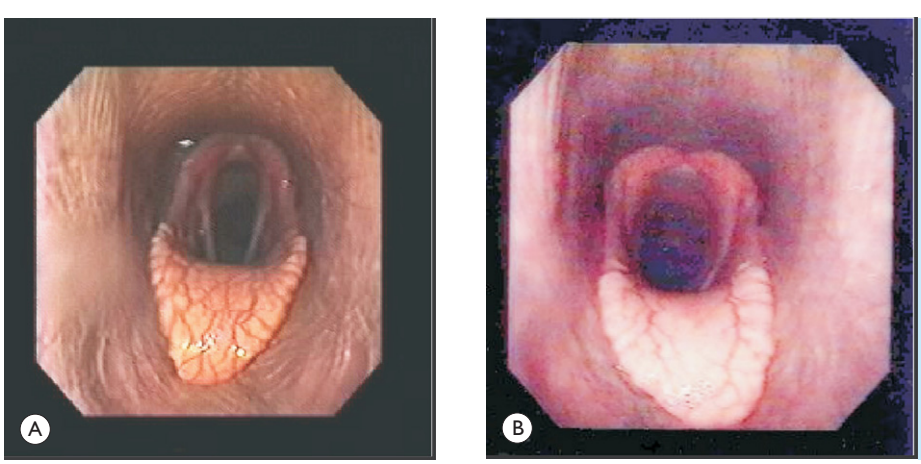


Fig. 2.5
Endoscopic views of an upper respiratory tract of a healthy horse during inspiration at rest (A) and during maximal exercise (B).

on a treadmill, the most important initial step in the process of a treadmill evaluation is to familiarize the horse to exercise on the treadmill. It cannot be stressed enough that the most essential part of the familiarization process is to have a competent horse-handling team; individuals familiar with the treadmill and skilled in handling fractious, excited, and often scared horses in an environment foreign to them. Although the philosophy regarding the familiarization process varies considerably among various referral centers and university hospitals, the most commonly employed system involves a 2–3 day process of non-exercising diagnostic evaluations and a multiple day familiarization protocol. However, this is not always the case, with several of the busiest centers employing a complete examination schedule conducted on an outpatient basis, all within 4–6 hours.

The initial stage of familiarization involves walking onto the treadmill platform repeatedly to allow the horse to become comfortable with its immediate surroundings. Then, several periods of starting and stopping the treadmill are utilized to help the horse become comfortable with the movement of the 'ground'. Once the horse becomes accustomed to walking as the treadmill is started, the speed can be slowly increased, encouraging the horse to change smoothly into gaits appropriate for the increased speeds, thus completing the initial familiarization stages. For those horses that routinely have ancillary running aids applied during competition (i.e. pacing harnesses, blinkers, head-check), additional familiarization should be conducted with these aids attached.

For most horses, the entire familiarization process is generally conducted over a time-span of less than an hour. Rarely, an individual horse will have a temperament unsuitable for familiarization in such a short time frame. In these cases, it may be decided to keep the horse at the facility for additional familiarization sessions, or at the discretion of the 'team', abandon any thoughts of high-speed treadmill evaluation! In the experience of most centers with high-speed treadmill evaluation capabilities, greater than 95% of the horses that reach the treadmill evaluation stage successfully complete the familiarization and proceed to the actual high-speed treadmill exercise evaluation.

Instrumentation

Following successful familiarization but prior to the actual high-speed treadmill evaluation, horses are instrumented to permit data collection during exercise. The most common monitoring instrumentation for diagnosing dynamic changes during exercise includes some type of ECG recording system, catheterization of a systemic artery (e.g. transverse facial artery), a means for monitoring core body/blood temperature, and placement of an endoscope to visualize the nasopharynx and proximal laryngeal structures. Occasionally, the presenting complaint may include the recent onset of exercise-induced pulmonary hemorrhage (EIPH). In these cases, the placement of a catheter to monitor pulmonary arterial pressures may be indicated.

To monitor the ECG during exercise, some form of telemetry system is generally utilized. A number of systems are commercially available, with the only requirement being the capability of recording a discernible ECG pattern during intense exercise. Because the horse is confined to the treadmill, it is not essential that a telemetry system be utilized; even a hard-wired system would be acceptable. It is, however, imperative that clear images of the ECG be recorded continuously during exercise and in the immediate post-exercise period. As previously noted, significant resting arrhythmias and/or myocardial dysfunction would preclude proceeding to a high-speed treadmill evaluation. However, several individual non-conducted beats or isolated VPDs are generally insignificant and will often not be apparent during exercise. The presence of this type of arrhythmia does not preclude the conduct of an exercise test.

A catheter placed in a systemic artery provides access to arterial blood during exercise. Sequential sampling of arterial blood during exercise is essential in evaluation of pulmonary gas exchange function as well as of exercise-related changes in blood electrolytes and acid–base status. Arterial blood gas values change extremely rapidly following exercise, within 5–10 seconds, thus precluding the use of virtually any post-exercise blood sample in the evaluation of lung gas exchange. The mechanics and exact placement of a systemic arterial catheter vary among the various facilities, with the most commonly utilized artery being the transverse facial artery. The type of catheter used is also a matter of individual preference, but most frequently some type of 20-gauge 'over-the-needle' catheter is utilized. In any event, the catheter must be securely attached to the horse (e.g. sutures or cyanoacrylate cement) and connected to extension tubing to permit collection of blood samples during treadmill exercise.

To temperature-correct measured blood gas values to those of the gas exchange region, it is essential that the blood temperature at the site of gas exchange be recorded. For the clinical treadmill examination, some type of rapid-responding thermocouple or thermister catheter must be placed in the central body core. This generally involves passing the temperature-monitoring catheter to the level of the heart via a jugular vein. Monitoring core body temperature is also of importance if heat dissipation abnormalities (e.g. anhidrosis) are suspected.[11,12] Figure 2.6 shows a catheter positioned in a transverse facial artery and a thermocouple catheter placed into a jugular vein.

Continuous visualization of the nasopharynx and proximal laryngeal structures during the high-speed treadmill examination is accomplished by placing a flexible endoscope through either of the nostrils to the level of the pharyngeal openings of the guttural pouches. While the exact type is not critical, a moderately flexible video or fiberoptic endoscope, 9–12 mm in diameter, with intense illumination and a wide field of view is most typically utilized. Some means of continuously recording the images obtained via the endoscope is also essential. Several commercial sources of veterinary video endoscopes are available, and are readily adapted to permit temporary fixation of the endoscope to the halter or bridle of the horse to maintain position during treadmill exercise.[10]

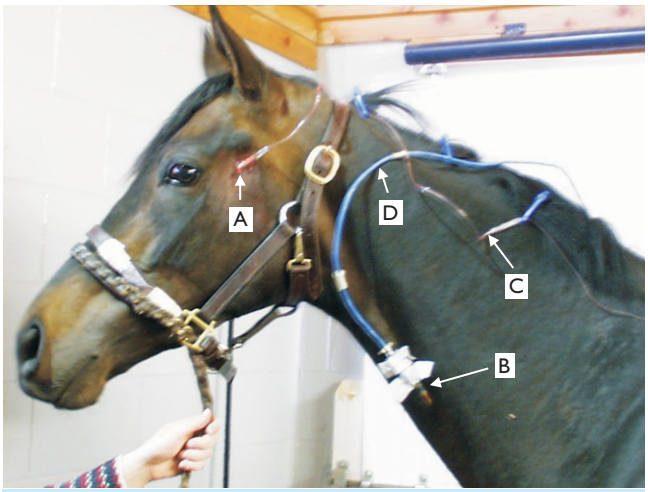


Fig. 2.6
Catheter placement for evaluation of arterial blood during treadmill exercise. (A) 20-gauge catheter secured with cyanoacrylate cement into the left transverse facial artery; (B) a thermocouple catheter passed via the left jugular vein; (C) catheter extension tubing to allow blood sampling during exercise; (D) thermocouple extension wire to allow recording of temperature signals from the sensor placed at the level of the right atrium.

Thorough diagnostic evaluation of the cardiopulmonary system during exercise may involve measurement of exercising pulmonary arterial pressures. Placement of a pressure-measuring catheter into the pulmonary artery, although somewhat invasive, is a relatively straightforward technique. A commercially available catheter introducer is placed into a jugular vein, and a pressure-monitoring catheter is passed through the introducer, advanced through the vein, the right atrium, the right ventricle, and into the pulmonary artery. Pressure waveforms are monitored during passage until the characteristic waveforms of the pulmonary artery are observed. Tip-mounted pressure transducer catheters are readily available, at modest cost, which permit not only accurate pressure measurements, but also simultaneous blood sampling, even during intense exercise. Although there are risks associated with the passage of a catheter through the heart, the associated problems rarely persist. These problems can include cardiac arrhythmias associated with myocardial irritation, thrombus formation, and possible damage to the myocardium and/or valve leaflets.[13] However, the diagnostic value of measuring pulmonary arterial pressure often outweighs the risks.

Recent reports also suggest that direct measurement of pressure changes within the right ventricle during exercise may provide valuable information regarding mild cardiac dysfunction. For these measurements, passage of appropriate pressure-measuring catheters into the right ventricle is identical to that described above for placement of a pulmonary arterial catheter except for the final positioning.[14]

Exercise tests

After placement of the necessary instrumentation described above, a standardized treadmill exercise test (STET) is conducted. Individualized STETs have been developed at various veterinary facilities; however, the differences are primarily related to equipment and/or personnel availability. A typical STET consists of a warm-up phase of walking, trotting, and moderate cantering (trotting/pacing in Standardbred race horses), followed by a high-speed test at as fast a speed as the individual horse is capable of sustaining for 1600 to 2400 meters. The exact intensity of the high-speed test is often dictated by the temperament of an individual horse, but in most cases speeds will approach 12–14 m/s. This generally represents 90–95% of the exercise intensity required to elicit maximum oxygen consumption in most fit athletic horses. Some clinical facilities conduct an additional high-speed test, 30–60 minutes following the first test, with the philosophy that a single test is not sufficiently strenuous to mimic racing conditions, and that two successive tests provide a better reflection of the fatigue and dynamic changes in certain variables associated with competition. Another commonly employed method of increasing exercise intensity during the STET is to elevate the treadmill to have the horses run uphill. While this does elicit greater exercise effort for any given speed than without treadmill elevation, it should be noted that different muscle groups are utilized during uphill exercise than on the flat. Therefore, this must be considered in the evaluation of potential performance-limiting abnormalities. It should also be noted that, for some horses, the inclusion of some uphill exercise during the STET may be appropriate. This is especially true for horses used in competitions that include jumping (i.e. steeplechasing, eventing).

During the high-speed test, the ECG and video images of the nasopharynx/larynx are continuously recorded. If pulmonary arterial pressures are being monitored, pressure waveforms are continuously recorded utilizing a computerized data collection system. Discrete samples of systemic arterial blood are collected anaerobically into heparinized syringes at various timed intervals during the test; a typical sampling protocol involves samples collected at rest, immediately following the warm-up period, after 30, 90, 150, 210 seconds of the maximal test, and within 60 seconds following cessation of exercise. The blood samples are tightly capped and stored on ice until analyzed, generally within 15 minutes of collection. Typical analysis would include blood gases (i.e. Po_2, Pco_2, pH), plasma electrolytes, hemoglobin concentration, lactate concentration, and multiple computed values (e.g. bicarbonate, base excess, total CO_2, anion gap, etc.).

In certain cases, part of the presenting complaint may include exaggerated noises associated with respiration. To help identify the source(s) of these reported respiratory noises, sounds associated with the upper respiratory tract and video images of the nostril region can be recorded during the treadmill examination.

Expected normal findings during STET

Normal ECG findings during exercise include a regular sinus rhythm with no ectopic beats. The heart rate is typically 60–80 beats/min during walking, 80–120 beats/min during trotting, 120–150 beats/min at a moderate canter (trot/pace in Standardbreds), 150–180 beats/min at a gallop (not maximal effort), and up to 220–240 beats/min at maximal effort. Heart rate and rhythm are also monitored during the immediate post-exercise period where the rate should drop to below 100 beats/min within 4–5 minutes, and have only occasional, transient sinus arrhythmias, second-degree atrioventricular block and/or isolated supraventricular or ventricular ectopic beats.[15]

The normal URT during a high-speed treadmill test will have little or no observable mucus. Additionally, during inspiration, arytenoid cartilages will fully abduct and move in synchrony, the epiglottis will remain on the floor of the nasopharynx (except during swallowing), the soft palate and walls of the nasopharynx should not adduct or in any way reduce the size of the nasopharynx, and the external musculature of the nostrils should expand the nasal openings during inspiration and maintain some tension (preventing fluttering) during exhalation.[9,16] Several researchers are attempting to correlate respiratory sounds with visual observations of pharyngeal/laryngeal abnormalities.[17,18] Published reports to date suggest that it may eventually be possible to obtain diagnostic information regarding certain URT abnormalities during routine exercise without a specific endoscopic treadmill examination. The caveat remains that such diagnostics would provide information only on the URT, potentially missing dynamic abnormalities in other body systems. Chapter 4 details abnormalities of the URT that are commonly associated with reduced athletic performance.

Arterial blood samples obtained during the treadmill examination are used to evaluate pulmonary gas exchange as well as electrolyte and metabolic changes associated with exercise. A number of these changes are related not only to the intensity but also to the duration of exercise. For these reasons, it is best to collect serial blood samples during the treadmill examination. Data for selected arterial blood parameters (those that exhibit the greatest exercise-related changes and thus are the most commonly utilized to diagnose related abnormalities) obtained during treadmill exercise in 119 clinically normal horses without evidence of cardiopulmonary or URT abnormalities are shown in Figs 2.7 and 2.8. Figure 2.7 shows average (± standard error of the mean) values for each of seven samples collected during the treadmill examination. Figure 2.8 shows the average values for the same variables but as a function of the maximum treadmill speed achieved by individual horses.

Core body temperature increases during exercise as a function of both exercise intensity and duration. Resting core body temperatures in a group of ~400 clinical cases averaged 37.3°C. The body temperature response to treadmill exercise is depicted in Fig. 2.7, while body temperature at the end of exercise plotted against maximum running speed for individual horses is shown in Fig. 2.8.

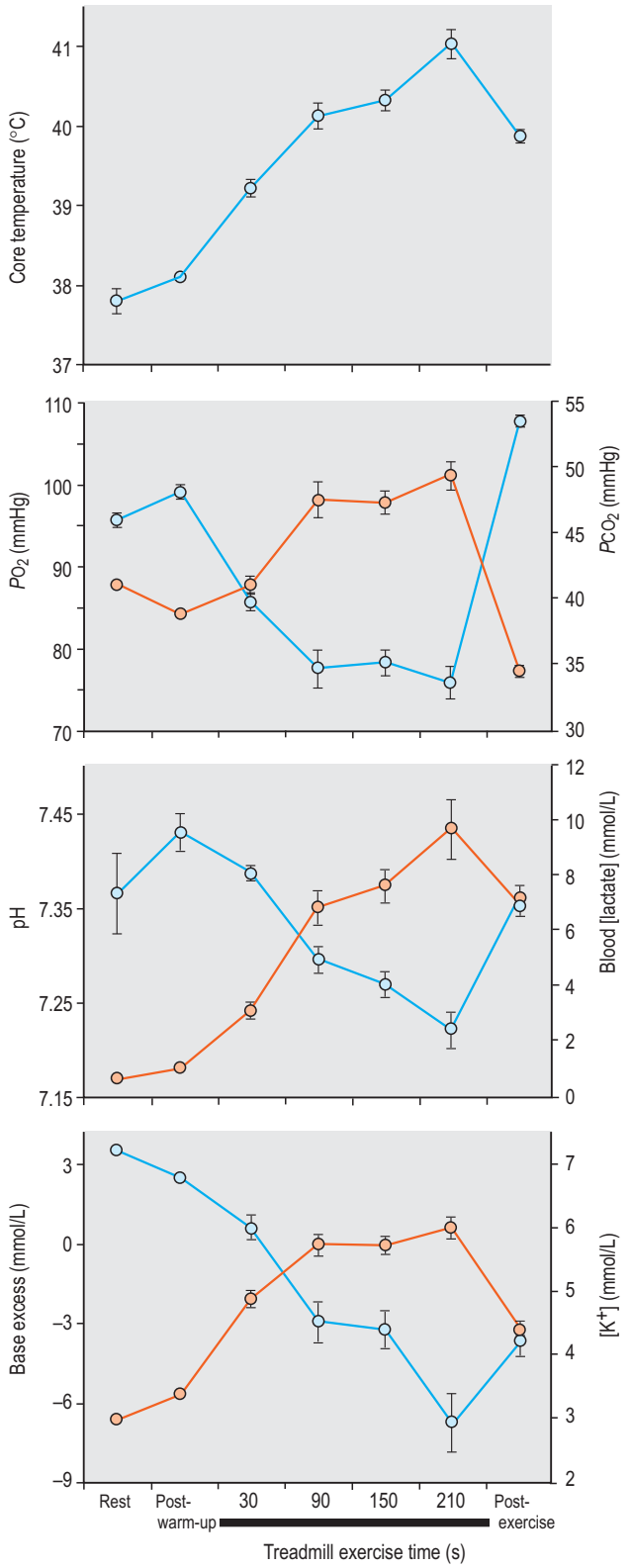


Fig. 2.7
Plots of selected blood variables at rest, following the warm-up period, during high-speed treadmill exercise at 12–13 m/s, and 30 seconds post-exercise. These data are from a subset of 34 individual horses from a total of 119 clinically healthy horses that completed a high-speed exercise test at a maximum speed of 12–13 m/s. Values are mean ± SEM. Left axis is used for values represented by blue lines; right axis for red lines.

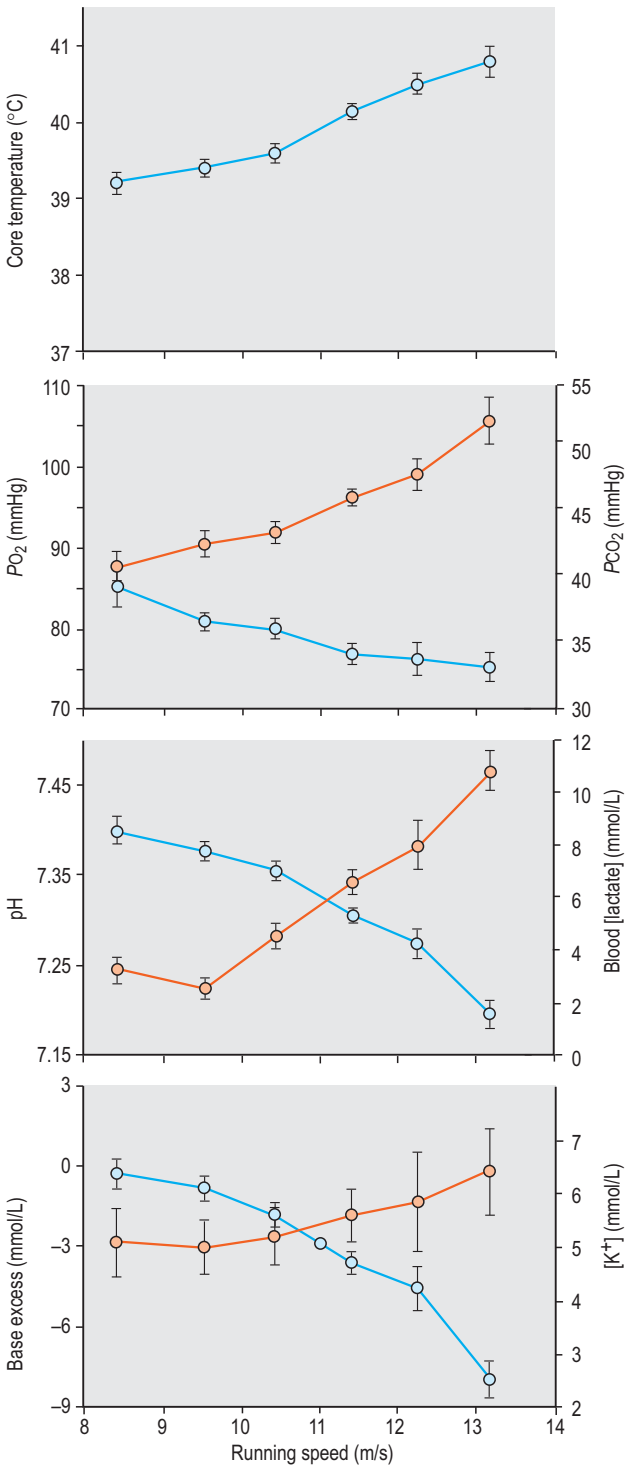


Fig. 2.8
Plots of the same blood variables as in Fig. 2.7 except, in this case, versus running speed. These values are those obtained from blood samples collected during the final 30 seconds of maximal treadmill exercise (i.e. the samples indicated in Fig. 2.7 at 210 seconds of treadmill exercise). The speeds indicated represent the maximal intensities attained by individual horses during treadmill tests. Values are mean ± SEM from a total of 119 horses determined to be clinically healthy that completed a high-speed exercise test: total number of individual horses at speeds of 8, 9, 10, 11, 12, and 13 m/s were 14, 19, 15, 25, 34, and 12, respectively. Symbols are as indicated in Fig. 2.7.

Immediate post-exercise assessment

Echocardiography

A resting cardiac examination is critical to ensure that the horse does not have overt disease as a contributor to decreased performance. On the one hand, subtle or paroxysmal abnormalities that might not be apparent at rest can significantly impact on exercise performance when maximal cardiac output is required. Conversely, some abnormalities appreciated at rest, such as a murmur with mild valvular regurgitation, might not negatively influence performance. As horses have a relatively high prevalence of murmurs and arrhythmias,[19–22] it can be a challenge to determine their significance as a cause of poor performance. Various abnormalities, such as systolic dysfunction, diastolic dysfunction, significant regurgitation, intracardiac shunts or dysrhythmias, can cause a reduction in athletic ability by reducing cardiac output. Some of these may be dynamic in nature, only exacerbated by strenuous exercise. Although the heart rhythm can be evaluated during exercise by telemetered ECG, myocardial function is much more difficult to evaluate, and, under most circumstances, this evaluation must be confined to the immediate post-exercise period.

In human medicine, immediate post-exercise stress echocardiography has been shown to be a very sensitive and specific indicator of exercise-induced myocardial ischemia and coronary artery disease.[23,24] Stress echocardiography consists of specific standardized views taken under resting conditions just prior to and immediately post-exercise. The corresponding images are displayed side-by-side in a continuous loop cine format at comparable heart rates, to compare wall motion and thickening from similar views before and after exercise. In humans, the left ventricular wall is divided into segments, and the wall thickening and motion pre- and post-exercise for each segment are evaluated and graded. The segments are scored normal, hypokinetic, akinetic or dyskinetic, and segmental dysfunction is considered to be a sensitive indicator of coronary artery disease and regional ischemia. To be most accurate, it must be completed within 2–3 min of cessation of exercise before values return to baseline. Recently, a similar technique has been advocated as a means of evaluating myocardial function in horses.[5] Normal myocardial function at rest is manifested by ventricular wall thickening and inward motion during systole with FS of approximately 30–40%. During exercise, the inward wall motion, wall thickening and FS should increase dramatically in response to the demand for increased cardiac output. This increased myocardial contractility persists very briefly into the post-exercise period. A recent study in exercising horses calculated myocardial contractility on the basis of dP/dt (the first derivative of the change in pressure with respect to time) via pressure catheters positioned in the left and right ventricles. Similar calculations have been used to assess both systolic and diastolic myocardial function in horses. This study

Table 2.2 Values for selected enzymes and proteins found in serum of clinically health horses

	Rest	Post-exercise
Total creatine kinase (CK) activity (U/L)	24.6 ± 6.9[a]	<1000[d]
	81–225[b]	85.8 ± 10.1[e]
CK isozymes (% of total)[f]		
BB	20.1 ± 7.1[a]	
	1.9 ± 0.8[e]	3.8 ± 1.9[e]
MB	1.3 ± 1.2[a]	
	11.2 ± 2.1[e]	12.9 ± 6.5[e]
MM_1	45.2 ± 6.2[a]	
	86.9 ± 2.6[e]	83.3 ± 6.5[e]
MM_2	33.6 ± 7.8[a] with MM_1[e]	
Aspartate aminotransferase (AST) activity (U/L)	141–330[c]	–
Total lactate dehydrogenase (LDH) activity (U/L)	275.8 ± 68.9[a]	313.0 ± 74.1[e]
LDH isozymes (% of total)		
LDH_1	23.7 ± 3.4[a]	
	12.6 ± 6.7[e]	8.8 ± 3.2[e]
LDH_2	28.0 ± 2.3[a]	
	23.3 ± 7.5[e]	13.7 ± 5.6[e]
LDH_3	32.9 ± 2.9[a]	
	50.6 ± 12.6[e]	62.0 ± 7.3[e]
LDH_4	13.1 ± 3.4[c]	
	10.1 ± 2.9[e]	12.5 ± 4.3[e]
LDH_5	2.3 ± 1.7[a]	
	3.4 ± 1.2[e]	3.1 ± 0.9[e]
Cardiac troponin I (cTNI) concentration (ng/L)	26 ± 11[b]	72 ± 57[b]

[a] From Fujii et al;[30] values are mean ± SD, n = 160.
[b] From Durando et al;[26] values are mean ± SD, n = 9.
[c] From Lumsden et al;[31] values are 95% confidence interval.
[d] From Martin et al;[1] upper limit for asymptomatic horses.
[e] From Rueca et al;[32] values are mean ± SD, for horses running >15 m/s.
[f] The designation BB, MB, MM_1, MM_2 is a term for the specific isoenzyme. BB is brain type, MM is muscular type, and MB is hybrid type (Fujii et al[35]).

demonstrated that contractility remains similar to exercising values for approximately 30 s, while the heart rate remains elevated.[14] Thus, for stress echocardiography to be a useful indication of exercising myocardial function, it must be performed within 30–60 s of the cessation of exercise.

Post-exercise blood samples, collected 1–4 h following the treadmill test, are evaluated for the activities of several circulating enzymes that can arise from damaged cells. The most commonly evaluated enzymes are creatine kinase isozymes (CK or CPK), aspartate aminotransferase (AST), and the lactate dehydrogenase (LDH) isozymes. In addition, the plasma concentration of cardiac troponin I (cTNI) has been evaluated.[25–27] Although not all of these enzymes are exclusively found in skeletal and/or cardiac muscle, unexpected differences between values in samples collected prior to the treadmill examination and those in the post-exercise samples can generally be attributed to abnormalities in either of these systems. Table 2.2 provides reference ranges for cTNI and the commonly measured enzyme activities, both at rest and post-exercise.

Differential cytologies of washes from either the trachea (TW) or the bronchoalveolar region (BAL) are frequently used to evaluate the potential contribution of lower airway disease to reduced athletic performance. Most clinicians agree that BAL fluid cytology is better correlated with specific lower airway abnormalities than is TW fluid and thus is the better sample to collect post-exercise.[28,29] However, the need for sedation and the more invasive nature of a BAL may preclude its use in some clinical settings, especially if the entire treadmill examination is performed in a single day on an outpatient basis. The cytologic profile of samples collected pre- and post-exercise will differ. Typical cell differential values for samples of TW and BAL fluid obtained before and approximately 1 h after treadmill exercise are given in Table 2.3.

Table 2.3 Normal values for cytology from tracheal and bronchoalveolar wash fluid

	Tracheal wash		Bronchoalveolar lavage	
	Rest[a]	Post-exercise[b]	Rest[c]	Post-exercise[c]
Nucleated cell differential				
macrophages	67 ± 11	63.0 ± 18.7	68.8 ± 8.8	58.9 ± 14.1
lymphocytes	10 ± 3.5	2.7 ± 2.1	22.9 ± 7.9	30.6 ± 9.3
neutrophils	20.5 ± 10.2	7.9 ± 6.7	3.8 ± 5.5	7.2 ± 13.7
eosinophils	2 ± 1	0.6 ± 0.7	NR	NR
mast cells	0	0.4 ± 0.6	NR	NR
epithelial cells	NR	25.3 ± 21.6	NR	NR
Hemosiderophages	6	6.5 ± 6.0	16.6 ± 19.4	14.4 ± 10.7

NR = not reported.
[a] From Christley et al;[33] values are mean ± SD, n = 9.
[b] Authors' unpublished data; values are mean ± SD, n = 101.
[c] From Couetil and Denicola;[34] values are mean ± SD, n = 23 rest, n = 36 post-exercise.

References

1. Martin BB, Reef VB, Parente EJ, Sage AD. Causes of poor performance of horses during training, racing, or showing: 348 cases (1992–1996). J Am Vet Med Assoc 2000; 216:554–558.
2. Seeherman HJ. Treadmill exercise testing. Treadmill installation and training protocols used for clinical evaluations of equine athletes. Vet Clin North Am Equine Pract 1991; 7:259–269.
3. Morris EA, Seeherman HJ. Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. Equine Vet J 1991; 23:169–174.
4. Durando MM, Young LE. Cardiovascular examination and diagnostic techniques. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: Saunders; 2003; 572–584.
5. Reef VB. Stress echocardiography and its role in performance assessment. Vet Clin North Am Equine Pract 2001; 17:179–189.
6. Reef VB. Evaluation of the equine cardiovascular system. Vet Clin North Am Equine Pract 1985; 1:275–288.
7. Long KT, Bonagura JD, Darke PG. Standardized imaging technique for guided M-mode and doppler echocardiography in the horse. Equine Vet J 1992; 16:342–347.
8. Marr CM, Bright JM, Marlin DJ, et al. Pre- and post exercise echocardiography in horses performing treadmill exercise in cool and hot/humid conditions. Equine Vet J 1999; Suppl 30:131–136.
9. Hammer EJ, Tulleners EP, Parente EJ, Martin BB, Jr. Videoendoscopic assessment of dynamic laryngeal function during exercise in horses with grade-III left laryngeal hemiparesis at rest: 26 cases (1992–1995). J Am Vet Med Assoc 1998; 212:399–403.
10. Parente EJ. Endoscopic evaluation of the upper respiratory tract. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: Saunders; 2003: 366–369.
11. Hubert JD, Beadle RE. Anhidrosis. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: Saunders; 2003: 816–818.
12. Mayhew IG, Ferguson HO. Clinical, clinicopathologic, and epidemiologic features of anhidrosis in central Florida Thoroughbred horses. J Vet Intern Med 1987; 1:136–141.
13. Schlipf JW, Dunlop CI, Getzy DW, et al. Lesions associated with cardiac catheterization and thermodilution cardiac output determination in horses. In: 5th International Congress of Veterinary Anesthesia, Guelph, Ontario, Canada, 1994.
14. Durando MM, Reef VB, Birks EK. Right ventricular pressure dynamics during exercise: relationship to stress echocardiography. Equine Vet J 2002; Suppl 34:472–477.
15. Holmes JR. Cardiac arrhythmias on the racecourse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987.
16. Rakestraw PC, Hackett RP, Ducharme NG, et al. Arytenoid cartilage movement in resting and exercising horses. Vet Surg 1991; 20:122–127.
17. Franklin SH, Lane JG, Burn JF. Spectral analysis of respiratory noise in horses with upper airway obstructions. In: Proceedings of the 2nd World Equine Airway Symposium. Edinburgh, UK; 2001.
18. Cable CF, Ducharme NG, Hackett RP, Erb HN. Spectrotemporal signature for identifying upper airway abnormalities in exercising horses. In: Proceedings of the 2nd World Equine Airway Symposium. Edinburgh, UK; 2001.
19. Scheffer CW, Robben JH, Sloet Van Oldruitenborgh-Oosterbaan MM. Continuous monitoring of ECG in horses at rest and during exercise. Vet Rec 1995; 137:371–374.
20. Bowen IM. Cardiac dysrhythmias. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: Saunders; 2003; 602–613.
21. Kriz NG, Hodgson DR, Rose RJ. Prevalence and clinical importance of heart murmurs in racehorses. J Am Vet Med Assoc 2000; 216:1441–1445.
22. Young LE, Wood JL. Effect of age and training on murmurs of atrioventricular valvular regurgitation in young thoroughbreds. Equine Vet J 2000; 32:195–199.
23. Berberich SN, Zager JRS, Plotnick GD, Fisher ML. A practical approach to exercise echocardiography: Immediate post-exercise echocardiography. J Am Coll Cardiol 1984; 3:284–290.
24. Beleslin BD, Ostojic M, Stepanovic J, et al. Stress echocardiography in the detection of myocardial ischemia. Head-to-head comparison of exercise, dobutamine, and dipyridamole tests. Circulation. 1994; 90:1168–1176.
25. Argiroudis SA, Kent JE, Blackmore DJ. Observations on the isoenzymes of creatine kinase in equine serum. Equine Vet J 1982; 14:317–321.
26. Durando MM, Reef VB, Kline K, Birks EK. Effect of cardiac catheterization on cTNI and CK-MB in exercising horses. Proc Am Coll Vet Intern Med 2001; 10:887.
27. Venge P, Lagerqvist B, Diderholm E, et al. Clinical performance of three cardiac troponin assays in patients with unstable coronary artery disease (a FRISC II substudy). Am J Cardiol 2002; 89:1035–1041.
28. Viel L, Hewson J. Bronchoalveolar lavage. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: Saunders; 2003; 407–411.
29. McKane SA, Canfield PJ, Rose RJ. Equine bronchoalveolar lavage cytology: survey of thoroughbred. Aust Vet J 1993; 70:401–404.
30. Fujii Y, Watanabe H, Yamamoto T, et al. Serum creatine kinase and lactate dehydrogenase isoenzymes in skeletal and cardiac muscle damage in the horse. Bull Equine Res Inst 1983; 20:87–96.
31. Lumsden JH, Rowe R, Mullen K. Hematology and biochemistry reference values for the light horse. Can J Comp Med 1980; 44:32.
32. Rueca F, Conti MB, Prorciello F, et al. Relationship between running speed, isoenzymes of serum creatine kinase and lactate dehydrogenase and left ventricular function in stallions. Equine Vet J Suppl 1999; 30:163–165.
33. Christley RM, Hodgson DR, Rose RJ, et al. Comparison of bacteriology and cytology of tracheal fluid samples collected by percutaneous transtracheal aspiration or via an endoscope using a plugged, guarded catheter. Equine Vet J 1999; 31:197–202.
34. Couetil LL, Denicola DB. Blood gas, plasma lactate and bronchoalveolar lavage cytology analyses in racehorses with respiratory disease. Equine Vet J Suppl 1999; 30:77–82.
35. Fujii Y, Ikeda S, Watanabe H. Analysis of creatinine kinase enzymes in racehorse serum and tissues. Bull Equine Res Inst 1980; 17:21–31.

CHAPTER 3

Exercise testing in the field

David Evans

Introduction

Exercise tests of equine athletes can be conducted in a treadmill laboratory, or in the field. There are advantages and disadvantages for conduct of exercise tests in both these locations. Field investigations have the advantage of conduct of the test in the environment likely to be used in competition. The surface, gaits and speeds used in a field test are therefore more closely aligned to the demands that horses face during exercise in the 'real world'. Field tests also account for the effects of jockey or driver. These advantages can also be disadvantages, because they can contribute to difficulties in standardization of field exercise tests. This chapter presents some of the limitations of treadmill exercise tests, and describes techniques that have been used for field exercise tests in galloping, trotting and pacing horses. The rationale for making the effort to perform field exercise tests is discussed. There have been many remarkable field studies that have measured the electrocardiogram, collected arterial blood and measured tracheal pressures in galloping horses. However, it is not the intention of this chapter to review in detail all equine field studies. The scope of this chapter will be limited mostly to field studies of cardiorespiratory function, and to the use of field studies to conduct fitness tests in athletic horses.

Limitations of treadmill tests

The arguments for using high-speed treadmills to evaluate fitness and health of horses are obvious. The physical environment can be controlled, and conduct of exercise tests with precise design is possible. The speeds and durations of each step of an exercise test are highly repeatable. There is also easy access to horses at suitable times during and after exercise for cardiorespiratory measurements and blood collections.

Horses should be acclimated to treadmill exercise before clinical exercise testing.[1] However, responses to acclimation runs are unpredictable in individual horses. Figure 3.1 illustrates the variability of heart rates and plasma lactate concentrations during treadmill exercise in horses that were given four treadmill tests on consecutive days. Several studies have shown that physiologic responses to treadmill exercise do not replicate responses to field exercise. Heart rate (HR) and plasma lactate concentrations in Standardbred horses pulling a 10 kilopond draught load were lower on the treadmill than on the racetrack.[2] It was also reported that HR and blood lactate in trotters were lower during exercise on a level treadmill than during exercise on a racetrack (Fig. 3.2).[3] Heart rates were expressed as V200 and VHRmax, the velocities at which HRs were 200 beats per minute or had just reached maximal HR. Blood lactates were expressed as V4, the velocity at which blood lactate was 4 mmol/L. This value is sometimes referred to as VLa4. Stride frequency was lower and stride length was greater on the treadmill. Interestingly, this study also showed that there were no differences in any measurements on two sand tracks of 720 and 1250 m in length. A study of ridden Warmblood horses also found that heart rates and blood lactate concentrations were lower on the level treadmill at speeds of 6.5–9.4 m/s compared with exercise over ground. The treadmill speed had to be increased by approximately 10% or the treadmill incline increased to 1–2% to give the same heart rates as in the field.[4]

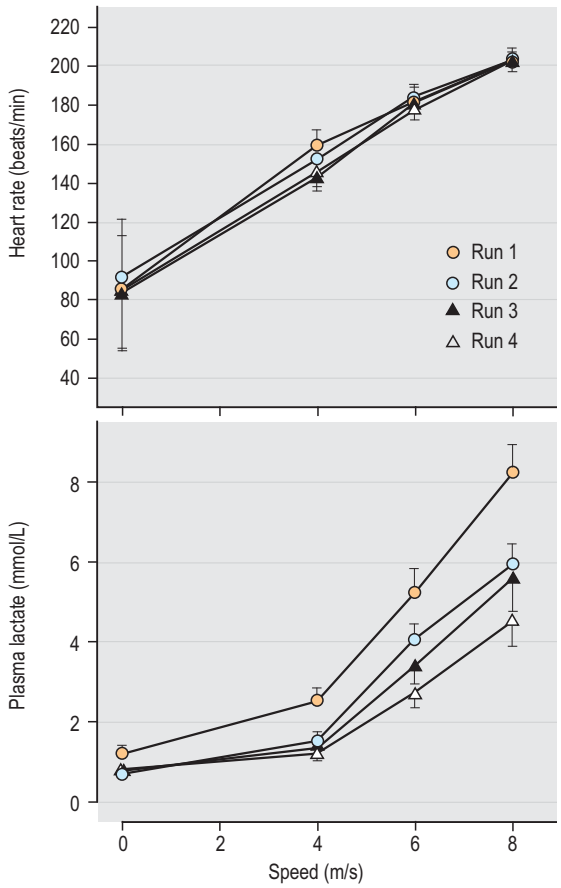


Fig. 3.1
Heart rates and plasma lactate concentrations (mean ± SEM) during treadmill exercise in six race horses that had four sequential acclimating runs over a 4-day period. Note the variability of heart rates during trotting at 4 m/s, and the high variability of plasma lactates at all velocities. From King et al,[1] with permission.

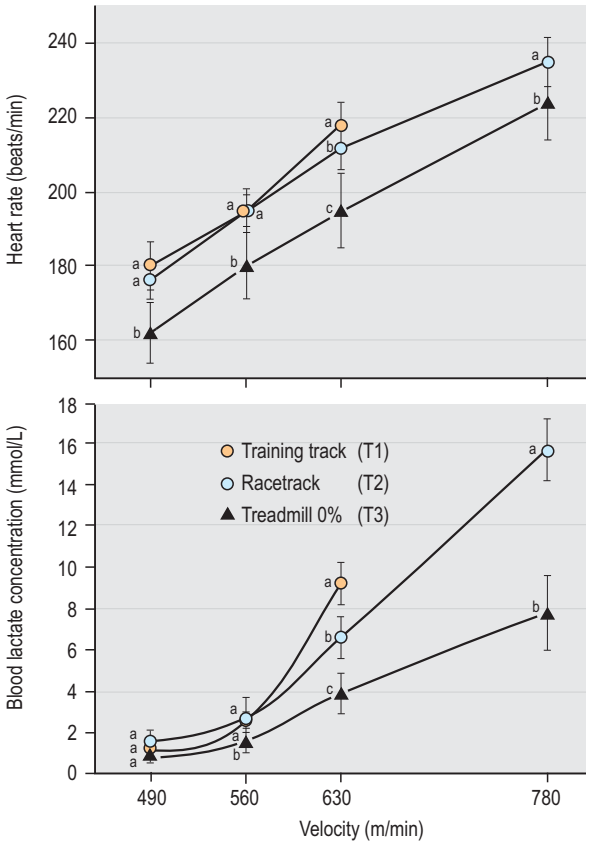


Fig. 3.2
Mean ± SD heart rate (HR) and blood lactate concentrations in five French Standardbred trotters at three different speeds during exercise tests performed on two different tracks (T1,T2) and on a non-inclined treadmill (T3). At each velocity, values with a different letter are significantly different. The treadmill tests produced lower HRs and blood lactate concentrations in most cases. From Couroucé et al,[3] with permission.

Locomotion during treadmill exercise is quite different to that on the track. As a consequence, even if horses are given tasks on treadmills that produce similar HRs, their gaits may be quite dissimilar. Stride frequencies at identical trot and gallop speeds are greater on a racetrack.[5] Design of treadmill exercise tests to replicate field exercise therefore seems to be a fruitless endeavor.

Treadmill exercise tests should be used when it is appropriate to do so, and field exercise tests also have a role in the management of athletic horses. In field tests, horses do not need acclimation, and the exercise is conducted in the physical environment that is more closely matched to that used in competition.

Field exercise tests

Heart rate and blood lactate measurements are the bases of an exercise test for athletic horses. Heart rates are usually expressed relative to a constant submaximal speed, such as V200, the velocity at which heart rate is 200 beats per minute. However, expression of the velocity at lower heart rates is equally valid, and some studies have used V140 and V170.

The blood lactate response to specific speeds of exercise has also been used in numerous studies of field exercise testing for assessing performance and fitness. Fitness has usually been described with speed at a lactate concentration of 4 mmol/L (VLa4). As the horse increases fitness, VLa4 increases. Alternatively, the blood lactate response to a single episode of submaximal exercise can be used. This 'one-step' approach might be more applicable in field tests. It obviates the need for time-consuming, standardized multiple increments of velocity, and the need for multiple collections of blood via a catheter secured in the jugular vein or by repeated venipuncture. Treadmill exercise tests have also measured the lactate 'break-point', the velocity at which blood lactate begins to accumulate in the blood,[6] but there has been no application of this technique in the field.

All exercise tests should attempt to answer a simple question for a trainer or owner of the horse. Ideally the exercise

test should be designed to answer one or more of the following questions:

1. Has the horse's fitness changed with recent training?
2. Is the horse 'fit' for its next race, where fitness refers to a horse that is healthy and suitably trained?
3. How does the fitness of horse A compare with horse B?
4. Does a horse with poor racing performance have suboptimal fitness?
5. Can an appropriate measure of fitness help with training of race horses?
6. Does a horse with suboptimal or unexpectedly poor performance have a disease? Is there evidence of a cardiac or respiratory limitation to performance?

Exercise tests to help answer all of these questions necessitate measurements of heart rate, oxygen uptake, and pulmonary ventilation. Nonetheless, blood lactate and heart rate measurements during or after suitable exercise tests can help with answers to questions 1, 3, 4, and 5. In the following sections, field exercise tests that have used heart rate and blood lactate measurements in Standardbred and Thoroughbred horses will be described.

There are several important principles to follow so that field fitness tests provide meaningful results and answer one or more of the above questions. First, the test protocol should be simple. Multiple steps of increasing speeds of exercise are frequently used in treadmill testing, but these forms of exercise testing in the field may not be popular with trainers because of the excessive time commitment. Exercise tests should also be easy to implement, and ideally should not disrupt normal training schedules.

There are several features of the exercise test that should be maintained wherever possible. These include consistency of:

1. Warm-up routine prior to testing
2. Rates and distances of acceleration during the exercise
3. Test distances or times
4. Speed during the exercise
5. Time after exercise at which blood is collected
6. Post-exercise activity
7. Environmental conditions.

The environmental conditions can be an important factor during the conduct of field exercise tests.[7] Heart rates and other variables were compared under high and low ambient temperature and relative humidity during a submaximal incremental field exercise test in horses tested in summer and in autumn. Heart rate was measured continuously, the other variables at rest and immediately after 4 minutes at 3.5, 4.5 and 7.0 m/s, separated by 3 minute rest intervals, and after 5 and 10 minutes recovery. Heart rates were significantly greater by a mean of 13 beats per minute during exercise in the hot versus cool conditions. It was concluded that differences in environmental conditions can affect assessment of exercise response. These factors must be considered when using fitness tests in the field. Sudden changes in environmental conditions might have considerable consequences for heart rates during exercise.

There has been slow adoption of the use of field exercise tests in commercial race-horse training establishments. Part of the reason for the slow adoption of these techniques has been the difficulty in the design and implementation of exercise tests in the field. Treadmills are useful because they help with the conduct of standardized exercise tests. However, few trainers use treadmills or have access to them. Understandably, some trainers might also have reservations about adopting new techniques that could disrupt busy training schedules.

However, many horse owners continue to be frustrated by lack of information about the fitness and performance capacity of their horses. Several recent studies have outlined new methods of performing exercise tests on racetracks. Some of these methods could easily be implemented in commercial training environments, so that they are a part of the routine management of the horses. The general approaches described below for use of heart rate and blood lactate measurements for fitness assessment can also be applied in endurance, event and other athletic horses. Ergospirometry, the measurement of breathing and oxygen uptake during exercise, is necessary for an ideal exercise test, but the technology is not yet suitable for routine use in the field.

Studies of heart rate in galloping horses

During the 1960s and 1970s, before the common availability of high-speed treadmills at research centers, there were many field studies with remarkable achievements. Telemetric electrocardiography was used widely in the 1960s and 1970s to study the HR and electrocardiogram (ECG) of race horses during exercise on racetracks.[8–13] Direct recording of the ECG with an on-board tape recorder was also used to study the heart rate during races.[14] These studies described typical heart rates during submaximal and maximal exercise in Thoroughbreds and Standardbreds. Studies of training exercise and races were included, as were descriptions of the recovery of heart rate after field exercise. Studies of heart rate were also combined with telemetry of arterial blood pressure at speeds up to 800 m/min.[15] These studies were mostly descriptive, and did not focus on design of exercise tests.

An exercise test typically consists of several bouts of exercise after a warm-up, which may or may not be separated by a rest period. Heart rate is usually measured during the exercise, and the velocity of each step of the exercise test is calculated by timing the event. The distances and durations of each step used in field tests have varied widely. Blood samples can be collected during rest periods after each step of the exercise test. Figure 3.3 shows a continuous record of heart rate over time during an exercise test in an Australian Thoroughbred event horse.[16] In this exercise test, each horse was exercised over a 450 m distance at speeds of approximately 250, 300, 450, and 600 m/min. Horses were given a brief period of walking between each step of the exercise test. Figure 3.4

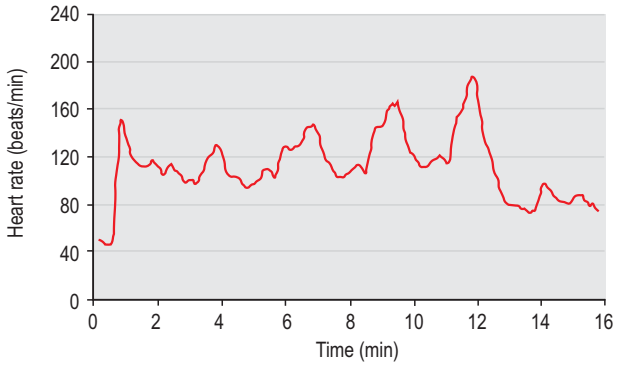


Fig. 3.3
Typical plot of heart rate versus time for the exercise test used in Thoroughbred event horses. There is an overshoot of heart rate at the commencement of the test (1 minute). The four heart rates during the four steps of the exercise test were recorded at 4, 7, 9 and 12 minutes. From Serrano et al,[16] with permission.

shows the use of a graph of heart rate and velocity for each step of the test to produce the typical linear relationship between heart rate and velocity. The graph also enables calculation of V200, the exercise velocity resulting in a heart rate of 200 beats per minute.[16] In this study of 17 horses, V200 ranged from 560 to 900 m/min. This wide range could reflect differences in inherent fitness, and differences in fitness due to training. An increase in fitness results in an increase in V200. Loss of fitness, cardiovascular and respiratory disease, lameness, and an increase in bodyweight could all cause a decrease in V200.

V200 can also be calculated with an incremental field exercise test in Thoroughbred race horses.[17] Commercial heart rate meters that log heart rate continuously and enable transfer of the data to a computer for analysis are suitable for this purpose. The exercise test consisted of about 1000 m trotting at 250 m/min, then galloping exercises at approximately 400, 460, 550, and 660 m/min for 600–800 m at each speed. Fine days and tracks in firm condition were used, and velocity was measured by stopwatch every 200 m of each step of the test. Mean HR and mean velocity were calculated for each 200 m section of the test.

This exercise test was used to investigate the influence of rider and track conditions, repeatability of V200 measurements and the effects of training on V200.[17] The HRs for the different sections of each step of the exercise test were all included, providing 17 HR and velocity measurements from one test. Figure 3.5 shows the relationship between heart rate and velocity in a Thoroughbred race horse using data obtained with this type of field exercise test. The method used in this exercise test has great potential. Use of a high number of data points should enable easy identification of outliers, and generation of a reliable line of best fit, as in Fig. 3.5. The technique also shows that it is possible to generate excellent HR–velocity relationships in field tests without use of protocols that necessitate strict adherence to steps of an exercise test with constant exercise speed. Trainers may more readily adopt this technique because it does not necessitate changes to training schedules, and it can be incorporated into the usual daily training routine. The methodology in this study demonstrates the importance of refining field exercise tests so that they are easy to undertake. The usual treadmill model of an exercise test, with an emphasis on 45–60 seconds of constant velocity exercise in order to achieve steady state conditions, may not be the most suitable method in the field.

The importance of taking into account the psychological state of the horse was also demonstrated.[17] In an excitable state, the slope of the regression line of HR on velocity was decreased because of high HRs during trotting. V200 was thus falsely high. This finding emphasizes the need for careful observation of horses during field exercise tests, and for questioning of trainers and jockeys concerning the emotional state of the horse during exercise. If in doubt, calculation of V200 should be delayed until the horse has completed a test in a relaxed state. The correlation between 31 values for

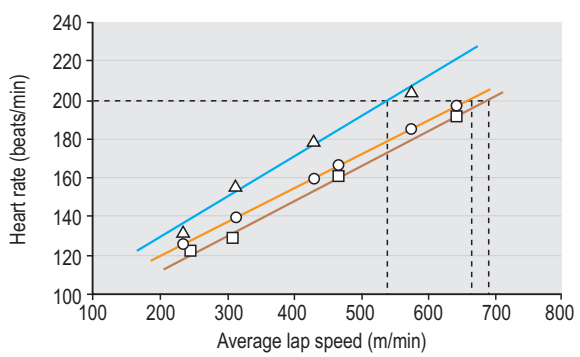


Fig. 3.4
Lines of best fit of the relationship between heart rate and velocity in a field exercise test used in two Thoroughbred event horses (Δ, □), compared with the average line of best fit (○) in 17 horses. Horse 2 (Δ) had higher heart rates than average at each of the four steps of the exercise test. The dotted lines show the method of calculating V200. From Serrano et al,[16] with permission.

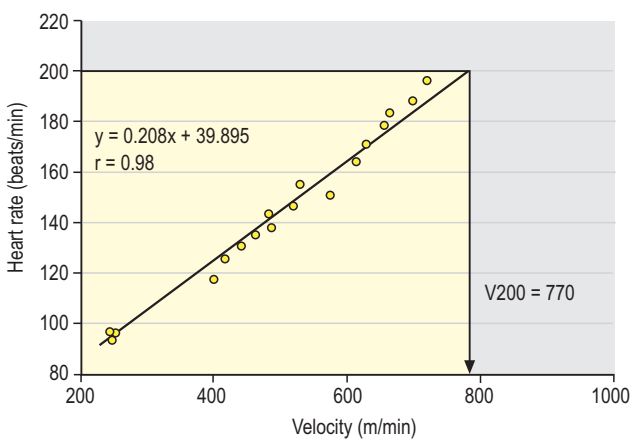


Fig. 3.5
Relationship between heart rate and velocity in a Thoroughbred race horse exercising under field conditions. From Kobayashi et al,[17] with permission.

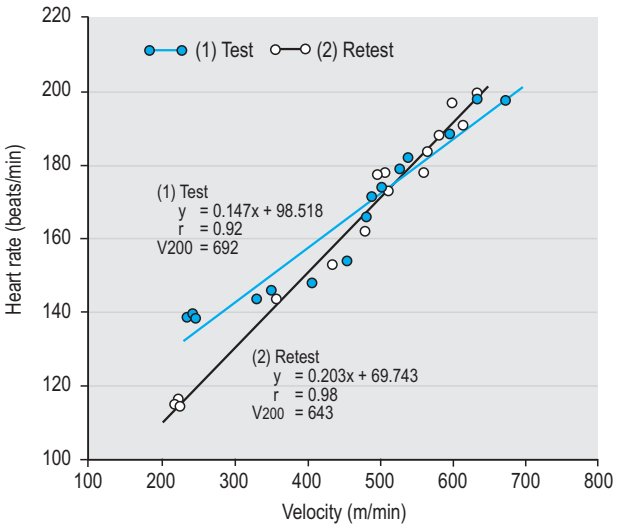


Fig. 3.6
Relationships between heart rate and velocity in a Thoroughbred race horse (1) exercising under field conditions after trotting in an excitable condition (●) and (2) when retested in a relaxed condition ( ). Note the pronounced increase in heart rates when trotting at 250 m/min in an excited condition. This effect has a marked influence on the slope of the line of best fit, which causes a false increase in V200. From Kobayashi et al,[17] with permission.

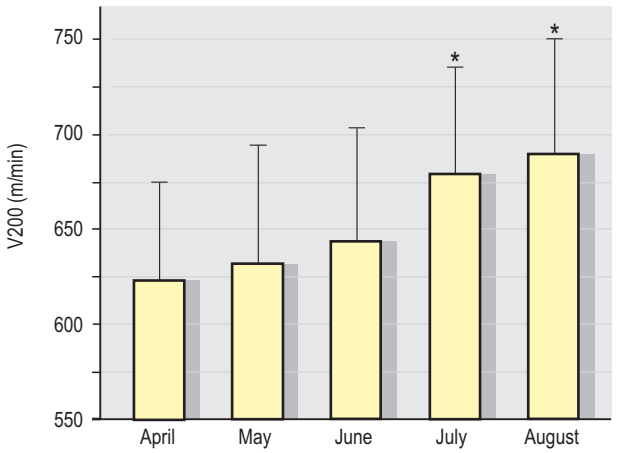


Fig. 3.7
Changes in V200 (± SD) as training progresses from April to August in 2-year-old Thoroughbreds. * Significantly different from April, May and June. From Kobayashi et al,[17] with permission.

V200 measured on two consecutive days was 0.88.[17] The differences in V200 were in the range of 0–50 m/min. Precision of V200 measurements in the field would probably be increased by use of more than one exercise test, and inspection of scatter plots to discard obvious outliers. These results suggest that the outliers will most likely be high HRs during trotting which could indicate excitability. Figure 3.6 shows the effect of excitability on heart rates during trotting, and the effect on V200. High HRs in this study were also associated with gait changes that were not 'smooth', and with phases of rapid acceleration. No major decisions about a horse's fitness or health should be based on the results of a single exercise test. Ideally, horses should be tested regularly, so that a record of results is established for an individual horse. If there is some doubt concerning the results in an individual exercise test, the test should be repeated.

As expected, the V200 was influenced by track type, with lower values on sand tracks than on grass or wood. Interestingly, the V200 was not significantly different in horses ridden by light (55 kg) and heavy (70 kg) jockeys in a crossover study.[17] However, the mean V200 was 35 m/min higher with light jockeys, and it seems sensible to avoid large differences in field studies of ridden horses.

One important rationale for field exercise tests is to accurately, reliably and precisely measure a variable or variables that indicate changes in state of training or health. Field studies of fitness have demonstrated that V200 in Thoroughbreds increased with training over a 5-month period (Fig. 3.7).[17] In 2-year-old horses, the average increase in V200 over the period was approximately 65 m/min, an increase of approximately 10%.

Telemetric electrocardiography has been used in combination with pneumotachography to measure heart rate, respiratory frequency, tidal volume, and respiratory gas flow rates in four Thoroughbred horses during field exercise at a speed of approximately 800 m/min.[18] Heart rate was also measured by telemetry during lunging exercise at the walk and trot, in combination with breath-by-breath measurements of pulmonary ventilation.[19] Studies of minute ventilation, flow rates, respiratory times and flow volume loops were conducted in normal horses and horses with airway diseases. Horses with bronchitis had higher heart rates during exercise than normal horses, as well as altered measurements of pulmonary ventilation. The authors concluded that the technique had considerable potential for diagnosis and evaluation of therapies. However, there has been little adoption of this method because of the limitations of the technology for measuring breath-by-breath respiratory gas flow rates during field exercise.

The results of many studies have demonstrated that higher than expected heart rates during submaximal exercise may be an indication of one of the following:

1. Lameness, or another painful condition
2. Dehydration
3. Exercise conducted in hot conditions
4. A loss of fitness, due to detraining or inappropriate training
5. Respiratory disease
6. Cardiovascular disease, or anemia
7. Increased body mass, or a greater percentage of bodyweight as fat or water
8. A physiologically inferior horse, probably due to a relatively small heart.

Ideal use of exercise tests therefore depends on regular use of heart rate measurements during the training months. Conduct of one exercise test in isolation is much less likely to provide meaningful information. Comparison of current

results with previous findings is most likely to give a trainer, veterinarian or owner information that can help manage the horse's training program. As well, the finding of a high heart rate during an exercise test may or may not indicate a problem with fitness or health. High heart rates during exercise, compared with recent findings in the same horse, are not a diagnosis. However, they are a warning sign, and such horses should be thoroughly examined to ascertain whether or not there is a new clinical or other condition that could explain the results. It is also best to be cautious about interpretation of unexpected findings. Tests should always be repeated if possible to confirm the validity of results.

Field tests of fitness in Standardbred horses

Field tests with multiple speeds and blood collections have been conducted in Standardbred trotters and pacers to assess performance on the basis of HR and blood lactate measurements. A simple exercise test for pacing horses consisted of four steps of exercise over 1000 meters.[20] Speeds of each step were 450–550, 600–700, 700–800, and greater than 800 m/min. The horse walked for 3–5 minutes between each of the four steps. Blood was collected into fluoride oxalate tubes 3 minutes after each step. Heart rates were also recorded during the exercise test to calculate V200. A plot of speed versus blood lactate was drawn. By drawing a line horizontal to the 4 mmol/L concentration, the VLa4 can be directly calculated. It was observed that superior horses had a lower blood lactate response to this exercise test.

In a study of Swedish Standardbred trotters, 10 horses performed a similar submaximal test on a track. The test consisted of five incremental heats at approximate speeds of 9.1, 9.5, 10.0, 10.5, and 11.1 m/s over 1000 meters. A blood sample was drawn from the jugular vein for plasma lactate analysis immediately after each heat. The plasma lactate response to exercise differed between horses, but no correlation was seen with a racing performance index in a small number of horses.[21]

Studies of larger numbers of horses that have a large range of racing abilities are more reliable. The relationship between VLa4, age and racing performance of Standardbred trotters has been investigated.[22] A total of 159 horses performed standardized exercise tests of three steps performed at increasing speeds. The velocity of the horses was measured with a tachometer on the sulky. Mean VLa4 values increased significantly ($P < 0.05$) with age between 2 and 4 years. Horses were defined as good performers (GP) when finishing between first and fifth place in a race or poor performers (PP) when finishing lower than fifth. VLa4 was significantly higher for GP than for PP ($P < 0.05$).

The VLa4 measurement is therefore a valid measurement for the evaluation of fitness in Standardbreds. The measurement could help trainers and owners to make more informed decisions about horses with poor performance, and assist with overall management of the racing career of a horse. Prospective owners may be more attracted to race-horse purchase if reliable measurements of fitness and performance capacity were more widely used. Veterinarians, trainers or owners interested in using these tests in Standardbred horses should develop their own exercise test routine on a single racetrack. It should also be noted that blood lactate concentration is likely to be increased by excitement during the test, and by 'pulling', an inefficient gait due to effort expended against restraint by the driver. Results from exercise tests in which horses pull hard against a jockey or driver should be regarded with suspicion, and the test repeated.

A review of exercise tests for French trotters exercising in the field concluded that track testing provided a more limited range of measurements than treadmill testing, but had the advantage of being performed in the horse's natural environment.[23] Various measurements such as heart rate during exercise and blood lactate concentration after exercise may be measured on the track, enabling calculation of physiological variables such as V200 and VLa4. Although VLa4 is calculated during submaximal intensity exercise, it is related to racing performance and seems to be the most important

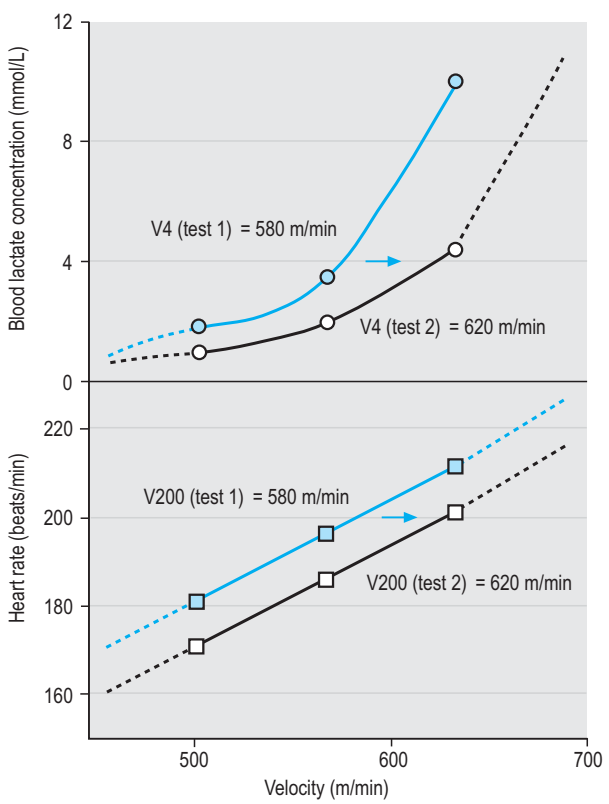


Fig. 3.8
Heart rate and blood lactate concentrations related to velocity in a French trotter before (blue lines) and after (black lines) 6 weeks of training. There is a shift to the right with improved fitness. The heart rates and blood lactate concentrations during exercise at 500, 580 and 630 m/min are lower after training. V200 and V4 have increased. From Couroucé,[23] with permission.

measurement to assess changes in fitness.[23] There is a significant influence of age on measurements of heart rate (V200) and VLa4 in trotters. Reference values for heart rate and blood lactate responses to field exercise in French trotters of varying fitness and age have been described.[24] The use of a graphical display of heart rate and blood lactate concentrations at different speeds of field exercise to calculate V200 and V4 in a trotting horse is illustrated in Fig. 3.8.[23] This figure also shows the typical effect of training on the relationships; both curves shift to the right. Figure 3.9 shows the normal values for some heart rate and plasma lactate indices in relation to exercise velocity in trotters of various ages,[24] and the influence of training is described in Fig. 3.10. High heart rates during field exercise tests may be associated with lameness or respiratory disease. The potential use of field exercise tests as an aid to the clinical evaluation of athletic horses is illustrated in Fig. 3.11, which shows the effect of subclinical respiratory disease on heart rates and blood lactate concentrations during a submaximal field test in trotters.[23]

A submaximal field exercise test consisting of two bouts of 1600 meters has been used to assess fitness in Standardbred

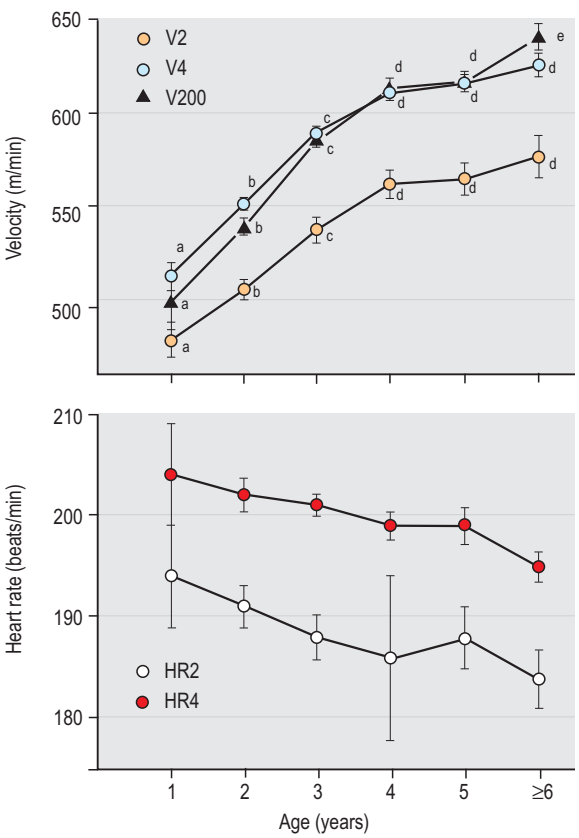


Fig. 3.9
Mean and 95% confidence interval values for several indices of fitness in French Standardbred trotters of various ages. V2 and V4, velocities at which post-exercise blood lactate concentrations are 2 or 4 mmol/L; V200, velocity at which HR is 200 beats/min. HR2 and HR4 refer to heart rates at blood lactate concentrations of 2 and 4 mmol/L. Values with different letters at each age are significantly different ($P < 0.05$). From Couroucé et al,[24] with permission.

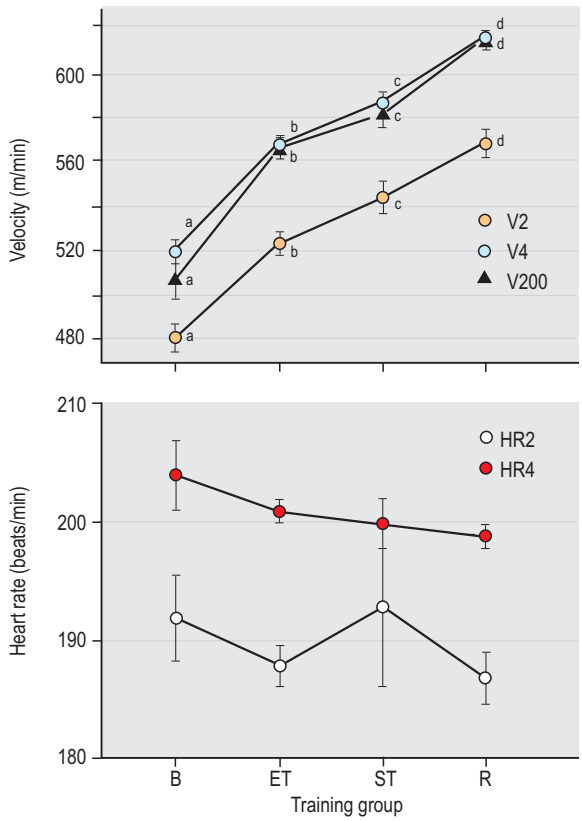


Fig. 3.10
Mean and 95% confidence interval values for several indices of fitness in French Standardbred trotters of various ages. B, at beginning of training; ET, after endurance training; ST, after sprint training; R, when racing. At each age, values with different letters are significantly different ($P < 0.05$). From Couroucé et al,[24] with permission.

pacing horses in two stables (A and B).[25] Five minutes of rest or walking between runs was allowed. Performance indices were compiled for each horse: number of race starts, number of race wins, number of race placings (1, 2 or 3), and lifetime earnings. Regression analysis was conducted to describe the relationship between plasma lactate concentrations and speed for tests one, two, and pooled results. Using the regression equation, observed (measured) minus expected (predicted) (O – E) lactate concentrations for tests were calculated and plotted against performance indices to determine their relationship. The association between lactate and velocity for the two tests was best described by exponential equations. This study found no relationship in either stable between O – E and performance indices (number of race wins, number of race placings, lifetime earnings and average $/start) for test run one, two or pooled lactates. At one of the stables there was a significant association between V4 (velocity predicted to produce a blood lactate concentration of 4 mmol/L) and log lifetime earnings ($r = 0.51$, $P = 0.05$) and log average $/start ($r = 0.54$, $P = 0.04$). There were no significant correlations at the other stable. It was concluded that a two-step determination method of V4 was a suitable method for studying limits to performance in pacing Standardbred race horses. A

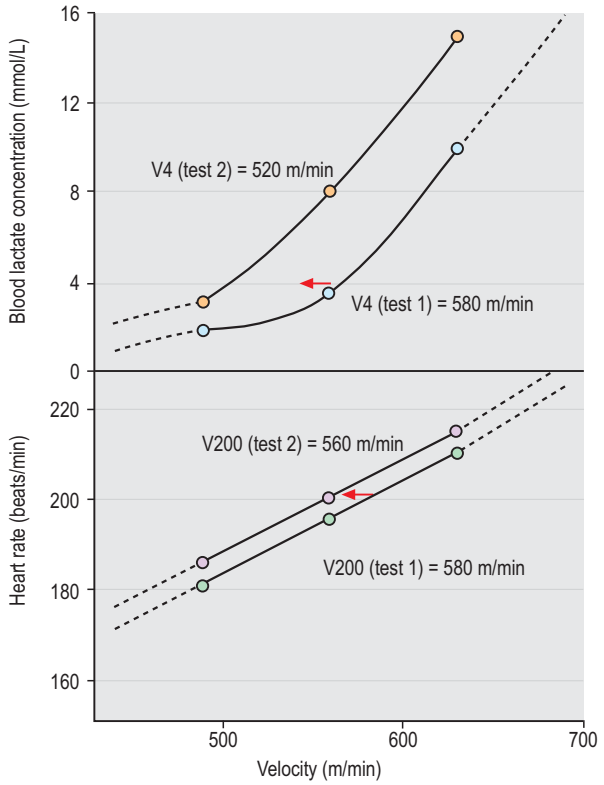


Fig. 3.11
Heart rate and blood lactate concentrations related to velocity in a French trotter before (test 1) and after (test 2) 6 weeks training, showing the influence of a subclinical respiratory infection. The heart rates and blood lactate concentrations during exercise at 500, 580 and 630 m/min are higher after training associated with the respiratory disease, and V200 and V4 have decreased. From Couroucé,[23] with permission.

major advantage of the technique used in this study was that the test was easily incorporated into the normal training routines. It was also noted that the correlations might be higher if studies of associations between fitness indices and performance included more horses with a wider range of racing abilities. Another limitation of such studies is that they do not include horses that have been discarded from training due to poor performance early in their racing career. More studies are needed of the variability in fitness of young, unraced horses. Does fitness in young unraced horses predict future racing performance? Is the rate of change in fitness equal in all horses when they are trained? Large-scale field studies may offer the best opportunities to investigate these questions.

Metabolic measurements after maximal exercise

Tests of the blood lactate response to submaximal exercise such as those described above are indications of endurance ability, or stamina. Lactate tests measuring VLa4 or VLa10 (blood lactate at a velocity of 10 m/s) are unlikely to be highly correlated with the ability of a horse to accelerate at the start or finish of a race, or the ability of a horse to sprint 600–800 m.

High levels of 'anaerobic stress' are found in Thoroughbred horses after approximately 50 seconds of maximal field exercise.[26] After only 400 metres of field exercise near racing speeds the blood lactate concentration increased from less than 1.0 mmol/L to over 14 mmol/L,[27] values similar to concentrations found after races. This rapid increase in blood lactate concentration during maximal exercise also occurs in Standardbreds and polo horses.[28] Measurement of the blood lactate concentration after maximal exercise has been used to estimate anaerobic capacity, defined as the ability of an individual to resynthesize ATP via anaerobic metabolism. Markers of anaerobic metabolism in skeletal muscle include concentrations of plasma lactate and uric acid after maximal exercise.[29]

The blood lactate concentration after maximal exercise to fatigue does not change with submaximal treadmill exercise training,[30] or after high-intensity training.[31] As well, the blood lactate concentrations after maximal exercise were not correlated with race performance in trotters[32] or Thoroughbreds.[33] This measurement is therefore not a useful marker of fitness.

Relationships between racing performance and plasma lactate and uric acid concentrations after racing were investigated in pacing Standardbred race horses.[34] Twenty horses were tested after races of 1760 meters and 28 horses after races over 2160 meters. Blood samples were taken 30–60 minutes before and 8 and 30 minutes after a race. There were no significant differences between the race distances for pre-race and 8 minute post-race plasma lactates. Significant low correlations were obtained for plasma lactate concentration 8 minutes post-race and the number of race wins ($r = 0.29$, $P = 0.04$), number of race placings (first, second or third) ($r = 0.34$, $P = 0.02$) and lifetime earnings ($r = 0.29$, $P = 0.04$). There were no significant correlations between performance indices and plasma uric acid concentrations in races of 1760 meters. For races of 2160 meters, correlations were found between plasma uric acid concentration at 8 minutes post-race and the number of race wins ($r = 0.37$, $P = 0.06$). As well, there was a significant correlation between uric acid concentration at 8 minutes post-race and lifetime earnings ($r = 0.35$, $P = 0.07$). These results imply that only 10–15% of the variability in retrospective career performance in pacing Standardbreds can be explained by these metabolic markers of the muscle anaerobic response to racing. Blood or plasma lactate and uric acid responses to maximal exercise are not useful measures of fitness on their own, but they could be included in multifactorial studies.

A study of the relationships between racing performance and several physiologic measurements was also conducted in 25 Standardbred trotters.[21] Blood samples and muscle biopsies were obtained 5–10 minutes after racing. The biopsies were analyzed for fiber type composition and enzymatic profile and blood samples for plasma lactate and ammonia concentrations. Fiber type composition varied among horses

(range 9–27% for type I, 32–54% for type IIA, and 27–46% for type IIB). Fiber type composition, muscle enzyme activities, plasma lactate and ammonia responses to racing were not correlated to a racing performance index.

The rate of accumulation of lactate in blood during maximal field exercise over distances up to 400 meters is closely related to speed in Standardbred, Thoroughbred and polo horses.[28] It was suggested that this lactate measurement could be a useful index of fitness. However, it is unlikely that any physiologic measurement after brief, maximal intensity exercise to estimate anaerobic capacity will be more closely correlated with fitness than a simple measurement of maximal speed during 40–50 seconds of exercise. In conclusion, the blood lactate response to maximal exercise has limited usefulness as a measure of fitness in horses. However, the blood lactate response to moderate, or submaximal speed exercise, expressed as VLa4 or another similar index, is a useful technique for differentiating poor performers and good performers, and for monitoring the changes in fitness during training programs.

Blood lactate measurements in submaximal field tests of fitness in Thoroughbreds

A major difficulty with field exercise tests has been control of the exercise performed by the horse. Ideal standardized tests necessitate control of exercise speeds, duration of exercise, and rates of acceleration. Use of stepwise exercise tests has been usual in treadmill studies, with incremental speeds used. Such tests enable descriptions of the relationships between speed and variables such as heart rate, blood lactate concentration, and oxygen consumption. Field exercise tests of this sort are not very practical for Thoroughbred race horses, and alternative methods are needed. Conduct of racetrack exercise tests for measurement of VLa4 or VLa10 is especially problematic in Thoroughbreds because it is difficult to obtain constant track conditions and constant speeds during exercise. Measurement of the lactate responses to a single or pair of exercise bouts could be a superior approach to field exercise testing in Thoroughbreds.

A standardized, two-step exercise test has been used to investigate the blood lactate running speed relationship in nine Thoroughbred race horses.[35] Each horse completed a two-speed field test at intervals of 6–8 weeks to determine the running velocity (v) that resulted in blood lactate concentrations of 4 (v(4)) and 12 mmol/L (v(12)). Changes of v(4) and v(12) in a horse between two consecutive tests were used to assess the effects of training history. The percentage of days with gallop workouts between two consecutive tests showed a significant correlation with changes in v(4) ($r = 0.71$, $P < 0.01$) and v(12) ($r = 0.56$, $P < 0.05$). The number of gallop workouts ($r = 0.60$, $P < 0.05$) and the total time of training ($r = 0.58$, $P < 0.05$) also correlated with the change of v(4). Furthermore the percentage of days without training was negatively correlated to changes of v(4) ($r = -0.75$, $P < 0.01$) and v(12) ($r = -0.56$, $P < 0.05$). These results imply that increases in fitness, as measured with the blood lactate response to submaximal exercise in a two-step field test, are more likely in Thoroughbred horses that have more galloping than trotting exercise, and have a higher number of gallops in a time period. More days without training was associated with reduced fitness, and more training at higher speeds was associated with greater fitness.

An alternative approach is to determine the blood lactate concentration during a single bout of strenuous, submaximal exercise. An appropriate speed of the exercise must be chosen. The aim is to have an exercise test that is demanding for some horses, but achieved easily in others. Typical speeds for such tests are 800 meters in 65–70 seconds in a Standardbred horse,[20] and in 55–60 seconds in Thoroughbreds.[36] These speeds would need to be confirmed in an individual stable, because they will depend on the quality of horses being trained, and possibly on track size and surface conditions.

The use of a single blood lactate measurement after exercise has been validated as a measure of racing ability in Thoroughbred horses, and as a simple method of monitoring responses to treadmill training. A correlation of over 0.6 was found between retrospective career racing performance in Thoroughbreds, and blood lactate concentration 2 minutes after treadmill exercise at 10 m/s.[33] During a treadmill training program, the blood lactate concentration after treadmill exercise at 9 m/s gradually decreased over 9 weeks of training.[30] This response was similar to changes in VLa4. These results suggest that exercise tests with multiple steps may not be absolutely necessary for fitness evaluation in horses, and that measurement of the blood lactate concentration after a standardized, one-step test may suffice.

The feasibility of a one-step field test for assessment of fitness in Thoroughbred horses has been investigated.[36] Each horse completed a 1000 m warm-up at a slow trot of approximately 3–4 m/s prior to each test. Subsequently the horses completed an 800 m gallop with jockeys instructed to maintain a constant running speed in the range of 13 to 16 m/s. This range of speeds was selected as they correspond with the speeds frequently used in training Thoroughbreds on Australian tracks. The time for the 800 m and each of the four 200 m sections was obtained by stop-watch. All timing was conducted from the same position at each track by the same observer. Speed was determined from the total time for the 800 m gallop. At the completion of each gallop, the horse was trotted for 5 min, and then jugular venous blood was collected for blood lactate assays.

After inspection of the scatter plots of the relationships between blood lactate concentration and velocity for data from each racetrack, regression analyses were conducted to describe the line of best fit. Figure 3.12 shows the relationship between blood lactate after field exercise and exercise velocity on a sand racetrack in 21 trained Thoroughbred race horses.[36] The variability of the velocity during the exercise tests was expressed as the coefficient of variation (CV) of the

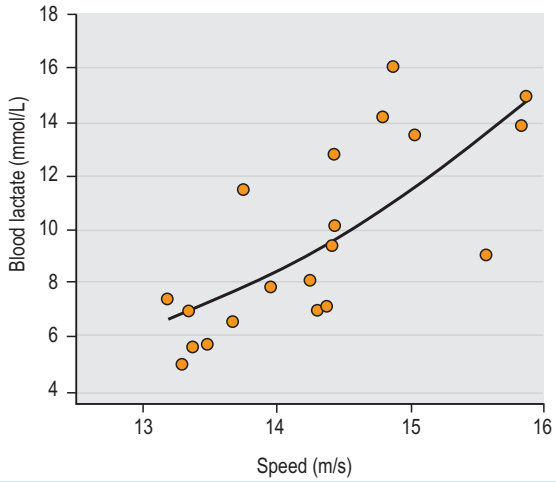


Fig. 3.12
Relationship between blood lactate concentration (mmol/L) after field exercise and velocity (m/s) during an 800 m exercise test on a sand racetrack in Thoroughbred horses. From Davie and Evans,[36] with permission.

times for the four 200 m sections of the exercise test. In horses tested more than once the result from the exercise test with the lowest CV was used in the regression analysis. Exercise tests were conducted at velocities in the range 13.2 to 15.9 m/s, and resulted in post-exercise blood lactate concentrations in the range 5.0 to 16.1 mmol/L. The mean speeds of the four consecutive 200 m sections of the exercise tests on the sand racetrack were 13.5, 14.6, 14.5, and 14.9 m/s. The jockeys were clearly unable to maintain a constant speed during the 800 m test.

A single step test that takes into account variability of velocity within a test, and is based on calculation of the difference between the measured and predicted lactate concentration, has potential application in field evaluations of fitness in Thoroughbred horses. Further studies are required to investigate whether the difference between the blood lactate response to exercise in an individual horse and the predicted concentration in a reference population is an accurate and reliable correlate of racing performance. Changes in this difference could also reflect changes in fitness over time.

The use of the difference between the measured and predicted lactate concentration as an index of the lactate response to exercise obviates the need for strict control over the target speed during the conduct of a field exercise test. Potentially it could be possible to conduct tests at any speed in an appropriate range, and compare the measured lactate concentration with the predicted concentration based on the equation for the line of best fit. This approach enables horses to be tested at different speeds, and comparisons between individual responses to exercise can be based on the rating. Superior English Thoroughbred race horses had a low blood lactate response to a single bout of exercise.[33] Therefore it could be expected that horses that consistently give a high 'rating' (that is, a high positive difference between measured and the predicted lactate concentration) could be expected to race poorly. Superior training in an individual horse should reduce the difference between measured and expected blood lactate concentrations.

The validity of results could be improved with some refinement of the technique. Accuracy and reliability of measurements could be improved if velocity did not increase during the exercise test. Anxiety or fear could also contribute to the variance, and these factors may not always be easy to recognize. The confounding effect of increases in speed may be more important in field tests that measure blood lactate concentration than in tests that measure heart rate, because the increase in speed can be related to the higher heart rate when the data are analyzed, as demonstrated in a study with Thoroughbred horses.[17]

A simple field exercise test for event horses has been described.[37] In this test, horses warmed up with 5 minutes of walking and then 6 minutes of trotting. Horses then galloped 400 m, 500 m, 600 m and 700 m/min over 1000 m with 5 min walking between these steps. This format enabled measurement of heart rates and blood lactate concentrations at each velocity of the exercise test, and calculation of V200 and VLa4. Such a test also assists horse trainers because it enables calculation of the velocity needed to train horses at a predetermined heart rate or blood lactate concentration.

A field exercise test with three steps was used with eight French Thoroughbred horses in France to investigate the use of heart rate measurements during and after track exercise as a suitable measure of changes in fitness.[38] The test consisted of a warm-up followed by three 3 min steps, one cantering and two galloping, followed by a recovery period. Heart rate was recorded during the entire test, and blood samples were taken during the 2 min rest periods following each step, and after the recovery period for the measurement of lactate concentrations. Fitness was described by the relationships between lactate concentrations, heart rate and velocity. The authors concluded that the efficiency score and the cardiac recovery index were good indicators of potential speed.

Total red cell volume measurements

Total red cell volume expresses the volume of erythrocytes in the circulation of the horse, including the volume in the spleen. Its measurement with dye dilution methods necessitates measurement of plasma volume and the induction of splenic contraction before the hematocrit (PCV) is measured, so that red cells sequestered in the spleen at rest are also measured. Splenic contraction has been induced by adrenaline (epinephrine) injections and moderately intense exercise.[39] Total red cell volume relative to bodyweight was significantly correlated with maximal trotting speed over 1000 m in 35 Swedish trotters ($r = 0.68$, $P < 0.001$).[40] These results suggest that this measurement is an important factor in the ability to trot rapidly, but there have been no studies of the relationship in other breeds. Unfortunately measurement of the total red cell volume in horses with a dye dilution

technique is not a simple procedure that can be readily applied in veterinary practice.

The hematocrit after maximal exercise in Thoroughbreds, which ranges from 60 to 70%, was not correlated with Timeform rating (a commercial measurement of relative racing ability) in English Thoroughbreds. It is not a valid fitness measurement.[33] However, the hematocrit can be measured after maximal exercise if results of resting hematology suggest that a horse is anemic. PCV should be greater than approximately 55% immediately after maximal exercise in trained Thoroughbreds. In Standardbred race horses overtraining was associated with a decrease in PCV measured after a 2400 meter time trial at maximal speed. Mean values were 56% in control horses and 52% in overtrained horses.[41] Total red cell volume did not decrease during overtraining, so the decrease in PCV may have reflected the decrease in velocity of the horses during the time trial, rather than a true decrease in the total red cell volume. A treadmill study has also found that onset of overtraining was not associated with red cell hypervolemia.[42]

Measurements of the hormonal response to intense exercise may be more useful for identifying the overtrained horse. Overtraining was associated with a decrease in the cortisol concentration measured after a maximal field exercise test in Standardbred pacers.[41] The exercise test consisted of 1200 meters pacing in 105 seconds, and then completion of the following 1200 meters in the fastest time possible. A decreased cortisol response to maximal exercise in the overtrained state was also found in a treadmill study of Standardbred horses.[43] The mean peak cortisol concentrations after intense treadmill exercise were 320 nmol/L before overtraining, and had decreased to 245 nmol/L when horses were overtrained. Overtraining should be suspected in horses with evidence of decreased performance in association with decreased bodyweight and plasma cortisol response to a standardized maximal or near-maximal velocity exercise.

Measurement of oxygen uptake in field exercise

Oxygen uptake is a fundamental measurement in any exercise test. It describes the rate of oxygen use in liters per minute, and is usually expressed relative to body mass. Calculation of oxygen uptake in the field necessitates measurements of air flow rates during breathing, and of oxygen and carbon dioxide concentrations in expired respiratory gas. The horse must wear a mask over its nose or face to enable these measurements. The technique is referred to as ergospirometry. In horses during maximal exercise, respiratory rates often exceed 120 per minute, and over 1500 liters of air are breathed per minute, at peak flow rates of 30–40 L/s or more at each nostril. Measurement of breathing (minute ventilation) and expired gas concentrations during intense exercise in horses is obviously a considerable technical problem, especially in the field.

Rates of oxygen uptake during submaximal exercise will depend on gait, economy of locomotion, body mass, and other factors. The maximal rate of oxygen uptake is the gold standard measurement for aerobic capacity. It is primarily limited by the maximal heart rate and cardiac stroke volume during exercise. A cardiac limit to performance can be best evaluated by measurement of oxygen pulse, the volume of oxygen ejected with each ventricular contraction. This measurement necessitates simultaneous measurement of oxygen uptake and heart rate during exercise.

A landmark study of heart rate, breathing and oxygen uptake in two trotters was conducted in Russia.[44] A truck carried equipment beside the trotting horses, which completed a stepwise exercise test with peak speeds of 11 m/s. Notable findings during exercise at 11 m/s were tidal volumes of 17 liters, pulmonary ventilation of 1200 L/min, and peak oxygen uptake of 64 L/min with a respiratory exchange ratio of 1.0.

The horse plus vehicle approach to field ergometry was also used in a study of four Quarter horses, one Appaloosa and one Thoroughbred at speeds ranging from 40 to 390 m/min, with and without a rider.[45] A tractor was used to pull a wagon, and on the wagon were the calorimeter and a gasoline generator. This study was conducted to enable calculation of the digestible energy intake needed to support the demands of exercise.

Field ergospirometry was described in 23 riding horses at a walk, trot and gallop, using an on-board oxygen sensor.[46] The key measurements of an ideal clinical exercise test were reported: heart rate, oxygen uptake, pulmonary ventilation, ventilatory equivalent for oxygen, oxygen pulse and economy of locomotion. The synchrony of stride and locomotion was noted, as was the transitory effect of swallowing on breathing. The limitation of the performance of the pneumotachometer and response times of the oxygen sensor probably precluded measurements at maximal speeds.

Field ergospirometry and blood lactate measurements were conducted in 12 Warmbloods in order to calculate the ratios of aerobic and anaerobic contributions to total energy output at speeds up to approximately 500 m/min.[47] Aliquots of expired gas were collected via tubes in the face mask, and the rider manipulated the bags that were used to collect the gas at each step of the exercise test. Oxygen debt was calculated from the oxygen uptake measurements made for 10 minutes after exercise, minus values before exercise. This value was referred to as the anaerobic contribution to energy output. It was reported that the percentages of energy expenditure that were anaerobic were 1%, 3%, 19%, and 30% at speeds of 100, 250, 350, and 530 m/min. This technology has not yet reported measurement of maximal oxygen uptake.

Breath-by-breath pneumotachography for clinical appraisal during field tests of ridden horses has made little progress in the last 20 years. A major technical challenge remains: specifically simultaneous measurement of heart rate, oxygen uptake and pulmonary ventilation during submaximal and maximal field exercise. Coupling of measurements of heart rate, breathing (pulmonary ventilation) and oxygen uptake during field

exercise will be a powerful technique for advancing knowledge in equine exercise physiology.

Tracheal stethoscopy

The use of tracheal stethoscopy in the field for the investigation of respiratory sounds in the horse has been described.[48] This technique has been used for the investigation of upper respiratory conditions such as idiopathic laryngeal hemiplegia. The technique has existed for many years, but has yet to find a place in routine clinical exercise testing in the field.

Conclusion

Heart rate and blood lactate measurements during standardized field exercise tests are relevant to the management of all athletic horses. These measurements can assist with performance prediction and evaluation of fitness changes, and can be used to alert owners and trainers to problems such as lameness and respiratory disease. More effort is needed to adapt new technologies and refine approaches to design of field exercise tests. It is unlikely that veterinarians, trainers or owners will be enthusiastic about equine fitness testing if the focus is not on simple approaches to field exercise tests. Simple tests, measuring the things that matter, is the approach in field studies in human sports laboratories. Heart rate and blood lactate measurements feature prominently in human field studies. Progress in technology transfer of applied exercise physiology might be greater if there was greater emphasis on field methods, using minimally invasive techniques. Every fitness test should answer a specific question, and results should be expressed in a way that helps a veterinarian, trainer or owner make more informed decisions about the training, fitness, health or management of horses.

A promising new technique for field fitness tests could be use of heart rate measurements in combination with measurement of velocity with differential global position system technology. Simultaneous logging of a horse's heart rate and velocity could be a powerful technique for field exercise tests.

The reliance on treadmills for most equine exercise research may have contributed to poor rates of technology transfer to equine veterinarians, trainers and horse owners. There are few established equine performance laboratories in the world, and many are located at considerable distances from racing populations. There will never be enough university-based treadmills to service all horses with sufficient facilities for fitness tests. Development of simple and user-friendly techniques for exercise studies of horses that do not depend on treadmills would therefore be a major advance.

New partnerships between equine exercise scientists and biomedical engineers could also generate new technologies for field studies. For example, field studies of breath-by-breath respiratory gas flows, and field ergometry, should be possible, building on the innovative studies performed in Germany.[18,46] The techniques for field ergomety have been developed for human athletes, and could be refined for use in horses. However, the technical challenge of reliably and accurately measuring respiratory flow rates of over 100 L/s in a horse galloping in the field at 1000 m/min has yet to be conquered. Field ergometry, coupled with measurements of heart rate, respiratory function and metabolic responses to exercise, would enable new fundamental studies in many areas of equine exercise physiology. Descriptions of the metabolic and energetic demands of different athletic events would be possible, and design of appropriate training programs would be facilitated. As well, clinical exercise testing would be more likely to be adopted by trainers and owners. Such 'high tech' clinical exercise tests would contribute to greater knowledge concerning limits to performance in different events (such as anaerobic or aerobic capacity, and maximal rates of oxygen uptake). Greater rates of technology transfer to industry participants are likely if researchers increase their use of normal horses in commercial training, and if technical developments free researchers from the constraints and limitations of treadmill fitness tests.

References

1. King CM, Evans DL, Rose RJ. Acclimation to treadmill exercise. Equine Vet J 1995; Suppl 18:453–456.
2. Gottlieb-Vedi M, Lindholm A. Comparison of standardbred trotters exercising on a treadmill and a race track with identical draught resistances. Vet Rec 1997; 140:525–528.
3. Couroucé A, Geffroy O, Barrey E, et al. Comparison of exercise tests in French trotters under training track, racetrack and treadmill conditions. Equine Vet J 1999; Suppl 30:528–531.
4. Sloet van Oldruitenborgh-Osterbaan M, Barneveld A. Comparison of the workload of Dutch warmblood horses ridden normally and on a treadmill. Vet Record 1995; 137:136–139.
5. Barrey E, Galloux P, Valette JP, et al. Stride characteristics of overground versus treadmill locomotion in the saddle horse. Acta Anat 1993; 146:90–94.
6. Kronfeld DS, Custalow SE, Ferrante PL, et al. Determination of the lactate breakpoint during incremental exercise in horses adapted to dietary corn oil. Am J Vet Res 2000; 61:144–151.
7. Hargreaves BJ, Kronfeld DS, Naylor JRJ. Ambient temperature and relative humidity influenced packed cell volume, total plasma protein and other variables in horses during an incremental submaximal field exercise test. Equine Vet J 1999; 31:314–318.
8. Banister EW, Purvis AD. Exercise electrocardiography in the horse by radiotelemetry. J Am Vet Med Assoc 1968; 152:1004–1008.
9. Marsland WP. Heart rate response to submaximal exercise in the Standardbred horse. J Appl Physiol 1968; 24:98–101.
10. Asheim A, Knudsen O, Lindholm A, et al. Heart rates and blood lactate concentrations of Standardbred horses during training and racing. J Am Vet Med Assoc 1970; 157:304–312.
11. Hall MC, Steel JD, Stewart GA. Cardiac monitoring during exercise tests in the horse. 2. Heart rate responses to exercise. Aust Vet J 1976; 52:1–5.

12. Steel JD, Hall MC, Stewart GA. Cardiac monitoring during exercise tests in the horse. 3. Changes in the electrocardiogram during and after exercise. Aust Vet J 1976; 52:6–10.
13. Senta T, Smetzer DL, Smith CR. Effects of exercise on certain electrocardiographic parameters and cardiac arrhythmias in the horse. A radiotelemetric study. Cornell Vet 1970; 60:552–569.
14. Krzywanek H, Wittke G, Bayer A, et al. The heart rates of thoroughbred horses during a race. Equine Vet J 1970; 2:115–117.
15. Hörnicke H, Engelhardt WV, Ehrlein H-J. Effect of exercise on systemic blood pressure and heart rate in horses. Pflugers Arch 1977; 372:95–99.
16. Serrano MG, Evans DL, Hodgson JL. Heart rate and blood lactate concentrations in a field fitness test for event horses. Aust Equine Vet 2001; 19:154–161.
17. Kobayashi M, Kuribara K, Amada A. Application of V200 for evaluation of training effects in the young Thoroughbred under field conditions. Equine Vet J 1999; Suppl 30:159–162.
18. Hörnicke H, Weber M, Schweiker W. Pulmonary ventilation in thoroughbred horses at maximum performance. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications, 1987:216–224.
19. Pollmann U, Hörnicke H. Characteristics of respiratory airflow during exercise in horses with reduced performance due to pulmonary emphysema or bronchitis. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications, 1987:760–771.
20. Wilson RG, Isler RB, Thornton JR. Heart rate, lactic acid production and speed during a standardised exercise test in Standardbred horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions, 1983:487–496.
21. Roneus N, Essen-Gustavsson B, Lindholm A, et al. Muscle characteristics and plasma lactate and ammonia response after racing in Standardbred trotters: relation to performance. Equine Vet J 1999; 31:170–173.
22. Couroucé A, Chatard JC, Auvinet B. Estimation of performance potential of standardbred trotters from blood lactate concentrations measured in field conditions. Equine Vet J 1997; 29:365–369.
23. Couroucé A. Field exercise testing for assessing fitness in French standardbred trotters. Vet J 1999; 157:112–122.
24. Couroucé A, Chrétien M, Valette JP. Physiological variables measured under field conditions according to age and state of training in French trotters. Equine Vet J 2002; 34:91–97.
25. Davie AJ, Priddle TL, Evans DL. Metabolic responses to submaximal field exercise tests and relationships with racing performance in pacing Standardbreds. Equine Vet J 2002; Suppl 34:112–115.
26. Snow DH, Harris RC, Gash SP. Metabolic response of equine muscle to intermittent maximal exercise. J Appl Physiol 1985; 58:1689–1697.
27. Littlejohn A, Snow DH. Circulatory, respiratory and metabolic responses in Thoroughbred horses during the first 400 metres of exercise. Eur J Appl Physiol 1988; 58:307–314.
28. Saibene F, Cortilli G, Gavazzi P, et al. Maximal anaerobic (lactic) capacity and power of the horse. Equine Vet J 1985; 17:130–132.
29. Schuback K, Essén-Gustavsson B. Muscle anaerobic response to a maximal treadmill exercise test in Standardbred trotters. Equine Vet J 1998; 30:504–510.
30. Evans DL, Rainger JE, Hodgson DR, et al. The effect of intensity and duration of training on blood lactate concentrations during and after exercise. Equine Vet J 1995; Suppl 18:422–425.
31. Hinchcliff KW, Lauderdale MA, Dutson J, et al. High intensity exercise conditioning increases accumulated oxygen deficit of horses. Equine Vet J 2002; 34:9–16.
32. Krzywanek H. Lactic acid concentrations and pH values in trotters after racing. J South Afr Vet Assoc 1974; 45:355–360.
33. Evans DL, Harris RC, Snow DH. Correlation of racing performance with blood lactate and heart rate in Thoroughbred horses. Equine Vet J 1993; 25:441–445.
34. Evans DL, Priddle TL, Davie AJ. Plasma lactate and uric acid responses to racing in pacing Standardbreds and relationships with performance. Equine Vet J 2002; Suppl 34:131–134.
35. Vonwittke P, Lindner A, Deegen E, et al. Effects of training on blood lactate running speed relationship in Thoroughbred racehorses. J Appl Physiol 1994; 77:298–302.
36. Davie AJ, Evans DL. Blood lactate responses to submaximal field exercise tests in thoroughbred horses. Vet J 2000; 159(3):252–258.
37. Muñoz A, Riber C, Santisteban R, et al. Investigation of standardized exercise tests according to fitness level for three-day event horses. J Equine Vet Sci 1998; 9:1–7.
38. Valette JP, Heiles PH, Wolter R. Multivariate analysis of exercise parameters measured during the training of thoroughbred racehorses. Pferdeheilkunde 1996; 12:470–473.
39. Persson SGB. On blood volume and working capacity in horses. Acta Vet Scand 1967; Suppl 19:1–189.
40. Persson SGB, Ullberg LE. Blood volume in relation to exercise tolerance in trotters. J South Afr Vet Assoc 1974; 45:293–299.
41. Hamlin MJ, Shearman JP, Hopkins WG. Changes in physiological parameters in overtrained Standardbred racehorses. Equine Vet J 2002; 34:383–388.
42. Golland LC, Evans DL, McGowan CM, et al. Effects of overtraining on blood volumes in Standardbred racehorses. Vet J 2003; 165:228–233.
43. Golland LC, Evans DL, Stone GM, et al. Plasma cortisol and B-endorphin concentrations in trained and overtrained Standardbred racehorses. Pflugers Arch 1999; 439:11–17.
44. Karlsen GG, Nadaljak EA. Gas and energy exchange in breathing of trotters during exercise (in Russian). Konevodstvo I Konesport 1964; 34:27–31.
45. Pagan JD, Hintz HF. Energy expenditure in horses during submaximal exercise. Proceedings of the 9th Equine Nutrition and Physiology Symposium 1985:182–187.
46. Hörnicke H, Meixner R, Pollmann U. Respiration in exercising horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:7–16.
47. Hanak J, Jahn P, Kabes R, et al. A field study of oxygen consumption and estimated energy expenditure in the exercising horse. Acta Vet Brno 2001; 70:133–139.
48. Attenburrow DP. The development of a radio stethoscope for use in the horse at rest and during exercise. Equine Vet J 1978; 10:14–17.

CHAPTER 4

Clinical exercise testing: overview of causes of poor performance

Ben B. Martin, Jr, Elizabeth J. Davidson, Mary M. Durando and Eric K. Birks

Introduction

Determining the cause of poor performance in equine athletes is difficult because many of the problems that cause poor performance are manifested only at medium- or high-speed exercise, and horses with poor performance may have multiple concurrent problems.[1,2] Comprehensive testing is often necessary to ascertain the definitive cause of poor performance. Traditional methods of evaluating horses with poor performance include performing a complete physical examination, a thorough lameness evaluation, and various clinicopathologic tests. However, the development of techniques for performing videoendoscopy during high-speed treadmill (HSTM) exercise, using telemetry to record exercising electrocardiograms, arterial blood gas sampling during exercise, post-exercise tracheal wash or bronchoalveolar lavage sampling for cytologic evaluation, and performing echocardiography immediately post-exercise, have combined to add a new dimension to the examination of horses with poor performance.[2–7] It is well known that multiple body systems may contribute to performance problems, including abnormalities of the upper respiratory tract, lower respiratory tract, cardiovascular, and musculoskeletal systems, as well as subclinical myopathies.[7]

Chapter 2 provided an overview of the diagnostic approach to poor performance in the horse, including the use of treadmill exercise testing. The purpose of this chapter is to describe the more common causes of poor athletic performance in the horse. The reader is referred to other chapters in this book for more complete description of the diagnosis and treatment of the conditions discussed.

Upper respiratory tract

Laryngeal hemiplegia (LH)

History

The most common complaints associated with LH are exercise intolerance and a high frequency inspiratory noise. Horses with LH are more commonly affected on the left side.[1,2] These horses typically have a grade III or grade IV LH, using the grading system previously published.[8]

Physical and videoendoscopic examination

Palpation of the larynx may be informative, as the muscular process can frequently be palpated secondary to atrophy of the cricoarytenoid dorsalis muscle. On resting endoscopic

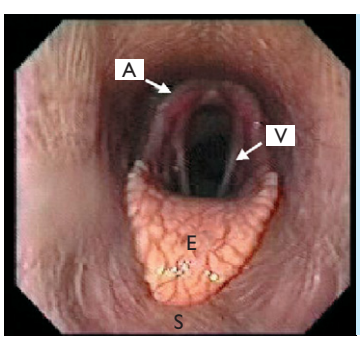


Fig. 4.1
Normal endoscopic appearance of pharyngeal and laryngeal structures. E, epiglottis; S, pharyngeal surface of the soft palate; A, right arytenoid cartilage; V, left vocal fold.

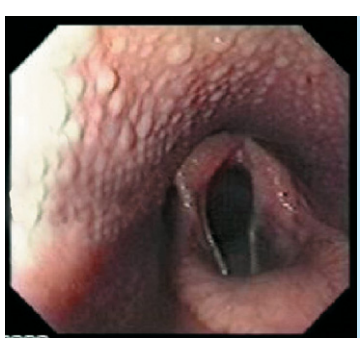


Fig. 4.2
Endoscopic appearance of pharyngeal and laryngeal structures of a horse at rest with grade III left laryngeal hemiplegia.

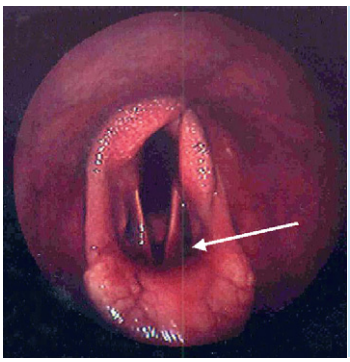


Fig. 4.3
Endoscopic view of pharyngeal and laryngeal structures of a horse 60 minutes post-exercise with grade IV laryngeal hemiplegia. Note frank hemorrhage suggestive of acute exercise-induced pulmonary hemorrhage (EIPH) (arrow).

evaluation, the arytenoid may be paralyzed or hang slightly in the airway (Figs 4.1–4.3). These horses are good candidates for treadmill evaluation because function during strenuous exercise helps to select the patients in which surgical correction is most likely to be successful.[8]

Treatment

Surgical intervention is the treatment of choice for LH when the arytenoid collapses into the airway (grade IIIC, grade IV). This may include placement of a prosthesis alone, or in combination with a ventricular saculectomy or cordectomy.[9,10] Surgical correction of grade II or IIIA or B is most often unsuccessful. Ideal surgical candidates are those with either grade IIIC or grade IV LH. Reported surgical success rate for grade IIIA and IIIB is 20–25%, versus 70–75% for grade IIIC and grade IV.[3] Horses with incomplete collapse of the affected arytenoid should continue to race or train until they become a grade III or IV. Attempts at cutting the recurrent laryngeal nerve in horses with partial collapse of the arytenoid to hasten progression to grade III or IV have met with limited success.

Prognosis

Treatment of uncomplicated LH carries a good prognosis for return to work and decrease in exercise intolerance, although some horses will continue to make an abnormal respiratory noise.[10]

Retroversion of the epiglottis

History

Horses have a history of significant exercise intolerance and of making a very loud gurgling, honking noise at medium to high speed.[11,12] This condition is uncommon, occurring in only 10 of 2100 horses examined at the University of Pennsylvania, New Bolton Center between 1992 and 2002.

Videoendoscopic examination

The resting videoendoscopic examination is usually normal, while videoendoscopy during exercise reveals an epiglottis that curls up in the center and rises directly dorsally to occlude most of the airway during inspiration (Fig. 4.4). There is a characteristic inspiratory noise.

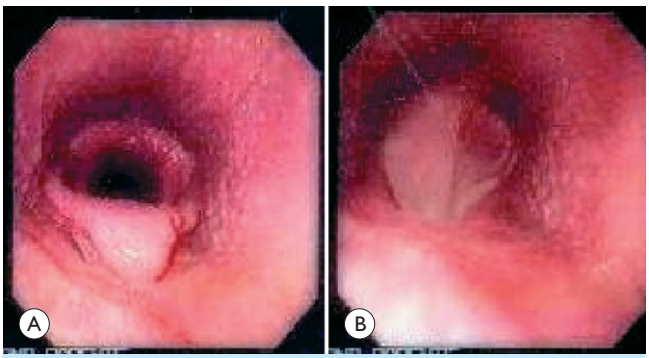


Fig. 4.4
Endoscopic view showing retroversion of the epiglottis during high-speed treadmill exercise upon exhalation (A) and inhalation (B).

Treatment

Several surgical treatments have been attempted including epiglottectomy, augmentation of the epiglottis, and placement of a suture to mimic the genio-hyoideus muscle.[11] The latter appears to have some promise, while the first two techniques have not been useful in the management of this condition.

Prognosis

The prognosis for return to previous performance ability is poor. Horses may, however, be used as pleasure horses that exercise at low to medium intensity.

Dorsal displacement of the soft palate (DDSP)

History

Most horses have a history of racing well for three-quarters of a mile, making an expiratory gurgling noise and slowing down rapidly. These two historical facts lead many clinicians to make a presumptive diagnosis of DDSP. Endoscopic examination immediately after racing or training is usually unrewarding. DDSP is the most common pharyngeal dysfunction in racing horses. Sport horses may also be hindered with DDSP. Retrospective analysis of 80 sport horses presented for poor performance identified this abnormality in six horses.[12]

Videoendoscopic examination

Resting videoendoscopy may be normal or suggestive of a problem. Examination of the pharynx during occlusion of the nostrils can provide useful diagnostic information. In particular, the time taken for the palate to displace and then return to its normal position should be noted. Prolonged displacement is suggestive of DDSP. After the endoscope has

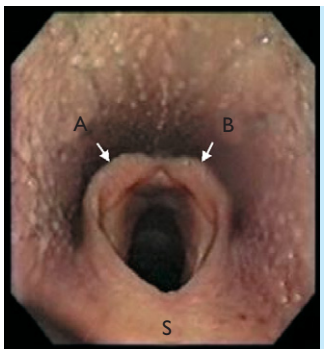


Fig. 4.5
Endoscopic view of a dorsally displaced soft palate (DDSP) at rest. The pharyngeal surface of the soft palate (S) and the arytenoid cartilages (right, A; left, B) are shown.

been removed from the trachea during examinination for tracheal mucus or blood, horses will frequently displace and then quickly replace the palate. This examination often provides an opportunity to examine the free border of the palate for ulcers or evidence of a previous surgery (notch or scar). Some practitioners feel that there is an association between an ulcer of the soft palate free border and DDSP during high-speed exercise. However, this is not a consistent finding in horses subjected to treadmill evaluation. DDSP (Fig. 4.5) may or may not be evident during a single exercising videoendoscopic examination; exercise to fatigue may be necessary to demonstrate the abnormality in some horses. Thirty to thirty-eight percent of horses may not make a respiratory noise during displacement, making diagnosis difficult.[5,13] DDSP can occur alone or in combination with other abnormalities. In one study, when DDSP occurred it was observed alone in 49% of horses and combined with at least one other abnormality in 51% of horses.[13]

Treatment

Surgical intervention is usually recommended when conservative management treatments, such as a tongue-tie, figure eight nose band, overcheck, can, spoon bit or anti-inflammatory throat sprays, have been unsuccessful. Various surgical interventions have been used in the treatment of DDSP, including radical myectomy,[14] sternothyroideus myotomy,[15] sternothyrohyoideus myectomy,[16] or staphylectomy,[17] with success reported to be 60–64%.[13–17] Because DDSP frequently occurs with other upper respiratory tract (URT) diseases, it is imperative that other upper respiratory conditions be identified and treated.[1,13]

Prognosis

The prognosis is guarded for successful return to athletic performance.

Axial deviation of the aryepiglottic folds (ADAF)

History

Horses with ADAF have a history of exercise intolerance and usually make a medium frequency, inspiratory noise during

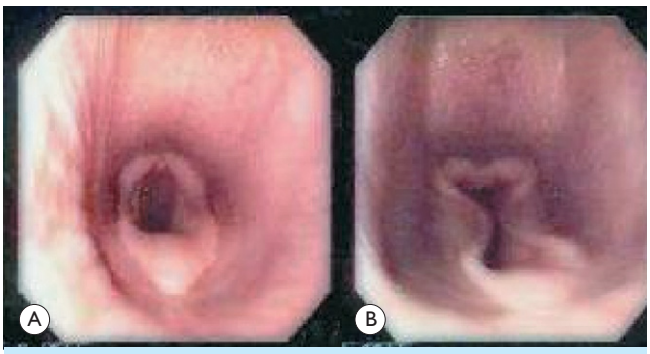


Fig. 4.6
Endoscopic view of axial deviation of aryepiglottic folds (ADAF) during high-speed treadmill exercise during exhalation (A) and inhalation (B).

exercise. ADAF occurs only at high speed and is characterized by axial collapse of the membranous fold extending between the corniculate process of the arytenoid cartilage and the lateral edge of the epiglottis (Fig. 4.6).[18] Some consider that ADAF represents a manifestation of the dysfunction that results in intermittent dorsal displacement of the soft palate (DDSP), but this remains uncertain.[18] ADAF occurred in 6% of cases examined videoendoscopically during a high-speed treadmill examination, and when ADAF was observed, it occurred alone in 64% of horses and in combination with another upper airway abnormality in 36% of horses.[1,18]

Videoendoscopic examination

Resting videoendoscopy is usually normal. Exercising videoendoscopic examination reveals collapse of the aryepiglottic folds (Fig. 4.6) alone or in combination with other URT abnormalities.

Treatment

Trans-endoscopic laser resection of the aryepiglottic folds is considered to be the treatment of choice.[18] Seventy-five percent of horses that received laser resection of the aryepiglottic folds successfully returned to racing 3 weeks to 3 months following treatment. However, with conservative treatment consisting of 2–12 months' rest, 50% of the horses in a recent study returned to successful racing.

Prognosis

The prognosis is excellent in ADAF alone. The prognosis with combined abnormalities is dependent upon the specific abnormalities.

Pharyngeal collapse (PC)

History

Horses with PC have a history of moderate to severe exercise intolerance and a low frequency, raspy inspiratory or roaring

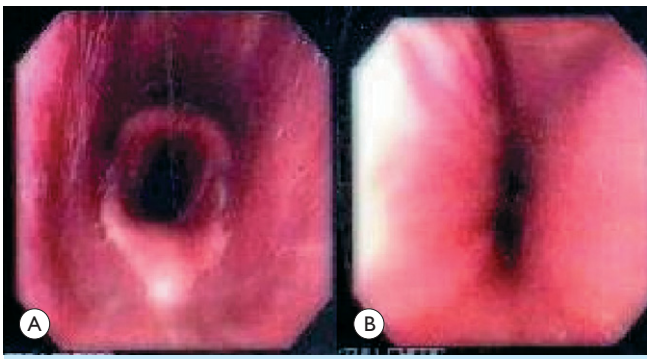


Fig. 4.7
Endoscopic view showing pharyngeal collapse (PC) during high-speed treadmill exercise. A, during exhalation, B, during inhalation.

noise. This abnormality has been identified in race horses[5] and sport horses,[12] and in 11.5% and 27% of horses completing a high-speed treadmill evaluation.

Videoendoscopic examination

As PC can only be identified during exercise,[5] a high-speed treadmill examination is required for diagnosis. Videoendoscopically, pharyngeal collapse can be classified as dorsal, lateral or circumferential (Fig. 4.7).[12] Severely affected horses struggle and it may be necessary to stop the test early. Elevated head and neck carriage such as that seen in Hackney ponies or American Saddlebreds can further increase the severity of PC.

Treatment

Conservative management of long-term rest (4–6 months), non-steroidal anti-inflammatory medication and a short course of oral corticosteroids may be successful in young, immature horses. The disease is most often career-ending in older (> 3 years old) race horses and sport horses. In horses that are maximally collected or have significant flexion of the neck during exercise (Hackneys, American Saddlebreds) it may be necessary to change careers.

Prognosis

In moderate to severe cases, the prognosis for any type of strenuous performance is poor. In rare instances, a young horse may mature out of the problem. In older horses, return to prior function is unlikely.

Lower respiratory tract

Lower respiratory tract (LRT) diseases can affect horses of any breed or discipline. In performance horses, exercise-induced pulmonary hemorrhage (EIPH) and inflammatory airway disease (IAD) are the two most common LRT diseases.[19] EIPH has been reported in 60–100% of performance horses.[19,20] IAD has been reported in 20–76% of horses receiving an endoscopic examination and transtracheal aspirate[21] or tracheal wash via the endoscope.[19] Certainly, many other LRT diseases/abnormalities are observed in horses. However, most of these are associated with generalized illness rather than non-specific complaints of 'poor athletic performance'.

History

Signs of EIPH can include epistaxis (rarely) after exercise[22] or, quite commonly, blood observed in the trachea post-exercise.[23–26] Coughing, increased swallowing, and/or prolonged recovery from exercise may occur following EIPH, but most often no signs are apparent. Signs of IAD in race horses (generally younger athletic animals subject to bouts of intense exercise) include coughing, mucus accumulation in the airways, exercise intolerance, prolonged recovery from exercise, nasal discharge, and worsening of signs when the weather is very hot, humid or cold. Perhaps the most common sign of IAD is exercise intolerance with or without other signs of respiratory disease.[27] Horses often have a history of fading at the 3/4 pole or in the home stretch.[27] EIPH and IAD may exist separately or together, and may occur with or without URT and/or cardiac dysfunction.

Physical examination

Often there are no abnormal findings during a resting physical examination. Horses with EIPH or IAD may or may not have abnormal lung sounds and a cough may or may not be elicited in horses with IAD. Some horses with a history of sudden, profuse epistaxis have been shown to have atrial fibrillation. Careful auscultation of the heart must be performed as a number of cardiac abnormalities can cause or exacerbate pulmonary problems.

Diagnostic tests

Both EIPH and IAD are best evaluated endoscopically following exercise. Blood visualized in the trachea and/or bronchi, or erythrocytes in tracheal or bronchoalveolar lavage (BAL) fluid, indicate EIPH. Although not directly diagnostic, visualization of large quantities of mucus in the airways is generally considered suggestive of IAD.[19,27]

Cytologic evaluation of samples obtained from the trachea or lower airways can often be of use in diagnosing pulmonary abnormalities. Lavage fluid may be collected from the trachea percutaneously or via an endoscope (transtracheal wash: TTW) or from the bronchial-alveolar regions (BAL). The ideal time for collecting post-exercise TTW and/or BAL samples is still debated, but most studies indicate that samples collected 45–90 minutes following exercise are the most suitable.[28] Numerous erythrocytes, in the absence of trauma, in lavage fluid (either TTW or BAL) indicate acute EIPH.[29] Hemosiderophages in lavage fluid indicate previous bleeding into

the airways, and, in horses in active competition, this finding is considered indicative of previous (in the past 1–21 days) episodes of EIPH.[19]

Normal values for differential cytologic evaluation of TTW and BAL fluids are presented in Chapter 2. Although the interpretation of differential cytologies in samples of lung fluid is still debated, an increase in the number or percentage (> 30%) of neutrophils is considered suggestive of IAD.[19,27]

As outlined in Chapter 2, systemic arterial blood samples can be used to evaluate lower airway function, as well as the functional significance of abnormalities in other body systems. While not specifically indicative of lung abnormalities, taken in conjunction with other clinical data, arterial blood gases can be of clinical importance and aid in diagnosis. It is important to keep in mind that arterial oxygen partial pressure (Pa_{O_2}) significantly lower than expected during exercise can occur not only from altered lower airway gas exchange, but also from reduced ventilation secondary to upper airway obstructions. Similar caveats are necessary when evaluating other arterial blood parameters. Thus, arterial blood gas values must be interpreted in light of results from the diagnostic tests pertaining to other body systems.[30]

Treatment

Treatment for EIPH has included the use of environmental management, pre-race administration of furosemide (frusemide), vitamin C, conjugated estrogens, vasodilators, and nasal strips. The effect of any of these treatments on EIPH remains controversial.[20,23] Treatment for IAD has two goals. The first is to decrease inflammation and the second is to increase the diameter of the distal airways. These goals are accomplished via the administration of inhaled corticosteroids and bronchodilators. These medications may be administered using several metered dose inhaler (MDI) systems (Equine AeroMask, Torpex, and the Equine Haler). The most versatile of these is the AeroMask, as it can deliver medication via MDI devices, nebulizer solution or dry powder inhaler. The Torpex device presently is used only to deliver albuterol sulfate. The Equine Haler can deliver any aerosolized drug using human MDI devices.[31]

Prognosis

Recent reports suggest that EIPH occurs in most, if not all, race horses.[23] Thus, simply finding evidence of EIPH does not suggest a reduced prognosis for future performance. However, the effects of repeated episodes of EIPH have yet to be critically evaluated. The current supposition is that each episode of EIPH results in increased scarring of the lung, leading to reduced gas exchange potential and thus reduced athletic potential. At the present time, no data exist that directly demonstrate any chronic effects of EIPH on athletic performance. Although epistaxis has not been positively correlated with the severity of EIPH, the general perception is that epistaxis indicates severe EIPH. Horses in which repeated episodes of epistaxis have been observed are generally retired from athletic competition.

The prognosis for managing early-recognized IAD is good. Treatment with bronchodilators and local anti-inflammatory agents generally leads to successful return to previous athletic performance.

Cardiovascular system

Abnormalities of the cardiovascular system can have a significant adverse effect on athletic performance, primarily via a reduction in cardiac output. Although less commonly recognized than diseases affecting the respiratory or musculoskeletal system, with the advent of newer diagnostic techniques for evaluation of cardiac function during and immediately after exercise, cardiac diseases are being diagnosed more frequently.[1,32] It can be difficult to determine the cardiovascular contribution to exercise intolerance, as frequently horses can have no, or only very subtle abnormalities at rest, while displaying significant abnormalities at near maximal effort. Conversely, 'normal' horses can have a relatively high prevalence of both murmurs and dysrhythmias,[32–36] which may be physiologic, disappear with exercise, and not contribute to reduced performance. Therefore, the significance of these findings may be unclear. For this reason, as discussed in Chapter 2, an evaluation during exercise is critical. Abnormalities can be divided into disturbances in cardiac rhythm, systolic or diastolic dysfunction, valvular regurgitation, and intracardiac shunts.

Dysrhythmias

Atrial fibrillation

History

In general, dysrhythmias more commonly contribute to performance problems than other types of cardiac dysfunction, and atrial fibrillation is the most common dysrhythmia associated with poor performance. Atrial fibrillation (AF) can be paroxysmal or sustained, with paroxysmal being implicated frequently as a cause of poor racing performance.[37–39] Epistaxis has been associated with AF.[40] This may be due, in part, to the alterations in left atrial, and hence pulmonary arterial pressures.[39] Dyspnea, hyperpnea and severe exercise intolerance have also been associated with AF, which decreases maximum cardiac output (under strenuous exercise conditions) by reducing left ventricular filling.[41,42] Horses with either paroxysmal or sustained AF frequently have no underlying detectable cardiac pathology.[43] These horses are excellent candidates for conversion to sinus rhythm, and once converted, should return to their previous level of performance. The large atrial mass and high resting vagal tone contribute to the development of AF. Electrolyte abnormalities (particularly K^+ depletion) have also been associated with development of AF. Therefore it is very important to ascertain drug administration history, such as the use of loop diuretics (e.g. furosemide (frusemide)).

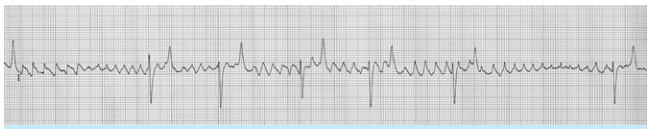


Fig. 4.8
Electrocardiogram (ECG) from a horse with atrial fibrillation. The ECG was obtained at rest and the heart rate was 50 beats/min. For all ECGs, a base apex lead system has been used, and paper speed is 25 mm/s.

Clinical findings and diagnosis

It is important to perform a complete cardiac evaluation of any horse in AF to determine the presence of underlying cardiac disease. Auscultation will reveal an irregular rhythm. Pulses will be irregular, of varying intensity, and pulse deficits may be palpated. If no underlying cardiac disease is present, heart rate will be within a normal range or only mildly elevated.[41] ECG will show an irregular R–R interval, no P waves, and fine to coarse fibrillation waves (Fig. 4.8).

Treatment and prognosis

The treatment of choice for uncomplicated AF is oral quinidine sulfate.[43] If the duration of AF is short (< 2 weeks) and no cardiac pathology exists, intravenous quinidine gluconate can be tried. Most horses without significant cardiac disease can be successfully converted to normal sinus rhythm. Although some horses revert back into AF, the likelihood of recurrence is higher in horses with AF of greater than 4 months' duration or those with evidence of underlying cardiac pathology.

Supraventricular and ventricular extrasystoles

History

Dysrhythmias other than AF, while less well recognized, can certainly decrease athletic capacity.[44,45] Both ventricular and supraventricular extrasystoles can decrease cardiac output, and thus maximal performance ability. Ventricular tachycardia (VT), defined as more than three consecutive ventricular extrasystoles, may be sustained or paroxysmal. While sustained VT is easily recognized, and has a clear-cut effect on performance, it might not be recognized on resting examination if it is paroxysmal and/or exercise-induced; however, these horses may demonstrate a sudden fall off in performance during a race. The influence on performance of premature depolarizations, whether supraventricular or ventricular in origin, can be more difficult to determine. When detected infrequently, and at rest, they are of questionable significance if they disappear with exercise. However, ectopic beats occurring during exercise interfere with normal cardiac function, and may be more significant.[32] If ectopic beats occur during maximal effort, or as the horse is speeding up or slowing down on the treadmill, they can decrease cardiac output enough to affect performance. Certainly, if ectopic beats are numerous there is likely to be an adverse effect on exercise performance. The immediate post-exercise period is a time of autonomic nervous system imbalance. Consequently, dysrhythmias, including occasional premature beats, are frequently observed during the post-exercise period. These dysrhythmias probably do not affect performance.

Clinical findings and diagnosis

If no rhythm disturbances are present at rest, the results of physical examination and electrocardiographic and echocardiographic tests may be normal. ECG examination during exercise is required to detect cardiac rhythm disturbances in these cases. If uniform VT is present at rest, a rapid, regular rhythm, with changes in intensity of heart sounds, will be ausculted. Pulse deficits may be present. A jugular pulse may be evident. Premature beats present at rest will be detected as occasional early beats, corresponding to the premature depolarizations. A compensatory pause may be heard after the premature beat if it is ventricular in origin, and pulse deficits may be present. The heart sounds may be variable in intensity, with the ectopic beat having an increased intensity. Paroxysmal VT present only during maximal exercise requires exercising telemetric ECG to diagnose. ECG will show abnormal QRS complexes occurring in a rapid regular rhythm. ECG findings associated with uniform VT include a series of abnormal, widened QRS complexes with a regular R–R interval (Fig. 4.9). P waves will not be associated with the QRS, and may not be visualized if buried in the preceding QRS–T complex. With premature depolarizations, the ECG will reveal an underlying regular rhythm, with occasional premature QRS complexes causing an irregular R–R interval. If the premature complexes are supraventricular in origin, the QRS complexes will typically be normal in appearance and a P wave will be seen associated with it, although the P–R interval may differ from others (Fig. 4.10). Usually there will

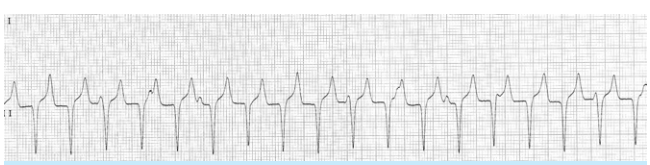


Fig. 4.9
Electrocardiogram from a horse with ventricular tachycardia. This horse was at rest with a heart rate of 120 beats/min. Note the P waves buried in differing portions of the QRS–T complex.

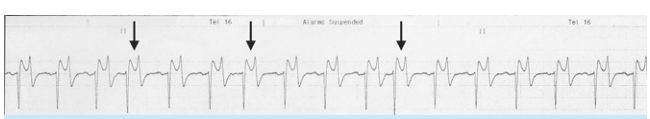


Fig. 4.10
Electrocardiogram (ECG) from a horse showing supraventricular premature depolarizations (SVPD; also known as atrial premature contractions, APC) (arrows). This ECG was obtained after exercise and the heart rate was 95 beats/min.

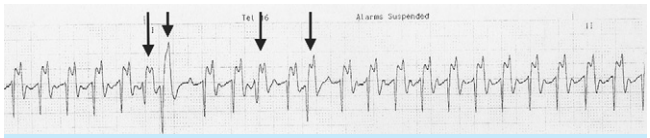


Fig. 4.11
Electrocardiogram (ECG) from a horse demonstrating ventricular premature depolarizations (VPD; also commonly called ventricular premature contractions, VPC) (arrows). Note compensatory pauses following VPD. This ECG was obtained immediately post-exercise and the heart rate was 160 beats/min.

not be a compensatory pause following the early beat. If the premature beat is ventricular in origin, the QRS complex will vary in configuration, and no P wave will be seen in association with it (Fig. 4.11). Ventricular premature depolarizations frequently are followed by a compensatory pause. While these arrhythmias may reflect primary myocardial disease, they may also be associated with hypoxemia, ischemia, electrolyte or metabolic disturbances, certain drugs, respiratory disease and toxemia.

Treatment and prognosis

Regardless of cause, rest for 4–8 weeks is recommended. Specific therapy is dependent on the type of dysrhythmia and whether underlying pathology is identified. In some cases of premature depolarizations, treatment with corticosteroids has been successful. If the premature complexes are frequent, anti-arrhythmic therapy can be instituted. Horses in VT may require specific anti-arrhythmic therapy along with correction of the primary problem.[44] Criteria for treatment include a sustained rapid rate (> 100 beats/minute), multifocal VT, R on T phenomenon, or if the horse is exhibiting clinical signs associated with the arrhythmia. Prognosis is favorable for most arrhythmias, if proper rest and correction of the underlying problem is accomplished.

Bradyarrhythmias

History and clinical findings

Severe bradyarrhythmias are not common. However, when present, they can cause weakness, syncope or profound exercise intolerance. Advanced second degree atrioventricular (AV) block, third degree AV block or sinus arrest not abolished by an increase in sympathetic tone or a decrease in parasympathetic tone are usually indicative of primary myocardial disease, although they are possibly associated with electrolyte or metabolic abnormalities.

Treatment and prognosis

Treatment consists of correcting the underlying cause, if one can be determined. Vagolytic drugs are not usually successful in restoring sinus rhythm. Corticosteroids may be used to decrease inflammation. However, the definitive treatment in most circumstances is a pacemaker. Although successfully used in horses, placement of a pacemaker is not practical in most instances.

Myocarditis/myocardial dysfunction

History

Clinical signs associated with myocarditis are dependent on the severity of the myocardial dysfunction, and can range from congestive heart failure with obvious clinical signs at rest, to subtle exercise intolerance that only manifests at maximal workloads.[32,46] Horses presenting with more severe cardiac dysfunction are not challenging to diagnose, as they are likely to have physical examination findings suggestive of heart failure, murmurs, and/or dysrhythmias. Horses with exercise-induced myocardial dysfunction are more difficult to diagnose, and may appear normal at rest, but may present with a history of fatigue and tiring early in a race.

Clinical findings and diagnosis

Clinical signs of congestive heart failure include a jugular pulse, ventral edema, tachypnea and rapid, weak pulses. Auscultation of these horses may reveal tachycardia with possible dysrhythmias and/or murmurs. Echocardiographic examination may demonstrate a moderate to severe decrease in fractional shortening, with chamber enlargement. If murmurs are present, Doppler examination may confirm valvular regurgitation. In horses that are less severely affected, the physical examination may be normal. The resting echocardiogram is also likely to be normal, or show only a mild decrease in the fractional shortening, with slightly less than normal thickening and inward motion of the myocardium. In these horses, it is critical to perform an exercise stress test to determine whether there is exercise-induced myocardial dysfunction.[32] Rather than the expected increase in fractional shortening, wall thickness, and inward wall motion, affected horses may have no change, or a decrease in these parameters (hypokinesis, dyskinesis, akinesis) immediately after high-intensity exercise.

Treatment and prognosis

Treatment of horses with exercise-induced myocardial dysfunction should include stall or pasture rest. If a non-infectious cause of myocarditis is suspected, corticosteroids may be useful. Prognosis is fair to good for return to function for these horses, with adequate rest.

Valvular regurgitation

Horses have a high prevalence of cardiac murmurs, many of which are physiologic or 'innocent' murmurs. However, even those associated with valvular regurgitation may not cause exercise intolerance unless the amount of regurgitation is moderate to severe. Mitral insufficiency is the abnormality

most likely to cause a decrease in athletic ability because of resultant left atrial enlargement and elevation in pulmonary artery pressure. Horses can successfully compete with significant tricuspid and aortic insufficiency unless accompanied by other abnormalities such as chamber enlargement, dysrhythmias, and mitral regurgitation.[33]

Ventricular septal defects

The effect on performance of ventricular septal defects (VSD) depends on the size, number, location, and type of work the horse must do. A small restrictive VSD might not impair performance at all, whereas a large one might decrease not only athletic potential, but life expectancy as well. Typically, if the VSD is < 2.5 cm in two perpendicular views, with a peak shunt velocity of > 4 m/s, and no other abnormalities are detected, performance will not be affected, although these horses might not be the most elite of race horses.[33,47]

Vessel thrombosis

Venous thrombosis, particularly jugular vein thrombosis, is a very common occurrence that does not usually impact performance. In most circumstances, collateral circulation develops if the vein does not recanulate. However, if severe and/or bilateral, so that venous drainage from the head is impaired, swelling and edema in the head and pharyngeal region may result, which may decrease athletic performance.[48] Although not common, thrombosis of the terminal aorta and/or iliac arteries can severely limit performance. It may be apparent at rest, with lameness, weak peripheral arterial pulses and slow filling of the saphenous vein in the affected hindlimb.[48] Exercise will often exacerbate clinical signs. Thromboses are definitively diagnosed with ultrasound of the suspected affected vessel.

Myopathies

Exertional rhabdomyolysis and subclinical myopathy

Exertional rhabdomyolysis (ER), recurrent exertional rhabdomyolysis (RER) and subclinical myopathy (SCM) can affect performance horses, with ER occurring in 2.8% of all horses and SCM occurring in 15.2% of horses with no clinical evidence of myopathy.[1,2] Horses with any of these conditions may have exercise intolerance. Although there are many causes of muscle disease in the horse,[49] this section will focus on ER, RER and SCM.

History

Horses with ER or RER may have signs of stiffness, muscle cramping, pain, muscle fasciculation, and weakness or exercise intolerance.[49] Horses with SCM typically do not exhibit any signs associated with ER or RER.[1] In fact, they usually appear clinically normal and the only pertinent information may be a history of poor performance or exercise intolerance.[1,2] A history should include the horse's recent exercise regimen, whether the horse has had a recent episode of 'tying up', the results of any diagnostic test, a listing of all medications and supplements administered to the horse, any present or prior lameness problems, and any history of respiratory problems.[49] Any horse with a recent bout of ER or RER (i.e. within 14 days) should not be subjected to a high-speed treadmill examination. In our experience, these horses have a recurrence of ER soon after treadmill schooling. Historically, young Thoroughbred females are the most likely to have RER, and this is thought to have a genetic component.[1,50]

Physical examination

During clinical episodes of ER, affected horses typically exhibit signs of pain, sweating, anxiety, muscle cramping, muscle atrophy, and unwillingness to walk (or lameness).[49] Dark colored urine may be present. One muscle group (e.g. the triceps group) or multiple groups of muscles may be affected. Horses with SCM may not exhibit any clinical signs and the diagnosis is based on laboratory findings. Close examination of the general muscle distribution and symmetry is important. Palpation of all large muscle groups should be done, along with running a blunt instrument gently over the neck, epaxial and gluteal muscles looking for excess fasciculation, wayward fasciculation or excessive guarding of muscle groups. Any of these adverse reactions may suggest primary or secondary muscle pain or muscle pathology.[49]

Diagnostic tests

If there is evidence of increasing lameness or of ER during any portion of the schooling for the high-speed treadmill evaluation, the examination is discontinued. Otherwise, the horse receives a complete HSTM examination and is monitored for post-exercise lameness and ER. If lameness is increased or if there is evidence of ER, appropriate management should be implemented.

The two most common serum or plasma enzymes evaluated are creatine kinase (CK) and aspartate aminotransferase (AST). Samples for CK and AST analysis are taken before and after exercise. It has been suggested that samples be collected 4–6 hours after exercise, when CK activity peaks.[52] However, other sample times are frequently employed for logistical or convenience reasons. For samples collected 30 minutes following exercise, a serum CK activity less than 1000 IU/L has been considered normal. In a recent retrospective study, 10/348 horses experienced clinical signs of ER.[1] CK activities in these horses 30 minutes post-exercise were 20 000–120 000 IU/L. In the same report, serum CK activities were elevated (15 000–220 000 IU/L) in 59/348 horses that had no obvious clinical signs of ER.

Elevations in AST can result from damage to both muscle and liver.[49] Post-exercise AST activities reach maximal

values later than does CK, and AST has a longer half-life; therefore activities can remain elevated as long as 2 to 3 weeks after insult.[52] Both CK and AST should be evaluated before and after treadmill exercise to determine if there has been any recent evidence of muscle damage.

An additional diagnostic test that may be helpful in cases of recurrent ER is nuclear scintigraphy. Nuclear scintigraphy may indicate the presence of deep muscle damage even with normal circulating muscle enzyme activities. This deep muscle damage may help explain subtle lameness or performance problems.

Treatment

Treatment of acute severe ER includes supportive care such as intravenous fluid therapy, acepromazine maleate, and monitoring of the CK activities. Clinical signs generally subside within a few hours of onset. Horses should not be returned to work until their muscle enzymes have returned to normal. Management of recurrent ER has included changing training methods, oral and injectable acepromazine, long warm-up periods, oral phenytoin, oral dantrolene sodium, acupuncture, afternoon turnout, and racing the horse from the field, along with numerous other methods. To date, none of these methods has been entirely satisfactory. Horses fed a high carbohydrate diet are more likely to have ER or RER.[53] In support of this, it has been suggested that a useful management technique to limit ER is feeding a low soluble carbohydrate, high fat diet.[49]

Prognosis

The prognosis for successful management of ER or RER is guarded. Horses responding to dietary management can have a good prognosis, as long as the dietary requirements are maintained throughout the remainder of the horse's career.

References

1. Martin BB, Reef VB, Parente EJ, et al. Causes of poor performance of horses during training, racing, or showing: 348 cases (1992–1996). J Am Vet Med Assoc 2000; 216:554–558.
2. Morris EA, Seeherman HJ. Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. Equine Vet J 1991; 23:169–174.
3. Morris E. Dynamic evaluation of the equine upper respiratory tract. Vet Clin North Am Equine Pract 1991; 7:403–416.
4. Parente EJ. Value of high-speed treadmill endoscopy. Proc Am Assoc Equine Pract 1998; 44:30–33.
5. Lumsden JM, Stick JA, Caron JJ, et al. Upper airway function in performance horses: videoendoscopy during high-speed treadmill exercise. Comp Cont Educ Pract Vet 1995; 17:1134–1144.
6. Reef VB. Stress echocardiography and its role in performance assessment. Vet Clin North Am Equine Pract 2001; 17:179–189.
7. Stick JA, Peloso JG, Morehead JP, et al. Endoscopic assessment of airway function as a predictor of racing performance in Thoroughbred yearlings: 427 cases (1997–2000). J Am Vet Med Assoc 2001; 219:962–967.
8. Hammer EJ, Tulleners EP, Parente EJ, et al. Videoendoscopic assessment of dynamic laryngeal function during exercise in horses with grade-III left laryngeal hemiparesis at rest: 26 cases (1992–1995). J Am Vet Med Assoc 1998; 212:399–403.
9. Marks D, Mackay-Smith MP, Cushing LS, et al. Use of a prosthetic device for surgical correction of laryngeal hemiplegia in horses. J Am Vet Med Assoc 1970; 157:157–163.
10. Speirs VC, Bourke JM, Anderson GA. Assessment of the efficacy of an abductor muscle prosthesis for treatment of laryngeal hemiplegia in horses. Aust Vet J 1983; 60:294–299.
11. Parente EJ, Martin BB, Tulleners EP. Epiglottic retroversion as a cause of upper airway obstruction in two horses. Equine Vet J 1998; 30:270–272.
12. Davidson EJ, Martin BB. Diagnosis of upper respiratory tract diseases in the performance horse. Vet Clin North Am Equine Pract 2003; 19:1–12.
13. Parente EJ, Martin BB, Tulleners EP, et al. Dorsal displacement of the soft palate in 92 horses during high-speed treadmill examination (1993–1998). Vet Surg 2002; 31:507–512.
14. Duncan DW. Retrospective study of 50 Thoroughbred racehorses subjected to radical myectomy surgery for treatment of dorsal displacement of the soft palate. Proc Am Assoc Equine Pract 1997; 43:237–238.
15. Llewellyn HR, Petrowitz AB. Sternothyroideus myotomy for the treatment of dorsal displacement of the soft palate. Proc Am Assoc Equine Pract 1997; 43:239–243.
16. Harrison IW, Raker CW. Sternothyrohyoideus myectomy in horses: 17 cases (1984–1985). J Am Vet Med Assoc 1998; 193:1299–1302.
17. Anderson, JD, Tulleners EP, Johnston JK, et al. Sternothyrohyoideus myectomy or staphylectomy for treatment of intermittent dorsal displacement of the soft palate in racehorses: 209 cases (1986–1991). J Am Vet Med Assoc 1995; 206:1909–1912.
18. King DS, Tulleners E, Martin BB, et al. Clinical experiences with axial deviation of the aryepiglottic folds in 52 racehorses. Vet Surg 2001; 30:151–160.
19. Martin BB, Beech J, Parente EJ. Cytologic examination of specimens obtained by means of tracheal washes performed before and after high-speed treadmill exercise in horses with a history of poor performance. J Am Vet Med Assoc 1999; 214:673–677.
20. Marlin DJ. Exercise-induced pulmonary hemorrhage. In: Robinson NE, ed. Current therapy in equine practice. 5th edn. Philadelphia: WB Saunders; 2003:429–432.
21. Sweeney CR, Humber KA, Roby KA. Cytologic findings of tracheobronchial aspirates from 66 thoroughbred racehorses. Am J Vet Res 1992; 53:1172–1175.
22. Takahashi T, Hiraga A, Ohmura H, et al. Frequency of and risk factors for epistaxis associated with exercise-induced pulmonary hemorrhage in horses: 251,609 race starts (1992–1997). J Am Vet Med Assoc 2001; 218:1462–1464.
23. Birks EK, Shuler KM, Soma LR, et al. EIPH: postrace endoscopic evaluation of Standardbreds and Thoroughbreds. Equine Vet J 2002; Suppl 34:375–378.
24. Pascoe JR, Ferraro GL, Cannon JH, et al. Exercise-induced pulmonary hemorrhage in racing thoroughbreds: a preliminary study. Am J Vet Res 1981; 42:703–707.
25. Raphel CF, Soma LR. Exercise-induced pulmonary hemorrhage in Thoroughbreds after racing and breezing. Am J Vet Res 1982; 43:1123–1127.

26. Sweeney CR. Exercise-induced pulmonary hemorrhage. Vet Clin North Am Equine Pract 1991; 7:93–104.
27. Hoffman AM. Inflammatory airway disease: definitions and diagnosis in the performance horse. In: Robinson NE, ed. Current therapy in equine practice, 5th edn. Philadelphia: WB Saunders; 2003:412–417.
28. Sweeney CR. Tracheal mucus transport rate in healthy horses. Am J Vet Res 1989; 50:2135–2137.
29. Meyer TS, Fedde MR, Gaughan EM, et al. Quantification of exercise-induced pulmonary haemorrhage with bronchoalveolar lavage. Equine Vet J 1998; 30:284–288.
30. Durando MM, Martin BB, Hammer EJ, et al. Dynamic upper airway changes and arterial blood gas parameters. Equine Vet J 2002; Suppl 34:408–412.
31. Rush BR. Aerosolized drug delivery devices. In: Robinson NE, ed. Current therapy in equine practice, 5th edn. Philadelphia: WB Saunders; 2003:436–440.
32. Reef VB, Maxson AD, Lewis ML. Echocardiographic and ECG changes in horses following exercise. Proceedings of the 12th Annual American College of Veterinary Internal Medicine Forum 1994; 12:256–258.
33. Reef VB. Heart murmurs in horses: determining their significance with echocardiography. Equine Vet J 1995; 19:71–80.
34. Patteson MW, Cripps PJ. A survey of cardiac ausculatory findings in horses. Equine Vet J 1993; 25:409–415.
35. Kriz NG, Hodgson DR, Rose RJ. Prevalence and clinical importance of heart murmurs in racehorses. J Am Vet Med Assoc 2001; 216:1441–1445.
36. Young LE, Wood JL. Effect of age and training on murmurs of atrioventricular valvular regurgitation in young thoroughbreds. Equine Vet J 2000; 32:195–199.
37. Amada A, Kurita H. Five cases of paroxysmal atrial fibrillation in the racehorse. Exp Rep Equine Health Lab 1975; 12:89–100.
38. Holmes JR, Henigan M, Williams RB, et al. Paroxysmal atrial fibrillation in racehorses. Equine Vet J 1986; 18:37–42.
39. Ohmura H, Hiraga A, Takahashi T, et al. Risk factors for atrial fibrillation during racing in slow-finishing horses. J Am Vet Med Assoc 2003; 223:84–88.
40. Deem DA, Fregin GF. Atrial fibrillation in horses: a review of 106 clinical cases, with consideration of prevalence, clinical signs, and prognosis. J Am Vet Med Assoc 1982; 180:261–265.
41. Kubo K, Senata T, Sugimoto O. Changes in cardiac output with experimentally induced atrial fibrillation in the horse. Exp Rep Equine Health Lab 1975; 12:101–108.
42. Deegen E, Butenkotter S. Behavior of the heart rate of horses with auricular fibrillation during exercise and after treatment. Equine Vet J 1976; 8:26–29.
43. Reef VB, Reimer JM, Spencer PA. Treatment of atrial fibrillation in horses: new perspectives. J Vet Intern Med 1995; 9:57–67.
44. Reimer JM, Reef VB, Sweeney RW. Ventricular arrhythmias in horses: 21 cases (1984–1989). J Am Vet Med Assoc 1992; 201:1237–1243.
45. Marr CM. Pathogenesis and clinical significance of ventricular arrhythmias. Proc Annu Am Coll Vet Intern Med 1998; 16:202–203.
46. Reef VB. Stress echocardiography and its role in performance assessment. Vet Clin North Am Equine Pract 2001; 17:179–189.
47. Reef VB. Evaluation of ventricular septal defects in horses using two-dimensional and Doppler echocardiography. Equine Vet J 1995; 19:86–95.
48. Leroux AJ. Vascular diseases. In: Robinson NE, ed. Current Therapy in Equine Medicine, 5th edn. Philadelphia: WB Saunders; 2003:625–630.
49. Valberg SJ. Skeletal muscle and lameness. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. Philadelphia: WB Saunders; 2003:723–743.
50. Ward TL, Valberg SJ, Gallant EM, et al. Calcium regulation by skeletal muscle membranes of horses with recurrent exertional rhabdomyolysis. Am J Vet Res 2000; 61:242–247.
51. Macleay JM, Valberg SJ, Sorum SA, et al. Heritability of recurrent exertional rhabdomyolysis in Thoroughbred racehorses. Am J Vet Res 1999; 60:250–256.
52. Kramer JJ. Clinical enzymology. In: Keneko JJ, ed. Clinical biochemistry of domestic animals, 3rd edn. Orlando: Academic Press; 1980.
53. McKenzie EC, Valberg SJ, Pagan JD. Nutritional management of exertional rhabdomyolosis. In: Robinson NE, ed. Current therapy in equine practice, 5th edn. Philadelphia: WB Saunders; 2003:727–734.

CHAPTER 5

Muscle physiology: responses to exercise and training

José-Luis L. Rivero and Richard J. Piercy

Muscular response to exercise

Overview

The skeletal musculature of the horse is highly developed and adapted to match the animal's athletic potential. In contrast to most mammals, in which 30–40% of body weight consists of muscle, more than half of a mature horse's body weight comprises skeletal muscle.[1] Total muscle blood flow in horses that are exercising at a level when O_2 consumption is at a maximum (VO_{2max}, 134 ± 2 mL/min/kg) has been estimated at 226 L/min, which represents approximately 78% of total cardiac output.[2] Such exercise therefore requires the co-ordinated application of many different body systems under the control of the nervous system (Fig. 5.1). Metabolites and oxygen reach skeletal muscle fibers via the respiratory, cardiovascular and hematologic systems; in turn the muscle fibers produce energy in the form of ATP which, via the contractile machinery, is converted into mechanical work. The structural arrangement of the musculoskeletal system provides the means with which to harness this energy to move the horse's limbs in a characteristic rhythmic pattern that is well established for each gait.

Equine muscle is considerably heterogeneous; the diversity reflects functional specialization and adaptive plasticity and has been studied extensively over the past 30 years. Muscle biopsy in particular has resulted in a greater understanding of the response of this tissue to exercise and training. Much of this work is summarized in the excellent review by Snow & Valberg[3] and therefore this chapter focuses specifically on new data obtained in the past decade, while assessing earlier studies from a later perspective.

Methodology

Percutaneous needle biopsy technique

Equine muscle physiology has centered around use of percutaneous needle biopsy (Fig. 5.2), a technique originally described for the M. gluteus medius by Lindholm and Piehl.[6] Although this muscle is very active during exercise[7] and shows considerable adaptation to training,[3] care must be exercised in interpreting data from a single biopsy,[8] because of the muscle's heterogeneity.[9,10] Other locomotory muscles (e.g. semitendinosus, biceps femoris, longissimus lumborum, triceps brachii and cleidocephalicus) can also easily be biopsied using the same technique. Muscle samples are useful for studies in vivo and in vitro using a range of morphologic, biochemical, and physiologic techniques. Muscle samples for histochemistry are frozen in isopentane precooled in liquid nitrogen. Samples for biochemistry are immersed directly in liquid nitrogen. In addition, a portion of the sample may be directly fixed for electron microscopy, thereby allowing measurement of capillary[11] and mitochondrial density.[12] Biochemical and physiologic studies can also be made on dissected and skinned single fibers.[13–15]

Laboratory methods

Biochemical analysis of homogenized equine muscle samples has enabled the study of broad metabolic responses to exercise and metabolic adaptation to training (see reference[3] for a review) through analysis of selected muscle enzyme activities, their substrates and intermediary metabolites. However, a limitation of this technique is that it does not enable differentiation between the various individual fiber types or the study of important morphologic features such as fiber size, capillary density and myonuclear location. Some of these disadvantages can be overcome by analyzing single fibers biochemically.[16,17] Histochemical evaluation of muscle, combined with image analysis,[18] has also provided invaluable information about the contractile and metabolic properties of equine muscles, specifically regarding fiber types, oxidative and glycolytic capacities, fiber sizes and capillary density.

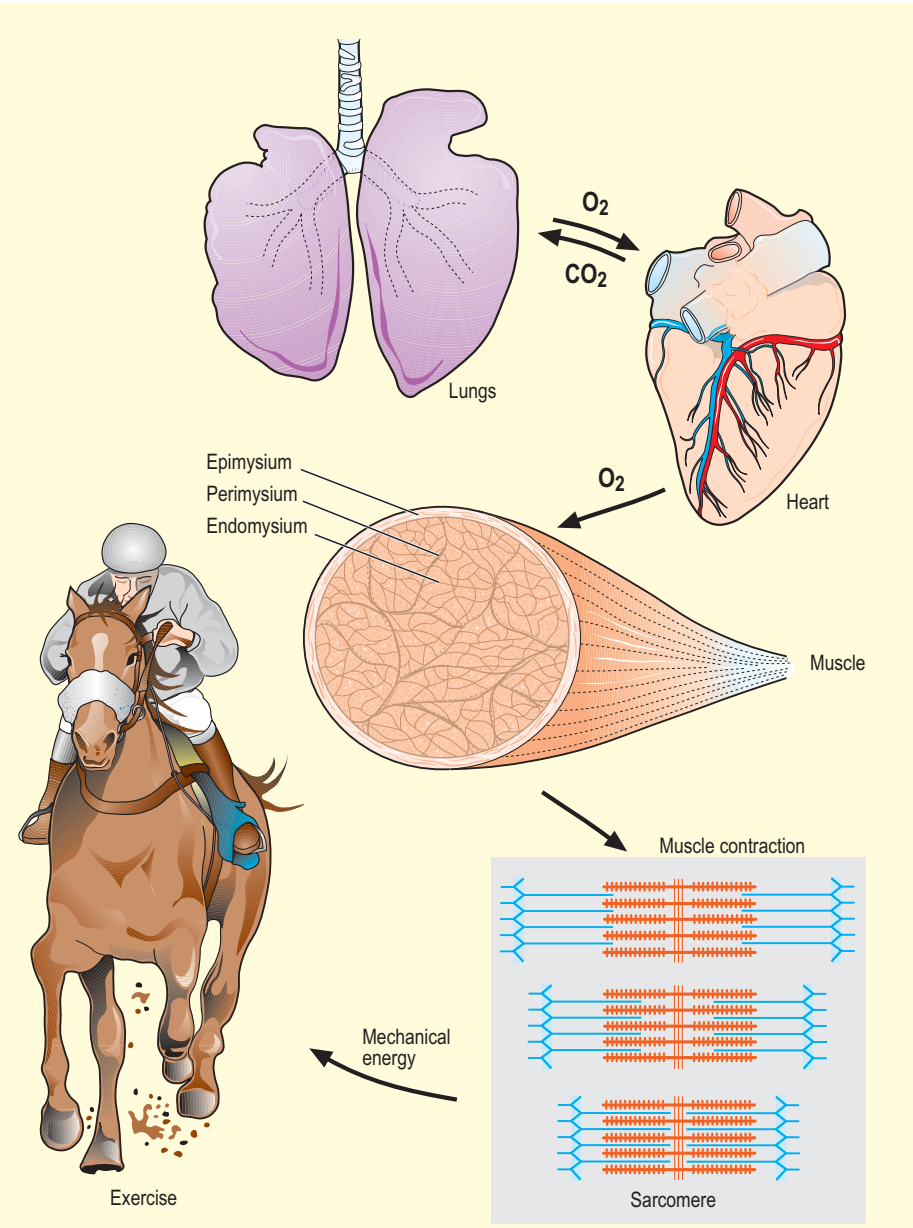


Fig. 5.1
Interaction between the main body systems (respiratory, cardiovascular, hematologic and muscular) involved in exercise. In the sarcomere, the thick myofilaments (myosin) are red and the thin myofilaments (actin) are blue.

However, subjective visual assessment of qualitative histochemical reactions (Fig. 5.3A,B) has until recently limited the application of these methods.[19] In recent years, more objective and quantitative histochemical methods have been applied to equine muscle.[20]

Cellular and molecular diversity within equine muscle has also been addressed, via study of myofibrillar and non-contractile proteins by immunohistochemistry,[21,22] gel electrophoresis,[23] a combination of both techniques,[24–26] and by enzyme-linked immunosorbent assay.[27,28] The past few years have seen the production of a considerable number of monoclonal antibodies to contractile and non-contractile muscle isoproteins, some of which can be used effectively in horse muscle via immunohistochemistry.[29–31] The technique's specificity provides, among other things, a more objective way to assess muscle fiber type (Fig. 5.3C).[32] Electrophoretic methods for the quantification of myosin isoforms have also recently been validated in the horse (Fig. 5.3D)[33] and immunoelectrophoresis has enabled the specific identification and relative quantitation of certain muscle-derived proteins.[34]

A major goal for future studies will be to refine molecular biology techniques and apply them to the field of equine exercise physiology in general and equine muscle physiology in particular. Northern blotting, reverse transcription followed by polymerase chain reaction and in situ hybridization will provide the means with which to study the molecular diversity of muscle proteins at the transcript (mRNA) level and before too long, microarray technology will enable a more global approach. This should prove invaluable when examining exercise and training effects, since altered transcript concentrations precede changes in protein expression.[35] Hence, during the early phase of transformation between fiber types,

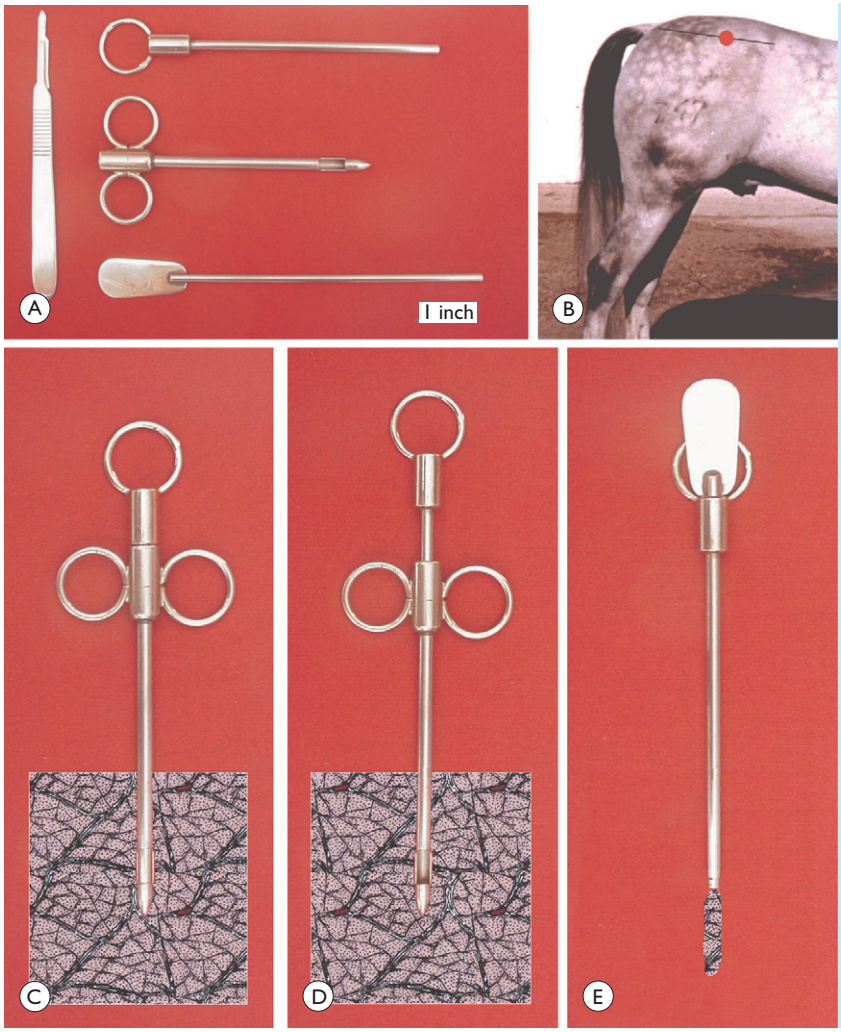


Fig. 5.2
(A) Percutaneous muscle biopsy needle; this needle, which has an outer diameter of 6 mm, was first introduced by Bergström[4] and was further modified with finger and thumb rings by Henckel.[5] (B) Site for the collection of biopsy specimens from the right gluteus medius muscle according to Lindholm & Piehl;[6] this fixed site is located one-third of the distance along a line running from the tuber coxae to the root of the tail. (C–E) An illustration of the various steps for the needle biopsy technique; (C) the needle biopsy, together with the internal cutting cylinder, is inserted into the muscle; (D) once within the muscle, the cutting cylinder is partially withdrawn so that the window is opened up, allowing muscle to enter the slot, and a piece is then cut by pushing down the internal cylinder; (E) between 50 and 150 mg of muscle tissue are usually acquired.

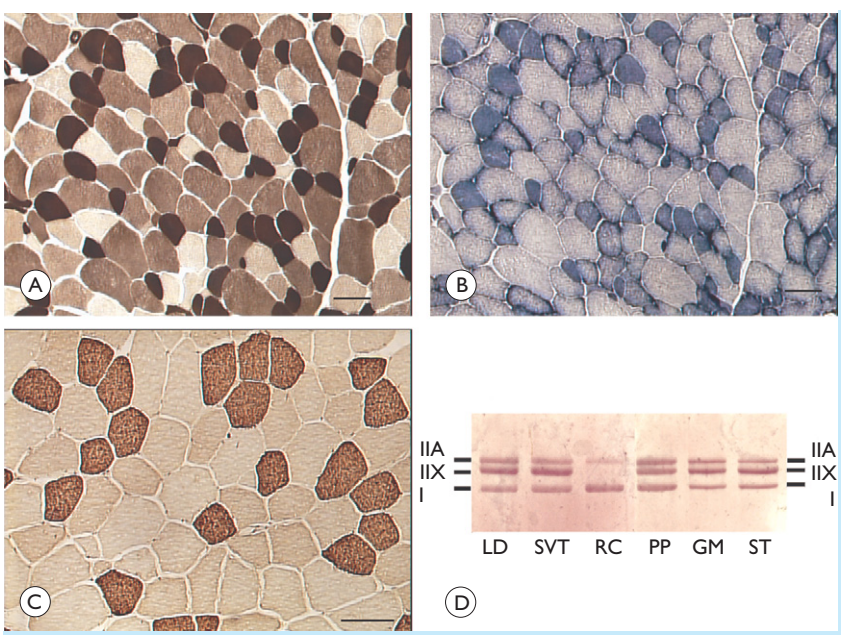


Fig. 5.3
Illustration of three integrated approaches for investigating skeletal muscle samples in horses: histochemistry (A, B), immunohistochemistry (C) and gel electrophoresis (D). (A) Transverse section of a gluteus medius muscle biopsy stained for demonstration of adenosine triphosphatase activity after acid preincubation (pH 4.4); the differential staining allows identification of the various fiber types. (B) Serial section of the previous sample stained to demonstrate succinic dehydrogenase activity; this histochemical stain is performed to allow examination of the oxidative capacity of myofibers. (C) Transverse section of the same sample stained by immunohistochemistry with a monoclonal antibody to the β-slow (type I) myosin heavy chain isoform; this method enables more objective delineation of muscle fiber types than histochemistry. (D) Coomassie blue staining to show myosin heavy chain composition of whole-muscle extracts on 8% sodium dodecyl sulfate polyacrylamide gel electrophoresis; isoforms are identified as IIA, IIX and I going from the slowest (highest) to the fastest band. LD, M. latissimus dorsi; SVT, M. serratus ventralis thoracis; RC, M. rhomboideus cervicis; PP, M. pectoralis profundus; GM, M. gluteus medius; ST, M. semitendinosus. Scales in A–C, 50 μm.

isoform-specific mRNA should be detectable some time before the associated protein.

Other techniques

In addition to cellular and molecular techniques, non-invasive analysis, such as nuclear magnetic resonance and electromyography,[36,37] is being increasingly applied to examine the effects of exercise and training on the neuromuscular system. Furthermore, electromyography, force plate and gait analysis have applications for assessing muscle activation patterns during locomotion.[7,38]

Muscle structure and function

Morphology

Development Most skeletal muscles are derived from paraxial mesodermal tissue following its condensation into segmentally arranged somites. Cells of certain lineages become compartmentalized within each somite as it differentiates: the dorsolateral compartment, known as the myotome, contains two subsets of myogenic precursor cells. The cells of one subset are destined to become the axial musculature, whereas cells of the other subset migrate into the periphery to form the muscles of the body wall and the limbs.[39] Myogenic precursor cells differentiate to form myoblasts. These fuse to become discrete populations of myotubes that subsequently fuse into myofibers (see Fig. 6.2).[40] At the same time, α-motor neurons establish their connections at neuromuscular junctions. Embryonic myogenesis shares many similarities with the regeneration of mature myofibers following injury, a subject that is covered in more detail in Chapter 6.

Gross anatomy Locomotor muscles are generally located proximally on the appendicular skeleton, thereby reducing the weight of the lower limb and decreasing the energy necessary to overcome inertia when the limb swings back and forth.[41] Movements of the distal limb are mainly passive and result from the release of elastic energy of the digital flexor tendons and suspensory ligament when the limb is unloaded.[42] However, myofibroblasts (with contractile properties) have been observed in these tendons.[43] Movements of the proximal limb result from active muscular contraction.[44] In general, most locomotor muscles are active during the propulsion stage of the stance phase of the stride in each limb.[45] Quantitative electromyography shows that muscles within the same group have significant differences in their activities when exercising at constant speed; furthermore, muscle activity, as measured by electromyography, is positively correlated with running speed.[46]

More than 90% of a muscle is made up of myofibers, with the rest consisting of nerves, blood vessels and the fat and connective tissue that separates the individual fibers (endomysium), the fascicles (perimysium) and the whole muscle (epimysium; Fig. 5.1). The connective tissue merges with both the origin and the insertion tendons of the muscle, as well as with internal tendons in compartmentalized muscles. Blood vessels and nerves course within the perimysium. Capillary arrangement in the skeletal muscle is optimized for oxygen delivery to tissue during exercise;[47] usually several capillaries are located within close proximity, sometimes circumferentially but more often running parallel to each fiber. The internal muscular architecture varies considerably both within and between equine muscles.[21,48,49] For example, different fiber lengths and pinnation angles have a significant impact on the power output and the degree of shortening of specific muscles, in accordance with their specific function.[50]

Histology The skeletal myofiber is an elongated cell (generally believed to be between 30 and 100 mm in length) with tapered ends. Fibers vary from 10 to 100 μm in diameter and are multinucleated (Fig. 5.4A). The nuclei are normally located at the fiber's periphery, in a subsarcolemmal position. Although the cytoplasm contains other organelles found in many cell types, it is mostly taken up by the contractile apparatus that consists of the contractile proteins and their supportive structures that are grouped together as myofibrils. In longitudinal sections, individual muscle fibers have numerous cross-striations (dark and light bands), that are orientated perpendicular to the fiber's long axis (Fig. 5.4B). Lighter I bands alternate with darker A bands. Within the I band there are dense striations called Z disks.

Ultrastructure The repeating unit between two adjacent Z disks is known as a sarcomere, the unit of muscular contraction. Each sarcomere includes half the I band on each side of the A band (Fig. 5.4C,D). I bands contain only thin filaments (8 nm diameter), whereas the A bands contain both thin and thick (15 nm diameter) filaments. Within the A band, the H band is defined as the central area where the thick filaments do not overlap with thin filaments (Fig. 5.4D). The central darker portion of the H band is designated as the M line (Fig. 5.4D). Transverse section of the sarcomere at the overlapping zone between thick and thin filaments reveals each thick myofilament surrounded by thin myofilaments in a hexagonal lattice arrangement (Fig. 5.4E). Muscle contraction occurs when, within each sarcomere, thin myofilaments slide over the thick myofilaments, bringing the adjacent Z disks closer together. Hence upon contraction, the I band shortens and the H band starts to disappear.

Thick filaments contain myosin and other myosin-binding proteins. Sarcomeric myosins have two heads and a long tail and consist of two heavy chains and two pairs of light chains (Fig. 5.5A). The myosin head is the motor domain that contains the adenosine triphosphate (ATP) binding site, the actin-binding site and the myofibrillar ATPase enzyme. The major components of the thin filaments are tropomyosin, the troponin complex (consisting of three subunits: troponin C (TnC), troponin T (TnT) and troponin I (TnI)), and two helical filamentous strands of actin (F-actin), made up of polymerized globular actin monomers (G-actin) (Fig. 5.5B). Elongated tropomyosin dimers lie within the major groove of the actin filament, spanning seven actin monomers; each troponin complex is also associated with a seven-actin repeat. The elongated NH_2-terminal of TnT extends for a considerable

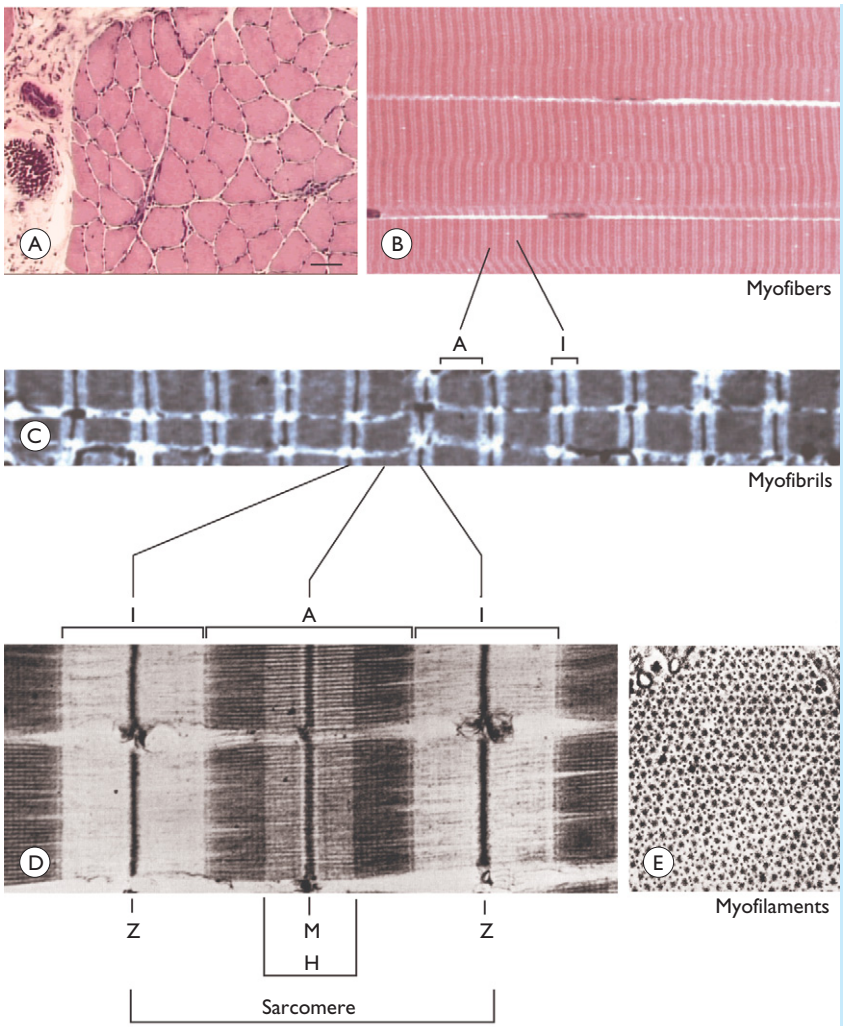


Fig. 5.4
Organization of the contractile apparatus from the cellular to the molecular level. (A) Transverse section from a specimen of the M. sacrocaudalis dorsalis medialis stained by hematoxylin and eosin and examined by light microscopy; scale = 50 μm. (B) Longitudinal section from the same specimen with the same stain. (C) Striated aspect of myofibrils when observed by electron microscopy at very low magnification, showing Z disks, A bands and I bands of sarcomeres. (D) Electron micrograph of longitudinal sectioned myofibrils at × 30 000 magnification. (E) Electron micrographs of transverse sections of one myofibril in the overlap zone (A band) between thick and thin myofilaments of sarcomere, illustrating the hexagonal arrangement of these filaments, × 150 000.

length from each tropomyosin molecule, spanning the gap between adjacent molecules.

Mitochondria are located beneath the sarcolemma and between myofibrils (Figs 5.6, 5.7). This intimate relationship means that ATP produced during oxidative phosphorylation is readily available for the contractile machinery. Intramuscular substrates, such as glycogen and lipids, are also stored between the myofilaments and under the sarcolemma (Fig. 5.7). Numerous other proteins, including myoglobin, glycolytic enzymes and various intermediate filaments are distributed throughout the cytoplasm.

The sarco(endo)plasmic reticulum (SR) of skeletal myofibers is an intracellular membranous system located between the myofibrils (Figs 5.6, 5.7), but has no physical continuity with the external surface membrane (sarcolemma). Much of its tubular network is orientated longitudinally to the myofibrils. The SR contains, amongst other molecules, a large amount of the enzyme Ca^{2+}-ATPase, the protein calsequestrin and the calcium release channel (ryanodine receptor or RYR1). At the AI junction of the sarcomere, the SR tubules become confluent and form terminal cisternae orientated perpendicularly to the long axis of the cell (Fig. 5.7D). Two adjacent cisternae are separated by a structure known as the T-tubule, which is a long tubular invagination of the sarcolemma, communicating directly with the extracellular space. Together the three structures make up a triad (Figs 5.6, 5.7).

The motor end-plate (see Fig. 5.11B) is a specialized region on each fiber, where the α-motor neuron interdigitates with the sarcolemma. The postsynaptic membrane contains numerous acetylcholine receptors. The remainder of the sarcolemma contains a variety of specific membrane proteins that function structurally and as channels, pumps and hormone receptors. Myofibers have a cytoskeleton of various intermediate filament proteins that link the contractile apparatus with a complex of proteins at the sarcolemma, known as the dystrophin-associated complex (see Fig. 5.14). Between the sarcolemma and the extracellular matrix is the basal lamina (Fig. 5.7E) which is generally closely apposed to the sarcolemma except where it leaves the sarcolemma to course over the surface of satellite cells (Fig. 5.8; see also Fig. 6.2).

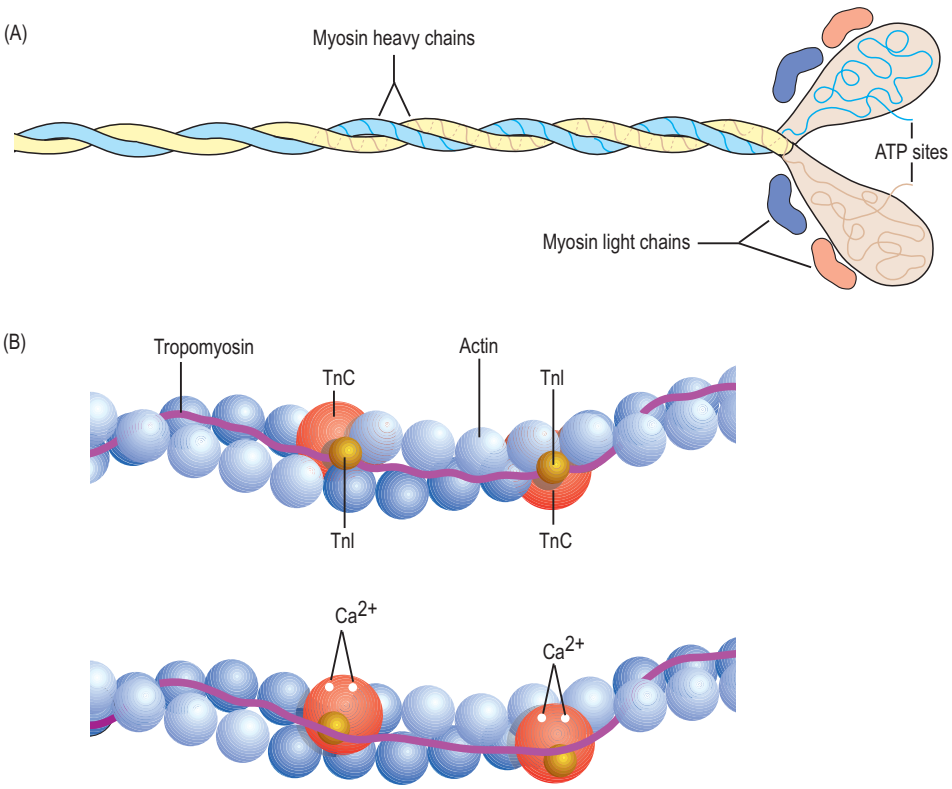


Fig. 5.5
(A) Diagram of the myosin molecule illustrating the α-helical coiled-coil tail, the folding of each heavy chain to form a globular head, the site of ATP hydrolysis, and the location of the four myosin light chains (regulatory and essential). (B) Model of the troponin–tropomyosin–actin that make up the thin myofilaments, during muscle relaxation (upper) and contraction (bottom). In the relaxed state, the inhibitory region of troponin (TnI, colored yellow) is attached to actin and tropomyosin, whereas troponin C (TnC, colored orange) is bound to Mg^{2+}. In this conformation, myosin cannot bind. In the contracted state, two Ca^{2+} ions bind to TnC, which in turn interacts with TnI. A conformational change to the troponin–tropomyosin complex exposes the myosin binding sites, thereby allowing the power stroke to occur.

General muscle physiology

The motor unit A motor unit consists of an α-motor neuron and the skeletal muscle fibers that it innervates (Fig. 5.9).[51] Since each time an α-motor neuron fires, the entire motor unit contracts, coarser movements are generated in those muscles that have many muscle fibers making up motor units (such as the locomotor muscles) compared with those with few (such as the extrinsic eye muscles). Muscle fibers within one motor unit are generally all of the same histochemical type, but they are normally widely distributed between fibers from other motor units and therefore give rise to the characteristic checker-board pattern that is apparent when using certain histochemical stains (see Fig. 5.3A). This is evident in denervated muscle (Fig. 5.10A,B) where there may be selective loss and atrophy of fibers of one histochemical type (Fig. 5.10A) or in reinnervated muscle following disease or injury, by patterns of fiber grouping (Fig. 5.10C).[52] Large-diameter α-motor neurons innervate fast-twitch fibers whereas smaller ones tend to innervate slow-twitch fibers.

Contractile force for a particular muscle is partly regulated by the rapidity of neuron discharge: muscle fibers contract with a twitch following a single discharge of a motor neuron but sustained contraction (tetanus) results from repetitive neuron firing. The force of a contraction increases with the rate of discharge up to a maximum limit that is determined by the properties of the muscle. Furthermore, a process known as recruitment, which reflects the gradual inclusion of larger motor neurons as greater force is required, also regulates force (see below). Relatively weak and slow contractions required for maintenance of posture therefore involve small-diameter α-motor neurons and slow-twitch fiber types, whereas locomotion and rapid movements rely on recruitment of larger diameter α-motor neurons and fast-twitch fibers.

Muscle proprioception Proprioception is the term given to the mechanism underlying the self-regulation of posture and movement through stimuli originating in sensory receptors embedded in joints, tendons, muscles and the labyrinth of the ear. In skeletal muscles and tendons these receptors are known as spindles and Golgi tendon organs and each type has been well characterized in the horse.[53–56] Signals derived within these sensory receptors are conveyed via a variety of well-defined reflex pathways that generate specific motor responses.

Muscle spindles consist of specialized intrafusal muscle fibers surrounded by a connective tissue capsule and lie parallel to regular muscle fibers (Fig. 5.11A). Sensory nerves (type Ia and type II) terminate on the intrafusal fibers in specialized sensory endings and generate afferent signals that are relayed to the spinal cord via the dorsal horn. Type Ia nerves carry both dynamic (rate of stretch) and static (amount of stretch) afferent signals whereas type II nerves sense only static muscle length. Motor innervation to the muscle spindle is provided by γ-motor neurons, which regulate the sensitivity of muscle spindles to muscle stretch. Golgi tendon organs are located within the connective tissues of tendons, joint capsules and muscles. They lie in parallel with the direction of mechanical force that they measure and from them, afferent type Ib fibers convey proprioceptive signals to the spinal cord.

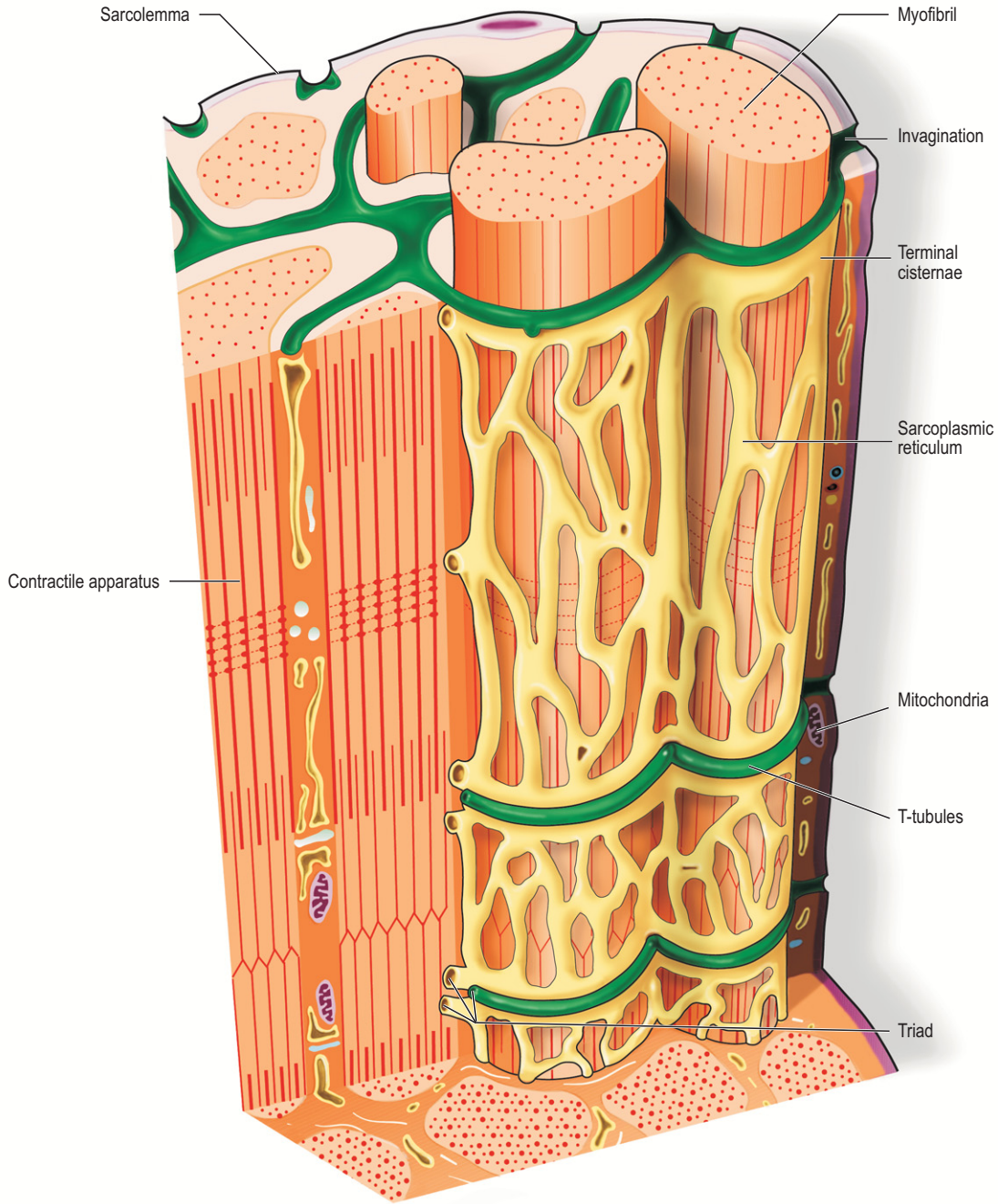


Fig. 5.6
Diagrammatic representation of the internal structure of a muscle fiber. Myofibrils are surrounded by the net-like tubular sarcoplasmic reticulum (SR); the SR converges at the junction between A and I bands of sarcomeres to form terminal cisternae. Between each pair of terminal cisternae there is an invagination of the sarcolemma called the T-tubule. Together, the three structures make up a triad. Mitochondria are dispersed between myofibrils.

Electrical and ionic properties of the sarcolemma
The sarcolemma maintains the interior of the fiber at a negative potential (the membrane potential) when compared to the extracellular fluid while the fiber is in a resting state. The negative potential is derived from the disequilibrium of ionic concentrations (mostly Na^+ and K^+) across the membrane and is generated partly by the action of the Na^+/K^+ ATPase pump, which extrudes three Na^+ ions for every two K^+ ions taken up. This results in the cytoplasm having a much higher K^+ concentration but much lower Na^+ concentration than the extracellular fluid. The remainder of the membrane potential is derived from the tendency of ions to diffuse down their electrochemical gradients across the semipermeable membrane.

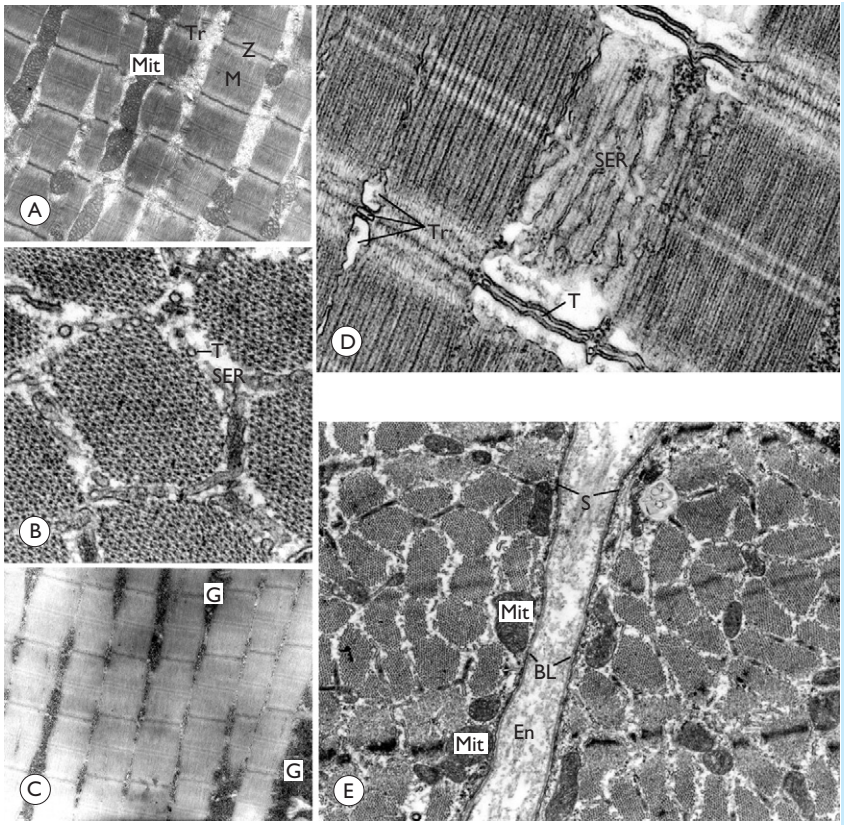


Fig. 5.7
Ultrastructural appearance of equine skeletal muscle cells when observed by electron microscopy. (A) Type IIA myofiber sectioned longitudinally; note the straight and thin appearance of Z lines, M lines in the middle of each sarcomere, a triad (Tr) and abundant mitochondria (Mit) within the intermyofibrillar spaces. (B) Transverse sectioned myofibrils showing the arrangement of the sarco(endo)plasmic reticulum (SER) and T-tubules (T); magnification ×54 000. (C) Type IIX muscle fiber sectioned longitudinally; note the abundant glycogen granules (G); magnification ×25 312. (D) Electron micrograph of an equine sarcomere showing the arrangement of the sarco(endo)plasmic reticulum (SER), T-tubule (T) and a triad (Tr); magnification ×58 125. (E) Two adjacent equine myofibers sectioned transversely showing the sarcolemma (S) and the basal lamina (BL), interposed between the sarcolemma and the extracellular matrix; there are also abundant mitochondria (Mit) located beneath the sarcolemma and between myofibrils; magnification ×35 835. (Frames A and C are courtesy of Drs LH Sucre and HJ Finol from the Universidad Central de Venezuela. Frames B, D and E are courtesy of Dr A Blanco from the University of Cordoba.)

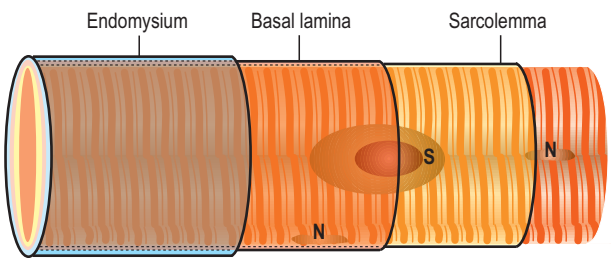


Fig. 5.8
Diagram illustrating the relationship of a satellite cell (S) to the sarcolemma, basal lamina and endomysium. N, myonucleus.

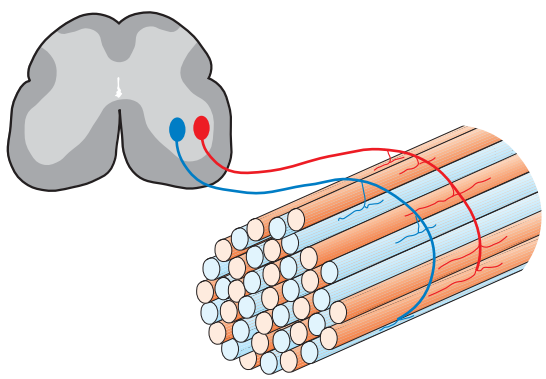


Fig. 5.9
Diagram illustrating the organization of motor units. A motor neuron from the ventral horn of the spinal cord supplies the motor innervation to a group of muscle fibers with similar contractile and metabolic properties.

Acetylcholine released from presynaptic nerve terminals at neuromuscular junctions (end-plates; Fig. 5.11B) binds to acetylcholine receptors and increases the conductance of the postjunctional membrane to Na^+ and K^+. The inward movement of Na^+ down its concentration gradient predominates, causing a transient depolarization (about 20 mV) in the end-plate, known as the end-plate potential. This depolarization is sufficient to activate sarcolemmal voltage-gated Na^+ channels (mutated in hyperkalemic periodic paralysis – see Chapter 6, p. 92), which open and therefore elicit propagation of an action potential along the membrane. Following this, and in response to depolarization, voltage-gated potassium channels open, resulting in the downswing of the action potential. The action potential therefore conducts rapidly along the sarcolemma in a wavelike fashion, away from the neuromuscular junction.

Excitation-contraction coupling Action potentials are conducted into the interior of muscle fibers via the T-tubules and there activate voltage-gated channels known as dihydropyridine receptors (DHPR). Unlike in cardiac muscle, very little calcium enters the muscle fiber from the extracellular space (via the DHPR).[57] Instead, a mechanical link between DHPR and the SR Ca^{2+} release channel (ryanodine receptor, RYR1) at the junctional feet of the triads results in the release of calsequestrin-bound Ca^{2+} from the SR's interior (Fig. 5.12). A positive feedback loop, known as calcium-induced calcium release, is responsible for further activation

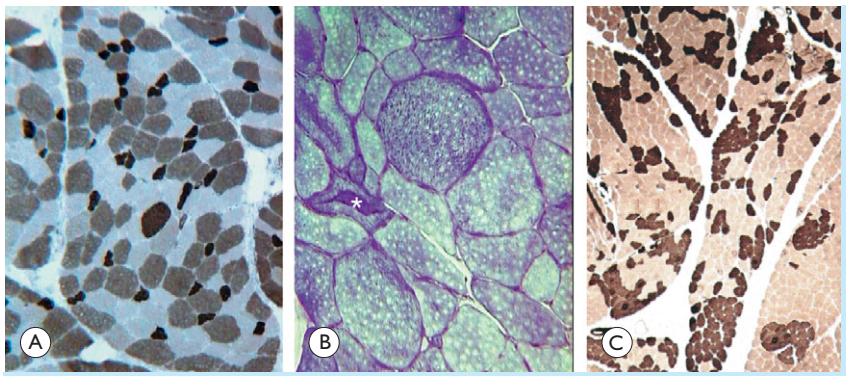


Fig. 5.10
Skeletal muscle histopathological signs of neurogenic atrophy in the horse. (A) Transverse section of the M. gluteus medius (7 cm depth) stained with ATPase at pH 4.5 from one horse with motor neuron disease; note the general, but particularly type I (black) fiber atrophy. (B) Transverse section of the M. vastus lateralis stained with periodic acid-Schiff (PAS) from a horse with femoral nerve paralysis; the asterisk shows a fiber with a target structure in its center, suggesting reinnervation following denervation. (C) Transverse section of the M. cricoarytenoideus dorsalis stained with ATPase (pH 9.4) from a horse with laryngeal hemiplegia showing disruption of the normal checkerboard pattern and fiber type grouping.

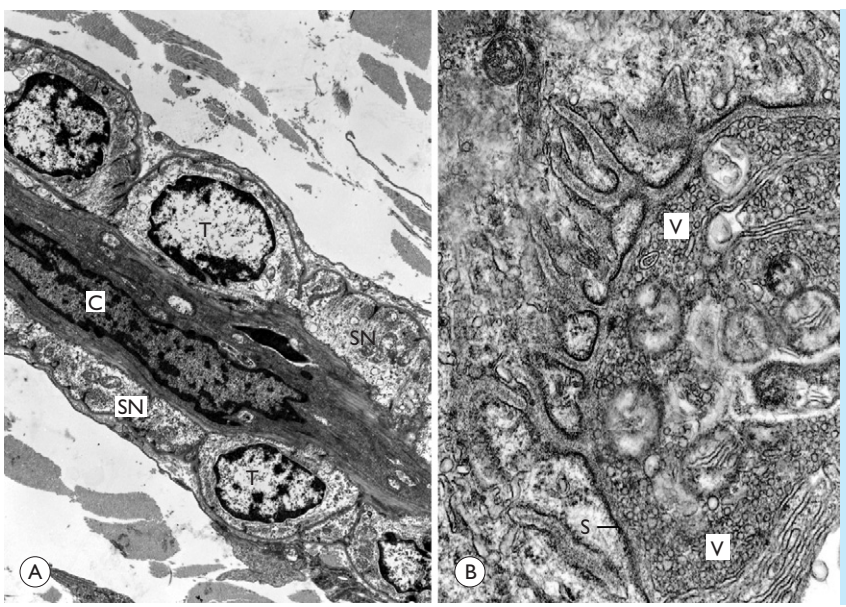


Fig. 5.11
(A) Electron micrograph of an equine muscle spindle; sensory nerves (SN) appose the abundant teloglia cells (T) which are surrounded by an internal capillary (C); magnification ×37 125. (B) Electron micrograph of an equine myofiber showing the neuromuscular junction (end-plate) of the sarcolemma (S); note the clear (acetylcholine-containing) vesicles (V) in the presynaptic nerve terminal; magnification × 43 000. (Courtesy of Dr A Blanco from the University of Cordoba.)

of RYR1 with the result that the calcium concentration within the cytoplasm increases about 100-fold from a resting concentration of approximately 50 nM.[57] The anatomical location of the terminal cisternae results in Ca^{2+} being released adjacent to the overlapping contractile apparatus.

Binding of Ca^{2+} to high-affinity binding sites on troponin C causes a conformational change to the troponin–tropomyosin complex (see Fig. 5.5B). This results in the exposure of the myosin-binding sites on F-actin and allows the myosin globular head to attach, as ATP is hydrolyzed, thus forming the crossbridge. Force generation, and the resulting shortening of the sarcomere are the result of a conformational change of the myosin head. Adenosine diphosphate and inorganic phosphate are displaced by actin, which is followed by dissociation of the actin–myosin bridge due to the binding of ATP to myosin again. The crossbridge cycle continues while the cytoplasmic Ca^{2+} concentration remains high. Relaxation is achieved when the Ca^{2+} is resequestered within the SR via the action of the Ca^{2+} ATPase pumps (see Fig. 5.13 for a summary).

Force transmission The force that is generated in the crossbridge cycle is transmitted via the contractile apparatus to intermediate filament proteins that act to maintain and stabilize the muscle fiber's shape during contraction. These intermediate filaments provide a structural link first to the sarcolemma and then to the extracellular matrix via a group of proteins known as the dystrophin-associated protein complex (Figs 5.14, 5.15).[58] Contractile forces are transmitted from each muscle fiber via the extracellular matrix and the connective tissues of tendons, and ultimately to the bones of the skeleton.

Oxygen availability ATP replenishment in (predominantly) oxidative fibers requires a readily available source of oxygen that is provided by the O_2-binding heme protein known as myoglobin.[59,60] The P_{50} for equine myoglobin (the PO_2 when it is 50% saturated) is about 2.4 mmHg at physiological temperatures and pH,[61] and therefore far to the left of hemoglobin and close to the PO_2 of muscle cells. During exercise, oxygen demand rises dramatically and is met by a 20–30 times increased blood flow through the muscle capillary beds.[2] Capillary dilation results partly from autonomic control and stretch imposed by the higher blood pressure, but also follows the local production of vasoactive substances that include potassium, adenosine and nitric oxide. The latter is produced by nitric oxide synthase, found both in the

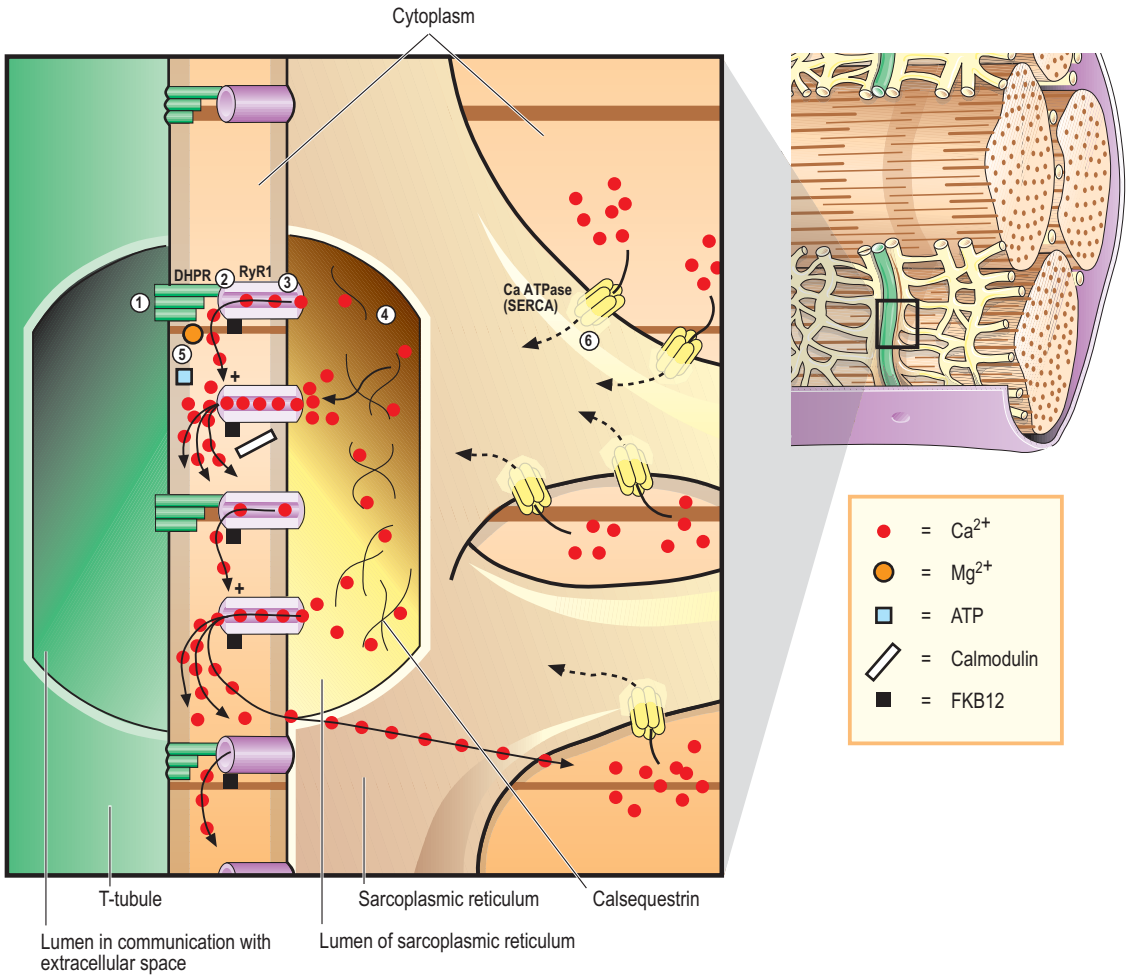


Fig. 5.12
Depolarization of the T-tubule membrane during the action potential activates voltage-gated Ca^{2+} channels (1) (dihydropyridine receptors) in the wall of the T-tubule. A mechanical link (2) with ryanodine receptors (RyR1) (3) located in the wall of the sarcoplasmic reticulum causes them to open and release calsequestrin-bound Ca^{2+} ions from the lumen of the SR (4). This Ca^{2+} stimulates further Ca^{2+} release via the calcium-induced calcium release mechanism. The process is modulated by other factors within the cytoplasm that include ATP, calmodulin and Mg^{2+} (5). After release into the cytoplasm, calcium activates the contractile apparatus by binding to troponin-C (Fig. 5.13). Reuptake into the SR occurs via the Ca^{2+}-ATPase pumps (6).

endothelium of the capillaries and bound to the dystrophin-associated protein complex within the contracting muscle fibers themselves (Fig. 5.16).[62]

Energy provision for muscular functions

Muscles cannot contract without a biochemical source of energy provided by the cleavage of high-energy phosphate bonds within ATP. In addition to the normal cellular metabolic requirements and the energy required for ion pumping up concentration gradients, ATP is required in the contractile crossbridge cycle: at the head of each myosin there is an ATP molecule that becomes hydrolyzed and releases energy (E) in a reaction catalyzed by the enzyme actomyosin ATPase:

$$ATP + H_2O \rightarrow ADP + Pi + H^+ + E$$

where ADP = adenosine diphosphate and Pi = inorganic phosphate.

Aerobic pathways Within mitochondria, β-oxidation of free fatty acids (FFA), the tricarboxylic acid (TCA) cycle and oxidative phosphorylation (via the electron transport chain) combine to produce ATP aerobically (Fig. 5.17; see also Fig. 28.25). During the process, the coenzymes nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD) are reduced to $NADH_2$ and $FADH_2$, respectively. Subsequently, $NADH_2$ and $FADH_2$ are reoxidized to NAD and FAD via the electron-transport chain in which oxygen acts as the final hydrogen acceptor to form water. Oxygen dissolved within the cytoplasm and bound to myoglobin is rapidly used up and hence must be replenished. Functional oxidative phosphorylation therefore depends on the dense capillary network between muscle fibers (Fig. 5.18). Acetyl-CoA is the substrate for the TCA cycle and its complete oxidation allows the formation of 12 molecules of ATP. Acetyl-CoA is derived from pyruvate, following anaerobic metabolism of glucose and glycogen within the cytoplasm (glycolysis) (Fig. 5.17); at

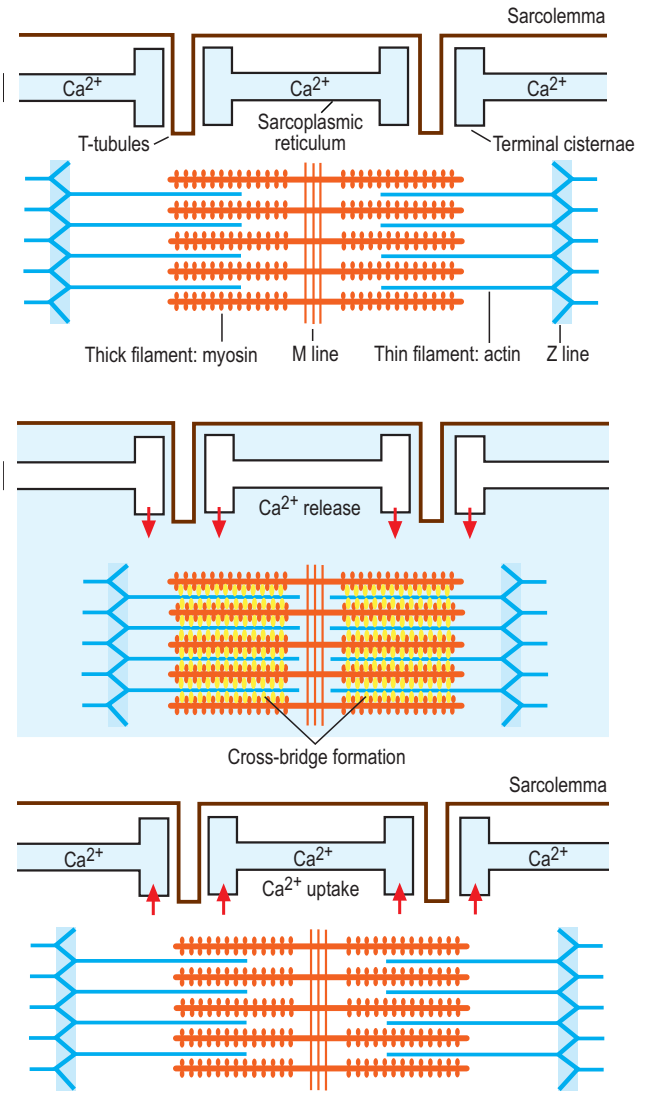


Fig. 5.13
Diagram illustrating excitation–contraction coupling and the role of calcium in the contractile mechanism. (Top) Calcium (light blue) stored in the SR during the relaxed state of the muscle. (Middle) A wave of depolarization moves along the sarcolemma and alters the membrane potential of the T-tubules. The altered membrane potential culminates in movement of Ca^{2+} ions into the cytoplasm from the SR (see Fig. 5.12). Thin filament inhibition is removed, allowing the globular heads of myosin to interact with actin and form a crossbridge that results in shortening of the total length of sarcomere. (Bottom) Muscle relaxation is achieved when Ca^{2+} is pumped back into the SR.

submaximal exercise intensities, most pyruvate produced via glycolysis is transported into mitochondria and is converted to acetyl-CoA. Thirty-six molecules of ATP are produced in the complete breakdown of glucose via these pathways. However, acetyl-CoA might also be derived from the oxidation of fatty acids, following their mobilization from the liver or adipose tissue. β-oxidation of FFA is highly efficient, as complete oxidation provides up to 146 molecules of ATP.

Anaerobic pathways In addition to the pathways described above, additional anaerobic mechanisms exist for ATP replenishment in muscle. They can be divided into two different mechanisms. The first system involves high-energy phosphate transformations involving the coupling of the creatine kinase (1), adenylate kinase (2) and AMP deaminase (3) enzyme systems:

1. ADP + phosphocreatine → ATP + creatine
2. ADP + ADP → ATP + AMP
3. AMP + H_2O → IMP + NH_3

The enzymes that catalyze these reactions help buffer ATP concentrations at the expense of lowering the cellular concentration of phosphocreatine and free ADP, while increasing the concentrations of creatine, adenosine monophosphate (AMP) and inosine monophosphate (IMP). These reactions occur in active muscles at top speeds, but provide only a small amount of ATP for a few seconds. Deamination of adenosine nucleotides leads to the production of ammonia (NH_3), uric acid and allantoin.[63]

The second anaerobic pathway involves glycolysis acting independently from the oxidative pathways. Glycolysis requires glucose-6-phosphate as a substrate, which may be derived from the phosphorylation of glucose by hexokinase or by the mobilization of stored intracellular glycogen that is metabolized first to glucose-1-phosphate via glycogenolysis (Fig. 5.17) and then converted to glucose-6-phosphate. Blood glucose is transported across the sarcolemma by means of specific glucose transporters that include GLUT-1 and GLUT-4 (Fig. 5.18).[64] GLUT-1 is normally located within the sarcolemma and provides basal glucose requirements; however, GLUT-4 receptors translocate to the sarcolemma in vesicles, in response to insulin or the demands of exercise (see Fig. 6.14, p. 91). The glycolytic pathways result in the formation of two pyruvate molecules which, in the absence of oxygen, are converted to lactate.

Integration of aerobic and anaerobic pathways Aerobic production of ATP is a relatively slow but highly efficient process, while anaerobic pathways produce energy rapidly but relatively inefficiently. Although both pathways are generally active during exercise, the relative contribution within each muscle depends on the nature, intensity and duration of the activity, the muscle's fiber type composition, the availability of oxygen and substrates and the relative concentrations of intermediary metabolites that may potentially activate or inhibit selected enzymes.[63,65] Hence, at the beginning of low-speed exercise, when oxygen is abundant, energy production depends largely on the degradation of glycogen via aerobic pathways.[63] Within a few minutes, glucose and FFA concentrations rise in the blood and following 20–30% glycogen depletion, there is a shift towards β-oxidation of FFA.[66] With higher energy demands, the muscle ATP/ADP ratio decreases, providing a stimulus for energy production via anaerobic mechanisms. The activity of the key regulatory glycolytic enzyme phosphofructokinase increases, resulting in greater production of pyruvate via glycolysis. The point where the availability of oxygen becomes a limiting factor in oxidative phosphorylation is reflected by partial reoxidation of $NADH_2$, as more and more pyruvate is converted to lactate. As exercise intensity increases, a greater proportion of the energy is supplied by the anaerobic pathway. The point when the increased rate of latacte production can be detected in the plasma is known as the anaerobic threshold. This threshold varies and depends on several factors

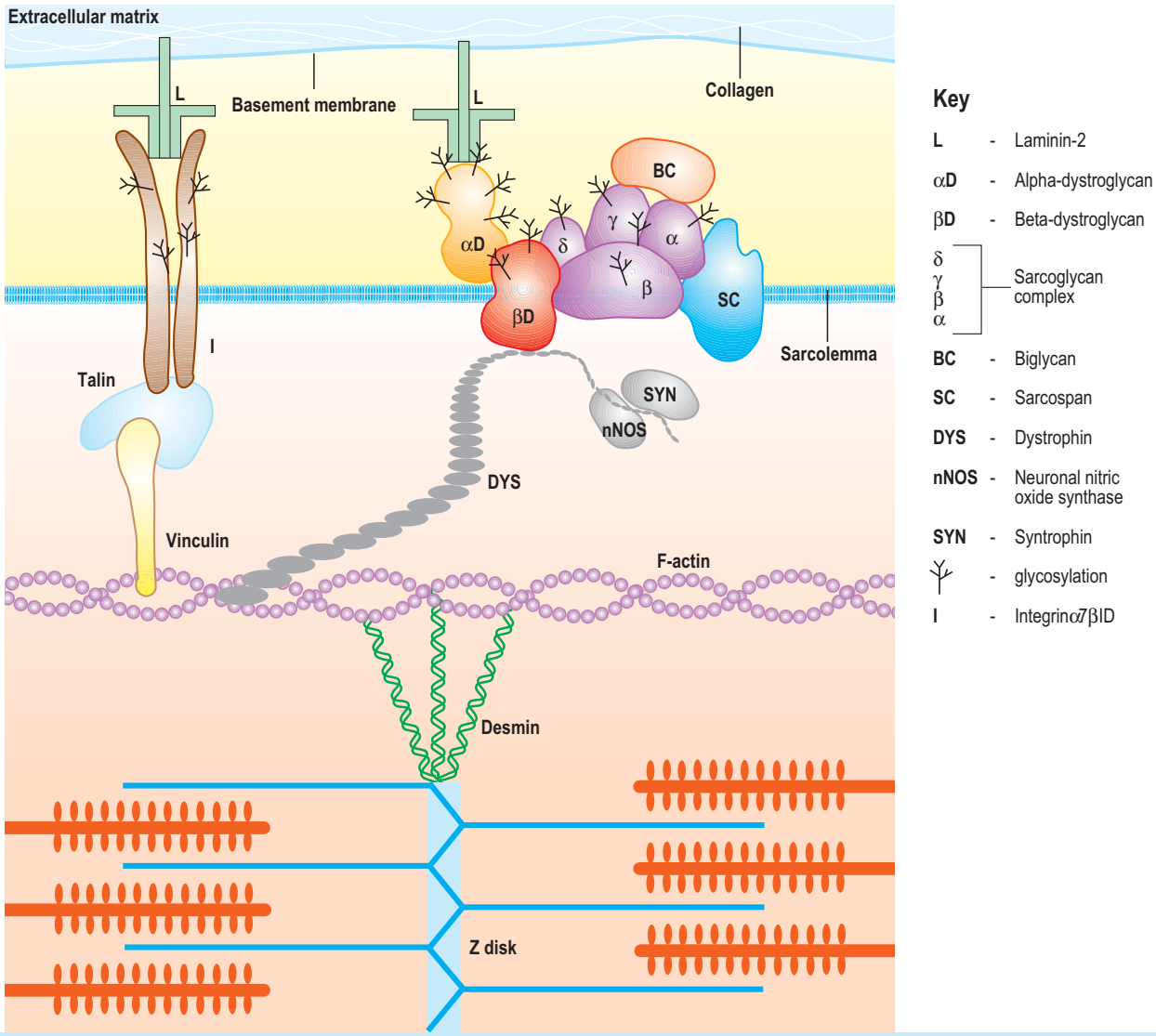


Fig. 5.14
Interconnections between the contractile apparatus, the dystrophin-associated complex (DAC) and the extracellular matrix. Further structural support is provided by integrin molecules that span the sarcolemma. Note nNOS makes up part of the DAC. In addition to a structural role, the DAC likely has a role in cell signaling.

including the muscle's fiber type composition and the level of fitness. Furthermore, the diet plays an additional role; for example, a fat-rich diet promotes oxidative energy production via FFAs,[67] thereby increasing the oxidative capacity of muscle[68] and sparing glycogen.[69] However, other substrates also influence the pathways employed during energy production: for instance, it has been shown that energy production can be steered towards that derived from glucose by the provision of additional glucose during exercise.[70]

Muscle heterogeneity

The ability of muscle tissue to perform efficiently in spite of very different types of exercise of varying duration is significantly enhanced by a muscle's heterogeneity. This functional flexibility is partly derived from the regulation of nervous control but also from the combined properties of the different fiber types.

Muscle fiber types

Fiber type differentiation There are important differences in the morphologic, physiologic, and biochemical properties of fibers both within and between muscles. These differences form the basis for the classification of fiber types. Better understanding of the expression patterns of groups of proteins within individual fibers has allowed refinement of fiber type classification in recent years. For example, myofibrillar proteins exist as different isoforms encoded by separate genes that are expressed in a myofiber type-specific

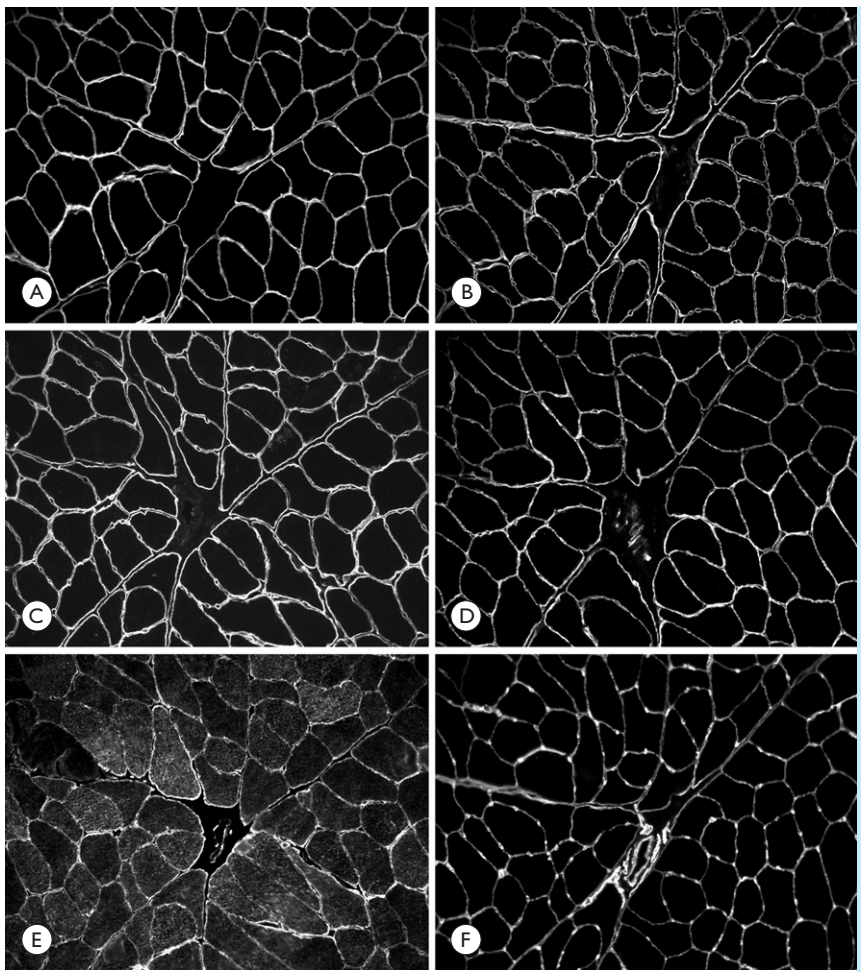


Fig. 5.15
Immunofluorescence labeling of serial 7 μm sections from the gluteus medius muscle of a normal Thoroughbred, showing proteins that link the contractile apparatus to the extracellular matrix. (A) Beta dystroglycan; (B) laminin alpha-2; (C) dystrophin; (D) integrin alpha-7-beta-1d; (E) desmin; (F) collagen IV. Working clockwise from desmin (E), contractile force is conveyed via dystrophin (C) to the dystrophin-associated complex (A and B) and ultimately to the extracellular matrix (F). Integrin alpha-7-beta-1d likely also plays a structural role. Compare with Figs 5.14 and 5.16. Note the capillaries located around each muscle fiber, and a central blood vessel that are also localized with the collagen IV antibody in (F).

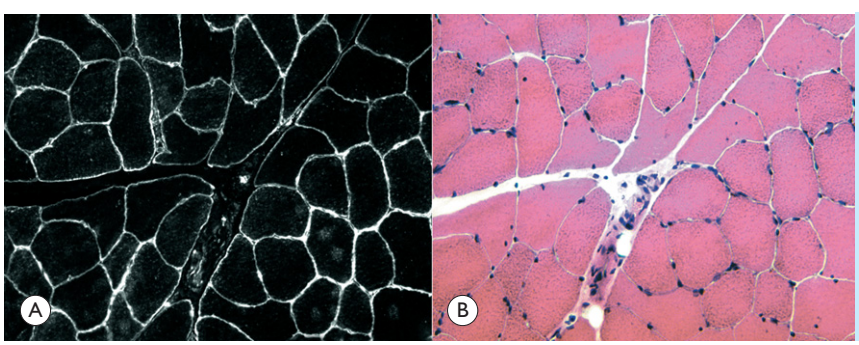


Fig. 5.16
Serial 7 μm (A) and 10 μm (B) sections from the gluteus medius muscle of a normal Thoroughbred. (A) Immunofluorescence labeling of neuronal nitric oxide synthase (nNOS). (B) Hematoxylin and eosin stain. Note the sarcolemmal distribution of nNOS, and compare with Fig. 5.14 and Fig. 5.15.

and co-ordinated manner.[71] Fiber types can best be differentiated by analyzing the specific myosin heavy chain (MyHC) isoform(s) expressed by each fiber, since MyHC composition closely reflects each fiber's phenotype.[20] Three MyHC isoforms have been characterized in adult equine skeletal muscles at the protein level: they are designated as types I, IIA and IIX[34] or IID[31] (henceforth IIX). The differential distribution of these MyHCs defines three pure fiber types containing a single isoform (types I, IIA and IIX) and two hybrid fiber types coexpressing two isoforms (I+IIA and IIAX) (Fig. 5.19). Hybrid IIAX fibers exist in equine locomotor muscles as a significant and stable population.[31,32] Recent studies have demonstrated either minimal (fewer than 0.6%)[72] or no expression of the MyHC-IIB isoform in the horse;[34] hence the fibers classified as type IIB in earlier studies are now more appropriately classified as type IIX.

Muscle fiber type properties Certain relevant differences between the various equine skeletal muscle fiber types

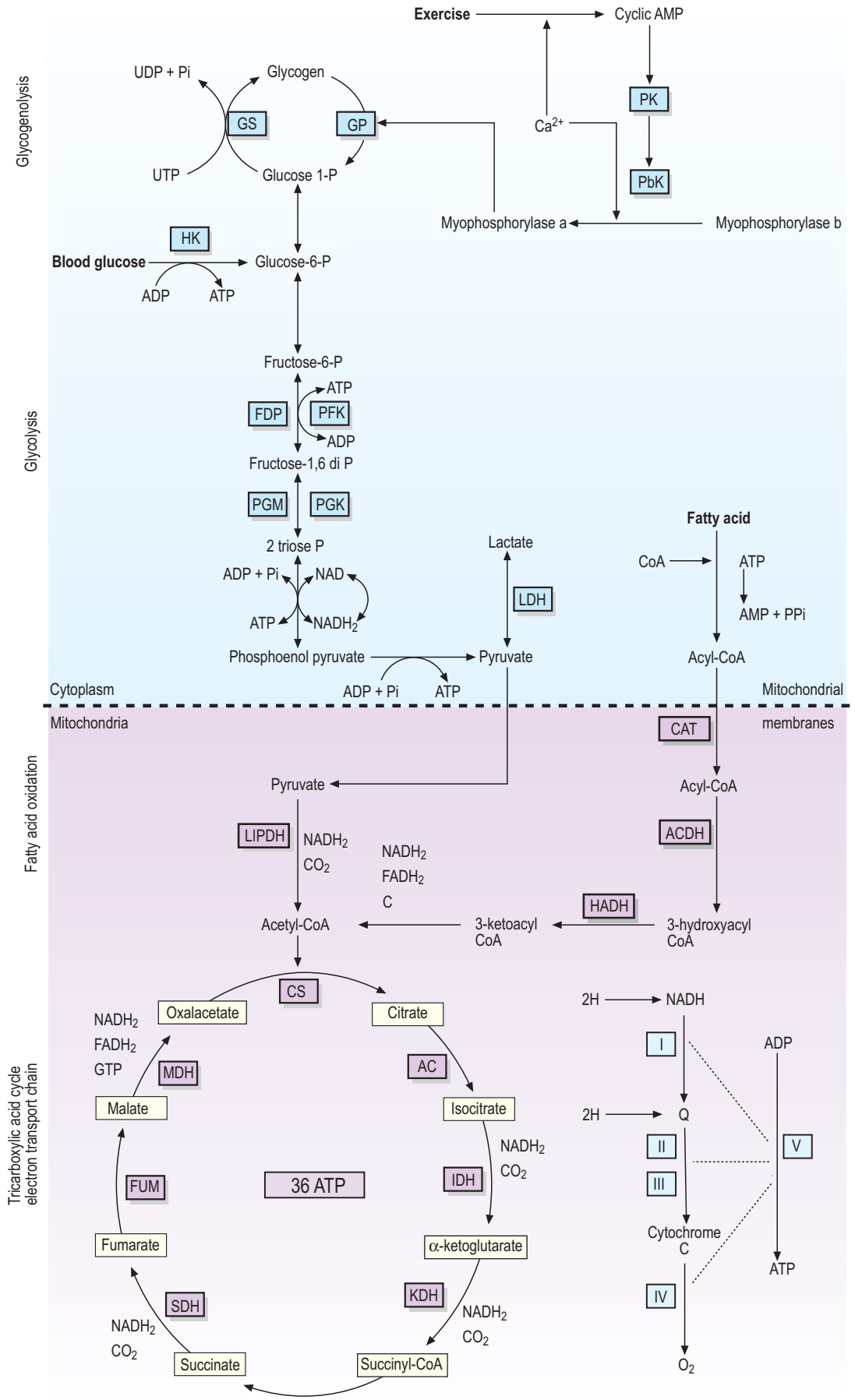


Fig. 5.17
Diagram summarizing the integration of metabolic pathways in muscle cells. Abbreviations: AC, aconitase; ACDH, acyl-CoA dehydrogenase; ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; CAT, carnitine acyltransferase; CoA, coenzyme A; CS, citrate synthase; FAD, flavin adenine dinucleotide; FDP, fructosediphosphatase; FUM, fumarase; GP, glycogen phosphorylase; GS, glycogen synthetase; GTP, guanosine triphosphate; HADH, 3-hydroxyacyl-CoA-dehydrogenase; HK, hexokinase; I, complex I; II, complex II; III, complex III; IDH, isocitrate dehydrogenase; IV, complex IV; KDH, ketoglutarate dehydrogenase; LDH, lactate dehydrogenase; LIPDH, lipoamide dehydrogenase; MDH, malate dehydrogenase; NAD, nicotinamide adenine dinucleotide; PbK, phosphorylase b kinase; PFK, phosphofructokinase; PGK, phosphoglycerate-kinase; PGM, phosphoglycerate-mutase; Pi, phosphate; PK, protein kinase; PPi, pyrophosphate; SDH, succinate dehydrogenase; V, complex V; UDP, uridine diphosphate; UTP, uridine triphosphate.

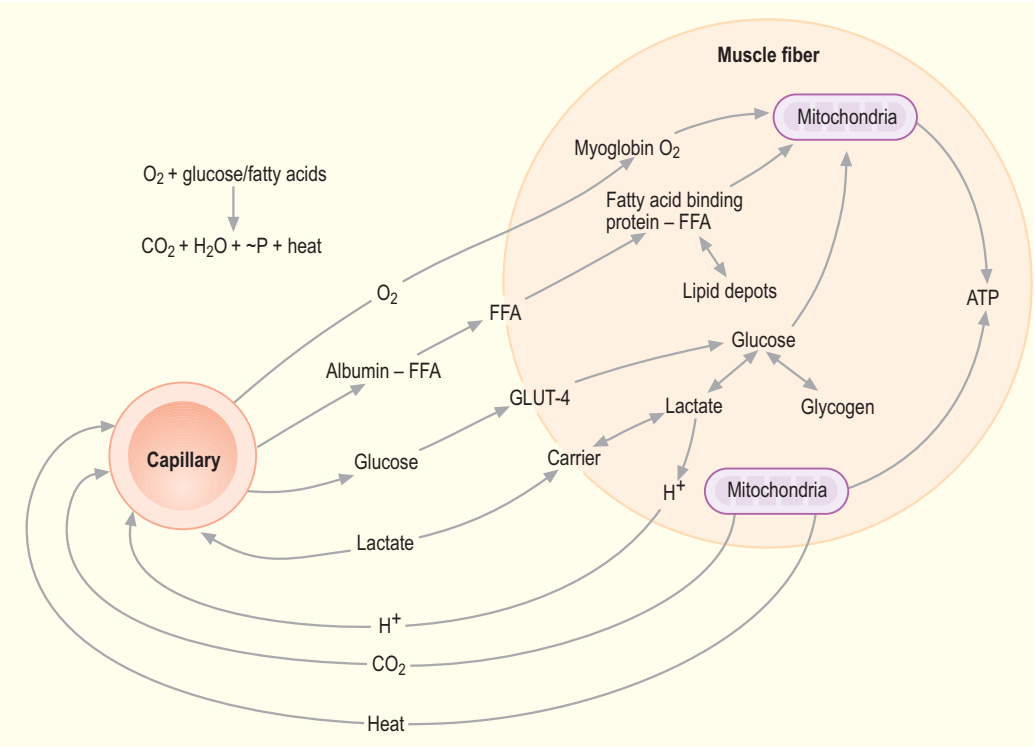


Fig. 5.18
Diagram of intermediary steps involved in the transfer of substrates to and from skeletal muscle fibers. FFA, free fatty acids; GLUT-4, glucose transport protein 4. (Adapted from Booth & Baldwin[64].)

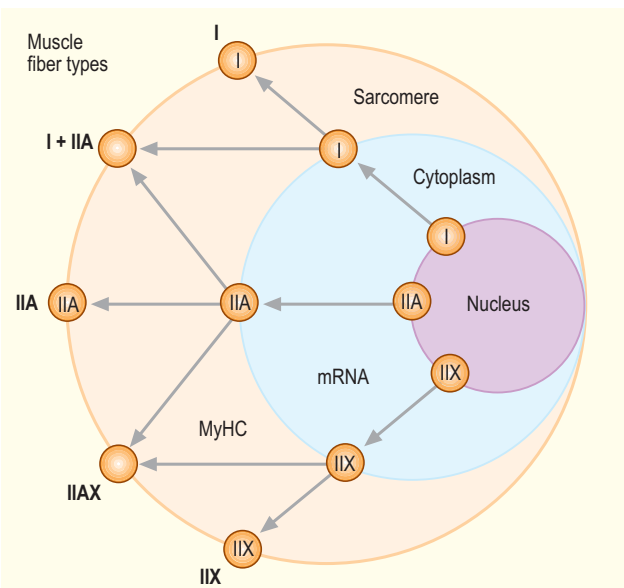


Fig. 5.19
Diagram illustrating the relationship between muscle fiber phenotype and the regulation of gene expression for the separate myosin heavy chain isoforms in adult horse skeletal muscle. Horses only express three myosin heavy chain isoforms: one slow or type I and two fast termed type IIA and type IIX. The differential expression of these isoforms defines three major fiber types, each containing a single isoform (i.e. types I, IIA and IIX) and two intermediate hybrid fiber populations containing either slow and fast IIA isoforms or the two fast isoforms.

are illustrated in Figure 5.20 and summarized in Table 5.1. When studied in combination, these differences allow more objective delineation (Fig. 5.21) and represent the considerable interdependence of contractile, metabolic and morphologic features. Type I fibers have a MyHC isoform that hydrolyzes ATP slowly, resulting in a slow crossbridge cycle, together with a small cross-sectional area, a high number of capillaries and a high oxidative capacity. However, their glycolytic capacity and glycogen content are relatively low. Together, these properties make type I fibers highly efficient and economical in producing slow repetitive movements and sustaining isometric force, but not significant power generation. In contrast, type II fibers have MyHC isoforms that create fast crossbridge cycling and therefore develop force rapidly. Within the type II group, type IIX fibers have a maximal velocity of shortening that is three times higher than that of IIA fibers.[14] Hence, IIX fibers are adapted for high power outputs for a limited time because they have a low oxidative capacity and limited oxygen availability (as reflected by their large cross-sectional area and relatively low capillary supply). Type IIA fibers, however, have a considerable number of both capillaries and mitochondria and rely on glycolytic and oxidative metabolism; they are therefore able to sustain high power outputs for longer than IIX fibers. Hybrid IIAX fibers are intermediate in their properties.[20] Although classified according to the MyHC composition, it is important to remember that other protein isoforms vary, each closely correlating with the fiber's function and with one another. Furthermore, fibers also differ with respect to other factors, such as the availability of high-energy phosphate,[74] GLUT-4

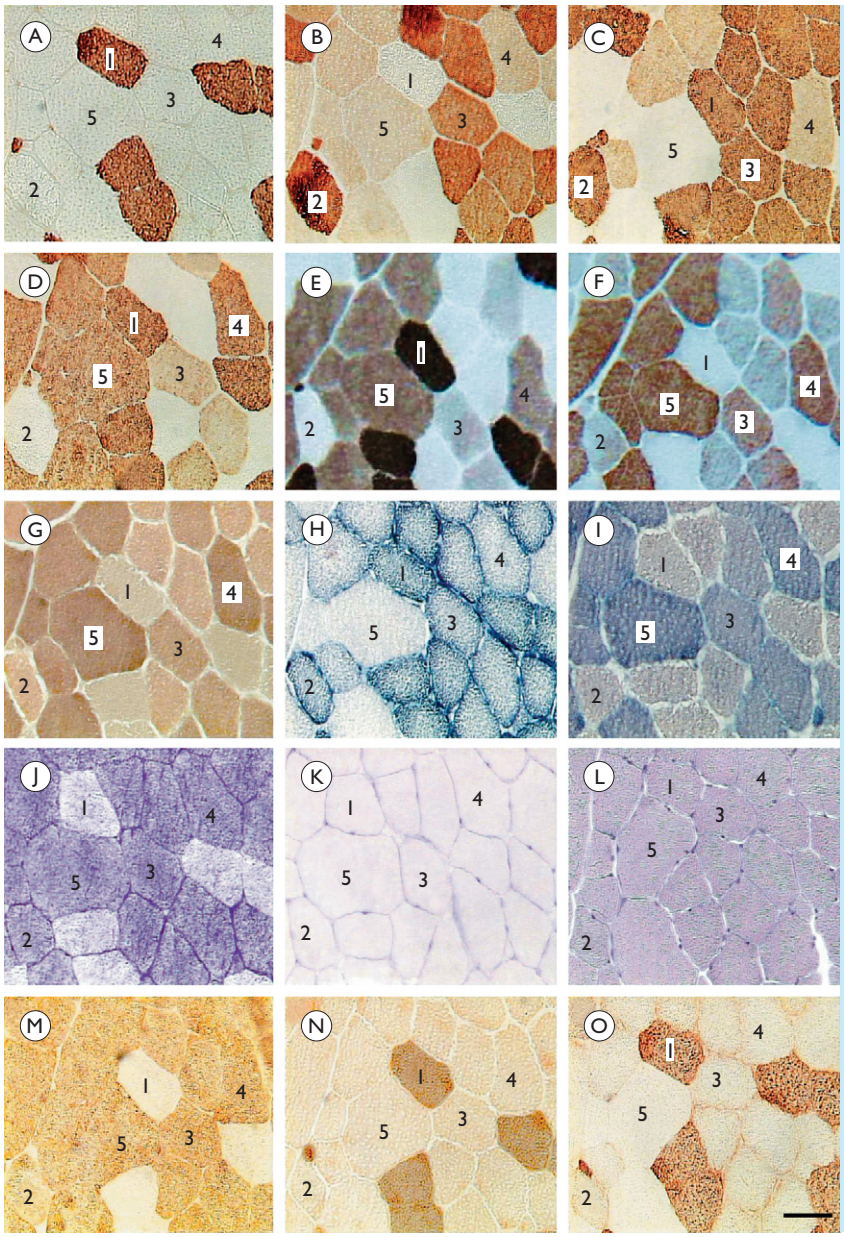


Fig. 5.20
Serial cryosections of adult horse M. gluteus medius stained by immunohistochemistry, enzyme histochemistry and histology. (A–D) Sections were stained with a number of monoclonal antibodies against specific myosin heavy chain (MyHC) isoforms: BA-D5 (A, anti MyHC-β/slow), SC-71 (B, anti MyHC-IIA), BF-35 (C, anti MyHCs β/slow and IIA), and S5-8H2 (D, anti MyHCs β/slow and IID/X). (E–G) Sections were assayed for myofibrillar actomyosin adenosine triphosphatase activity after acid (pH 4.4, E) and alkaline (pH 10.45, F) preincubations, and by Blanco and Sieck's quantitative histochemical procedure (G).[73] (H–I) Sections assayed for succinate dehydrogenase and (H), glycerol-3-phosphate dehydrogenase activities (I) and periodic acid-Schiff (PAS) for selective staining of glycogen (J). (K–L) PAS with α-amylase digestion, for visualizing capillaries (K) and hematoxylin and eosin for visualizing myonuclei (L). (M–O) Sections were stained by immunohistochemistry with monoclonal antibodies specific against SR Ca^{2+}-ATPase (SERCA) isoforms and phospholamban: CaF2-5D2 (M, anti-SERCA1a), MA3-910 (N, anti-SERCA2a) and 05-205 (O, antiphospholamban). The fibers labeled 1, 2, 3, 4 and 5 are types I, IIA, IIAx, IIaX and IIX, respectively. Calibration bar 50 μm.

protein expression (Fig. 5.22),[64] the calcium sensitivity of force production[15] and carnosine and taurine contents.[75–77]

Muscle fiber recruitment Although muscle can be separated into individual fiber types, the basic functional unit of skeletal muscle remains the motor unit (see section above on general muscle physiology). Motor units are commonly classified according to the MyHC profile of their constituent fibers (hence I, IIA and IIX; Fig. 5.23). This is possible because fibers within a single motor unit show relatively homogeneous, although not identical, biochemical and histochemical properties.[78] Although the motor unit's structure, function and hence role in motor control have been studied extensively in experimental animals, they have not been widely studied in larger mammals. However, specific muscle fiber type recruitment has been examined in horses by observing glycogen depletion patterns during and after exercise of varying intensity and duration (Fig. 5.24).[3] In horses, it appears that motor units are selectively recruited in a specific pattern that changes according to the gait, in addition to the intensity and duration of exercise. For the maintenance of posture, only type I motor units are recruited. As intensity and duration increase, further motor units are recruited, in the rank order: I → IIA → IIAX → IIX. Type IIX motor units are only recruited at near-maximal exercise intensity (sprint and jumping) and during extremely prolonged submaximal exercise.[63]

Muscle fiber type distribution between and within muscles Fiber-type composition varies extensively between muscles and in accordance with the functional requirements of the muscle.[79] For example, significant components of the forelimb musculature consist of postural type I fibers, while propulsive muscles of the hindlimb contain a high proportion

Table 5.1 Quantitative fiber type features of equine skeletal muscle. Values are mean ± SE of 208 individual fibers.

	Muscle fiber types[1]				
	I	**IIA**	**IIAx**	**IIaX**	**IIX**
No. of fibers	51	80	25	25	27
Anti-MyHC monoclonal antibodies[2]					
BA-D5 (OD)	0.60 ± 0.02 b		0.34 ± 0.02 a		
SC-71 (OD)	0.30 ± 0.02 a	0.52 ± 0.03 d	0.46 ± 0.02 c	0.34 ± 0.01 b	0.34 ± 0.01 b
BF-35 (OD)	0.47 ± 0.03 c	0.49 ± 0.03 d	0.46 ± 0.03 cd	0.36 ± 0.02 b	0.30 ± 0.02 a
S5-8H2 (OD)	0.44 ± 0.02 d	0.33 ± 0.01 a	0.37 ± 0.02 b	0.41 ± 0.01 c	0.41 ± 0.01 c
Myofibrillar ATPase activity[3]					
Ac-mATPase (OD)	0.77 ± 0.02 d	0.28 ± 0.03 a	0.34 ± 0.03 b	0.47 ± 0.02 c	0.50 ± 0.02 c
Alk-mATPase (OD)	0.27 ± 0.02 a	0.37 ± 0.03 b	0.46 ± 0.04 c	0.52 ± 0.02 d	0.54 ± 0.02 d
Qu-mATPase (OD/min)	0.30 ± 0.02 a	0.39 ± 0.02 b	0.42 ± 0.01 c	0.45 ± 0.01 d	0.51 ± 0.01 e
Metabolic properties[4]					
SDH (OD/min)	0.49 ± 0.02 d	0.46 ± 0.03 c	0.37 ± 0.02 b	0.34 ± 0.02 b	0.24 ± 0.03 a
GPD (OD/min)	0.33 ± 0.02 a	0.36 ± 0.03 b	0.41 ± 0.01 c	0.46 ± 0.01 d	0.47 ± 0.01 d
PAS (OD)	0.34 ± 0.02 a		0.45 ± 0.03 b		
Fiber size, capillaries and myonuclei[5]					
CSA (μm^2)	3124 ± 723 a	3339 ± 763 b	4623 ± 807 c	5039 ± 1293 c	7635 ± 2930 d
cap/10^3 μm^2	2.06 ± 0.94 b	1.96 ± 0.57 b	1.60 ± 0.41 ab	1.38 ± 0.21 a	1.23 ± 1.07 a
nuc/10^3 μm^2	2.26 ± 0.65 b	2.32 ± 1.02 b	1.65 ± 0.36 ab	1.44 ± 0.78 a	1.11 ± 0.70 a
Anti-SERCA and PLB antibodies[6]					
CaF2-5D2 (OD)	0.33 ± 0.03 a		0.44 ± 0.03 b		
MA3-910 (OD)	0.48 ± 0.02 b		0.38 ± 0.03 a		
05-205 (OD)	0.54 ± 0.03 b		0.37 ± 0.02 a		

[1] Hybrid I + IIA fibers are not considered in this analysis; IIAx = hybrid fibers with a predominant myosin heavy chain type IIA content; IIaX = hybrid fibers with a predominant myosin heavy chain type IIX isoform.
[2] See Fig. 5.20's legend for origins and specificities of antibodies.
[3] *Ac-mATPase* myofibrillar ATPase after acid (pH 4.45) preincubation; *Alk-ATPase* myofibrillar ATPase after alkaline (pH 10.45) preincubation; *Qu-mATPase* quantitative myofibrillar ATPase activity (pH 7.6).
[4] *SDH* Succinate dehydrogenase activity; *GPD* glycerol-3-phosphate dehydrogenase activity; *PAS* periodic acid-Schiff.
[5] *CSA* Cross-sectional area; *cap* number of capillaries; *nuc* nuclear number.
[6] *SERCA* Sarco(endo)plasmic reticulum Ca^{2+}-ATPase; *PLB* phospholamban; see reference[20] for sources and specificities of these antibodies.
Within a row, means with different letters are statistically different ($P < 0.05$), where *a* expresses the lowest value and e the highest. In the absence of significant differences between type II fibers, values are presented as pooled means for all type II fibers (*n* = 157 fibers).
OD Optical density.

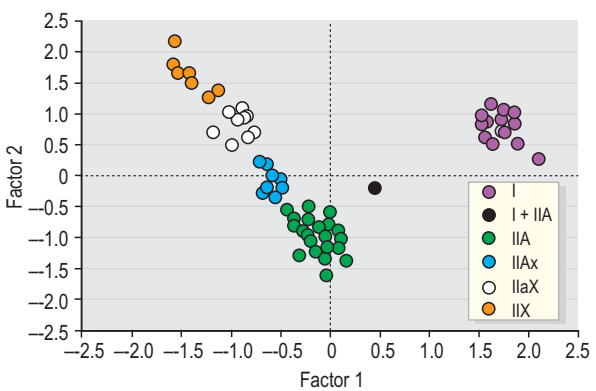


Fig. 5.21
Principal component analysis of muscle fiber type features in a representative sample (*n* = 82 fibers) to show graphically the spatial discrimination of myosin heavy chain (MyHC)-based fiber types. This scatter plot shows the spatial distribution of a set of equine muscle fibers upon the basis of muscle variables included in Table 5.1; this analysis resulted in an optimal discrimination (100%) of all muscle fiber types; Factor 1 axis discriminates between type I (right) and type II (left) fibers, whereas Factor 2 axis discriminates type IIA (bottom) and IIX (top) fibers.

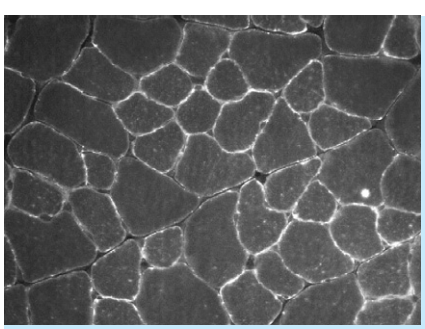


Fig. 5.22
Transverse section of rat extensor digitorum muscle samples labeled by immunohistochemistry with a monoclonal antibody to GLUT-4 (glucose transport protein). Note the higher intensity of staining in the periphery of the smaller fibers (presumably types I and IIA) compared with the larger ones (presumably IIX and IIB).

of fast-twitch type II fibers (Fig. 5.25A,B). Variation is also seen between muscles belonging to the same synergic group. For example, most of the triceps muscle mass consists of type II fibers, but the medial head is composed of nearly all type I fibers.[80] Significant regional variations in fiber composition within a muscle have also been reported in several horse

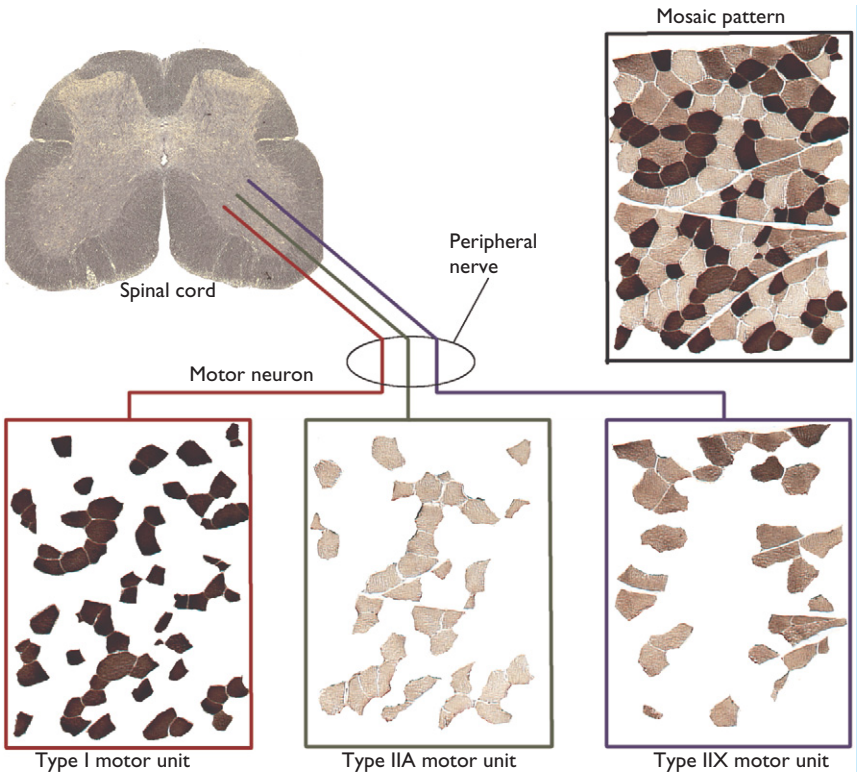


Fig. 5.23
Diagram showing the spatial distribution of muscle fibers integrating three different motor units classified according to myosin heavy chain isoform expression as types I, IIA and IIX. Note how muscle fibers within each motor unit are dispersed between those of others resulting in the characteristic mosaic or checkerboard distribution seen in transverse section.

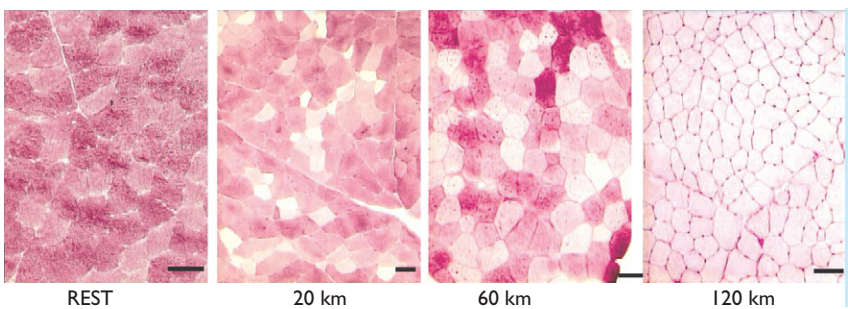


Fig. 5.24
Transverse sections of gluteus medius muscle biopsies (6 cm depth) to show muscle glycogen depletion patterns in a horse competing in an endurance ride of 120 km. Note the increase in the number of myofibers without glycogen when the intensity and duration of the exercise increase. Bars, 75 μm.

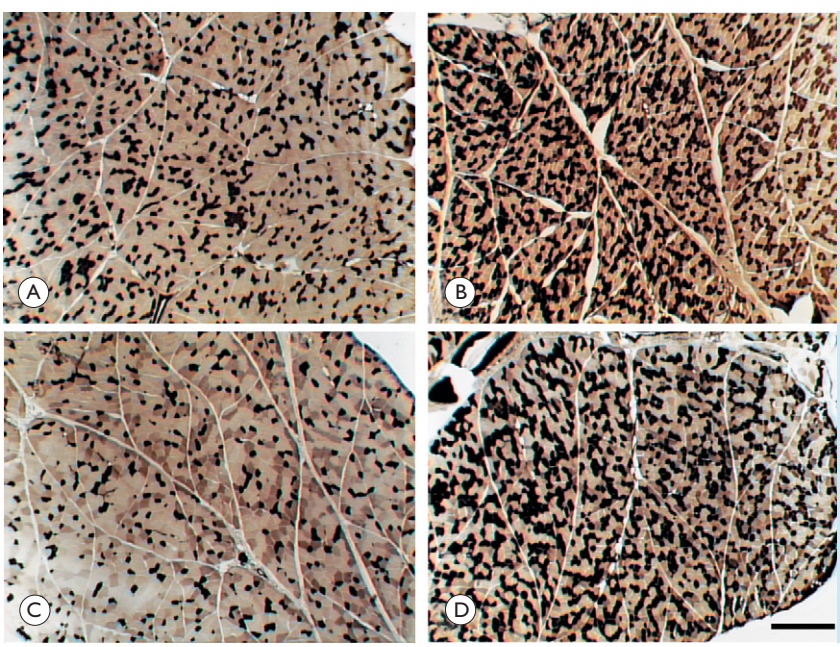


Fig. 5.25
(A, B) Transverse sections stained for myofibrillar adenosine triphosphatase activity after acid preincubation (pH 4.4) demonstrating the differential muscle fiber type composition in two locomotor muscles with different functions: M. semitendinosus (A) vs M. rhomboideus cervicis (B). Note the higher percentage of type I fibers (black staining) and the lower proportion of types IIA (white) and IIX fibers (gray) in the rhomboideus muscle compared with the semitendinosus muscle. (C, D) Transverse sections stained with myofibrillar adenosine triphosphatase activity after acid preincubation
(pH 4.4) from two muscle samples removed from the equine gluteus medius muscle at two different sampling depths: 2 cm (C) vs 8 cm (D). Note the higher percentage of type I fibers and the lower proportion of type IIX fibers in the deeper region of the muscle than in the superficial region. Scale bar, 1000 μm.

muscles.[8,9,24,25,32,48,49,81] Most locomotory muscles have greater numbers of oxidative type I and type IIA fibers in the deep portions and a predominance of glycolytic type IIX in more superficial portions (Fig. 5.25C,D). This compartmentalization reflects the relationship between structure and function: the deeper regions appear best suited for posture maintenance and low-level but longer duration muscular activity, whereas the more superficial regions are involved with short-duration, rapid, propulsive force generation. In general, groups studying equine muscle physiology have formed conclusions based on data derived from a single biopsy sample site (see reference[3] for review of relevant citations); however, it is apparent that this approach may be too simplistic. Several studies by the first author's group have demonstrated a greater muscular response to training in the deeper region of the M. gluteus medius compared with more superficial regions.[82–84]

Relationship to performance Some studies in horses have shown that performance is correlated with selected muscle characteristics (see reference[3] for a review). Unsurprisingly, endurance capacity is correlated with (1) high percentages of type I and IIA fibers[85] and (2) high activities of oxidative enzymes,[86] whereas sprint capacity is correlated with high percentages of type II fibers.[87] It is therefore feasible to differentiate the endurance potential of horses based on the fiber type composition of certain muscles,[88] although different conclusions have been obtained in Thoroughbreds[81] and Trotters.[89,90] Nevertheless, trotting speed is highly dependent on the ability of muscle to produce energy via anaerobic glycolysis.[89] Interestingly, some myofiber properties are correlated with kinematic profiles. For example, stride length and frequency are positively correlated with both the percentage of IIA fibers[91] and fiber size.[92] The stance time of the stride is inversely correlated with the percentage of IIX fibers[93] and fiber diameter.[92] Furthermore, some relevant muscular adaptations to training occur with concomitant modifications in the temporal characteristics of the trot.[94]

Control and regulation

Myogenic factors Multiple factors, both myogenic and non-myogenic in origin, regulate the expression of proteins that comprise the various muscle-specific organelles in each muscle fiber (Fig. 5.26) and, in combination, these factors also regulate the percentage of individual fiber types found within each muscle. During development and maturation (and regeneration following injury – see Chapter 6) these factors change, resulting in a significant alteration in protein expression. However, generally, the myogenic lineage from which a muscle fiber develops defines the ultimate fiber type.[71] All fibers during embryonic development express an embryonic MyHC isoform. At birth, some fibers are found to express type I MyHC: these are destined to become mature type I fibers in the adult. Other fibers express a neonatal MyHC isoform that is gradually replaced by either IIA or IIX, or both MyHCs: these subsequently become type II fibers in the adult. Horse skeletal muscle has also been found to express the α-cardiac MyHC isoform,[31] but its significance is unclear. The influence of genetic factors on equine muscle fiber types is clearly illustrated by dramatic variations observed between different breeds of horses (Fig. 5.27)[79,95,96] and between separate genealogical bloodlines within the same breed.[97] Furthermore, there is a tendency for fiber type ratios (type I : type II) to be inherited.[87,98] During growth and maturation, muscle fibers change in their size and histochemical properties: there is a gradual conversion of fast to slow phenotype that is especially pronounced in the first year postpartum,[99] but that may continue until about 6 years of age[100–102] or older.[103]

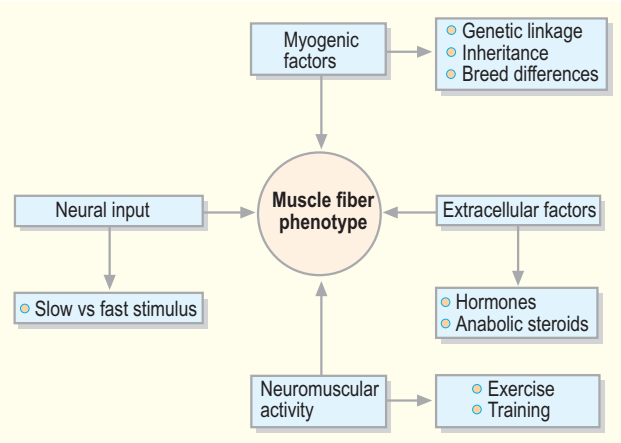


Fig. 5.26
Schematic diagram summarizing regulation of muscle fiber type. Fiber type is determined by a combination of four factors: (1) the myogenic lineage from which the muscle fiber developed; (2) the innervating motoneuron that regulates fiber type via patterns of activity and basal activity and/or via other mediators such as neurotrophic factors; (3) activity levels influenced by exercise and training; and (4) extracellular factors. The extracellular factors include hormones (e.g. thyroid hormone and growth hormone), growth factors (e.g. insulin-like growth factor and anabolic steroids), substrate availability (e.g. β-guanidinoproprionic acid), and various other currently unidentified factors such as certain extracellular matrix proteins.

Non-myogenic factors In addition to the underlying myogenic lineage, additional factors influence muscle fiber phenotype. Muscle fibers are syncyteal (multinucleated), with their myonuclei arranged peripherally throughout the length of the fiber. The volume of cytoplasm associated with a single nucleus is known as the myonuclear domain.[104] Hence, each individual nucleus regulates the expression of proteins within a particular cytoplasmic region. In horses, myonuclear domains of type I fibers are smaller than those of IIX fibers, but similar in size to those of IIA fibers (Fig. 5.28).[20] These observations have been related to the different activity patterns of the various fiber types:[105] the more active type I fibers have a higher rate of both protein synthesis and protein turnover than the less frequently recruited faster fiber types.

Neural input also has a significant influence on muscle fiber growth and type (fast/slow, glycolytic/oxidative) through altered regulation of gene expression.[106] This is convincingly demonstrated by dramatic changes observed in muscles follow-

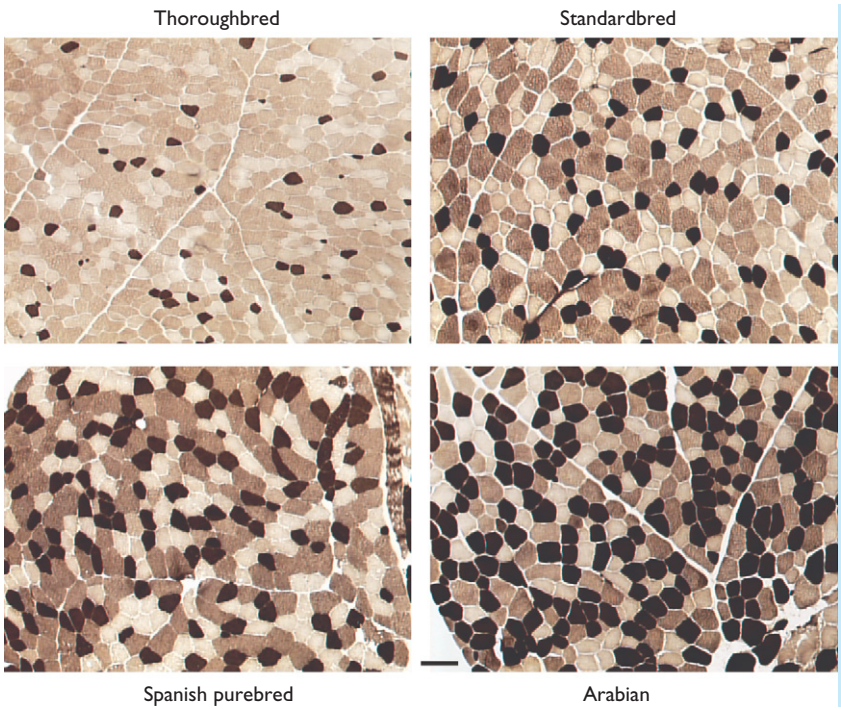


Fig. 5.27
Transverse sections of M. gluteus medius specimens stained with myofibrillar adenosine triphosphatase after acid preincubation (pH 4.4), removed at the same depth, from four different breeds of athletic horse. Note how the percentage of type I (oxidative) fibers and the fiber size increases from the fastest breed (Thoroughbred) towards the slower, more endurance-suited breed (Arabian). Bar scale, 150 μm.

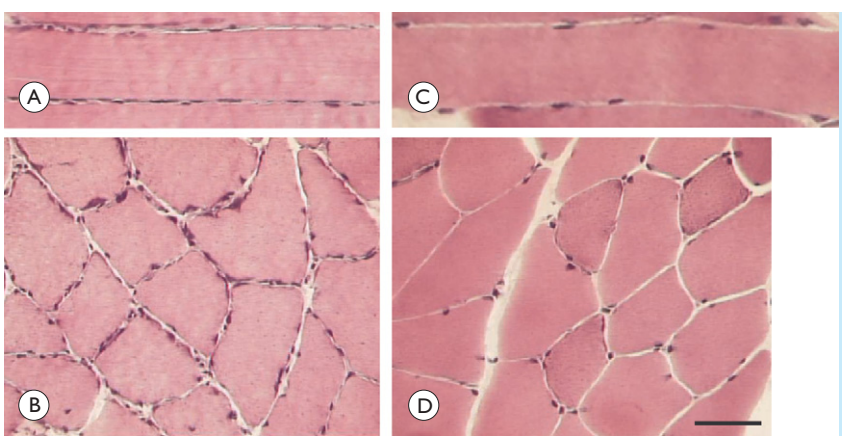


Fig. 5.28
Representative images of longitudinal (A and C) and transverse (B and D) sections stained with hematoxylin and eosin of a muscle containing predominantly slow fibers (type I) (M. sacrocaudalis dorsalis medialis, A and B) compared with a muscle containing predominantly fast-contracting (type II) fibers (superficial region of the M. longissimus lumborum, C and D). Note the increase in myonuclear number in the fibers from the slow-contracting muscle compared with the fast-contracting muscle. Scale bar, 50 μm.

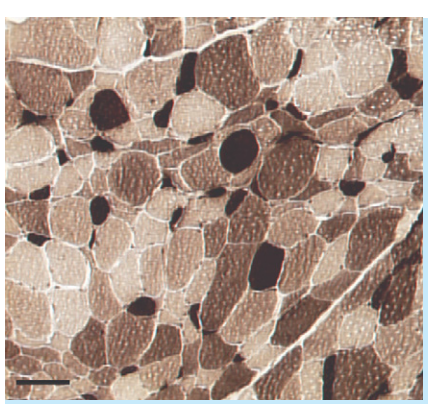


Fig. 5.29
Transverse section of a M. vastus lateralis muscle sample from a horse with denervation atrophy (femoral paralysis) stained with myofibrillar adenosine triphosphatase after acid preincubation. Note selective angular atrophy of some type I (black) and type IIA (white) fibers, while other type I and IIA fibers, presumably belonging to other motor units, are of normal size. Bar, 50 μm.

ing denervation (Figs 5.10, 5.29). Such regulation is particularly evident in slow type I fibers, because their basal neurogenic dependence is significantly greater than faster fiber types (type I > IIA > IIX).[51] Additional factors that are known to influence myofiber diversity include hormonal and drug (anabolic steroid)-induced changes,[3,100–102] that may vary depending on the underlying fiber type.[107] Of particular interest, and as discussed in the sections that follow, neuromuscular (contractile) activity associated with exercise and training has a significant impact on fiber type adaptation and the expression of fiber-specific protein isoforms.

Muscular responses to exercise

When aerobic metabolism can meet energy demands (during submaximal exercise), oxygen uptake correlates with increas-

ing speed.[65] However, the slope of the linear relationship may vary according to the load, incline, track surface and ambient temperature.[65] At a certain point energy demand outstrips oxygen uptake and the shortfall must be met by anaerobic metabolism.[65] Muscle fatigue may occur during either aerobic or anaerobic exercise: in the following sections, we consider the major metabolic changes that occur within muscle, that are believed to contribute to the development of fatigue.

Aerobic exercise

Muscle and liver glycogenolysis starts to occur soon after the start of aerobic exercise. Glucose derived from the liver is subsequently transported into myofibers to join the glycolytic cascade via glucose-6-phosphate formation (see Fig. 5.17). However, although elevated glucose-6-phosphate concentrations have been detected after submaximal exercise in horses,[108] circulating epinephrine (adrenaline) released during exercise stimulates the release of FFAs from adipose tissue and/or liver stores, which partially inhibit glucose utilization during moderate-intensity exercise.[109] Nevertheless, during prolonged submaximal exercise, blood glucose may still account for up to 25% of the total energy output.[63] This reliance on glucose derived mainly from the liver results in an early sparing of muscle glycogen. As energy demands increase, higher rates of pyruvate oxidation tend to cause a further shift towards FFA β-oxidation. The overall effect is that muscle glycogenolysis declines over time during aerobic exercise, whereas FFA oxidation increases.[66]

Although lipids are the predominant fuel utilized during prolonged submaximal exercise, fatigue occurs long before the complete metabolism of lipid deposits.[3] At submaximal workloads, fatigue has been associated with intramuscular glycogen depletion (Fig. 5.30)[63] because FFA oxidation cannot produce sufficient ATP without a source of pyruvate. During prolonged activity, glycogen depletion patterns occur in parallel with the progressive recruitment of fiber types, i.e. initially in type I fibers, then in IIA and finally in glycolytic IIX (see Fig. 5.24). Therefore, muscular fatigue does not occur at the same time in all fibers but in a progressive manner that results in gradual compromise to performance. Following exercise, glycogen repletion occurs in the reverse order (i.e. IIX → IIA → I) and may take up to 72 hours,[110] or sooner with the administration of dextrose[111] or nandrolone.[112]

Although glycogen depletion appears to play a major role in fatigue onset during aerobic exercise, a variety of other factors are also implicated, including AMP deamination, hyperthermia, dehydration, electrolyte depletion and lack of motivation.[63,113,114] The onset of fatigue itself may be hard to assess objectively but recent evidence suggests that electromyography may prove useful in the experimental setting.[36]

Anaerobic exercise

The effects of high-intensity exercise on horse skeletal muscle and development of fatigue have been comprehensively reviewed by Snow & Valberg.[3] In recent years, further research has confirmed many previous observations and provided new insight on mechanisms underlying the onset of fatigue. The functional demands imposed by high-intensity exercise require the recruitment of most motor units within a given muscle; at this time, intramuscular glycogen and blood glucose act as the predominant fuels to replenish ATP during anaerobic glycolysis. In addition, some ATP is derived from the deamination of adenosine nucleotides. In contrast to aerobic metabolism, there is relatively little reliance on FFA oxidation.

Lactate accumulation and pH decline Limitations imposed by oxidative metabolism result in greater amounts of the end-product of glycolysis (i.e. pyruvate) being converted to lactate rather than acetyl-CoA; in the process, NAD is used to regenerate more ATP. As a consequence, muscle lactate concentrations increase during anaerobic exercise.[89,90,115–117] This rise is correlated with the proportion of type II fibers within muscles.[118] Initially, intracellular lactate accumulation is removed from the cell by active transport into the blood (see Figs 5.18, 5.31).[119] Saturation of this mechanism results in a sudden exponential rise in intracellular lactate accumulation, known as the anaerobic threshold, that generally occurs when the plasma lactate concentration reaches about 4 mmol/L.

The rise in intracellular lactate, together with free H^+ ions, results in a significant reduction in cytoplasmic pH[120] that has been suggested to be the major cause of fatigue during anaerobic exercise (Fig. 5.30).[63] Muscle pH may decline to as low as 6.25–6.50 and lead to impairment of both structure and function. Significant disturbance to both mitochondrial and SR ultrastructure has been documented in horses that exhibit

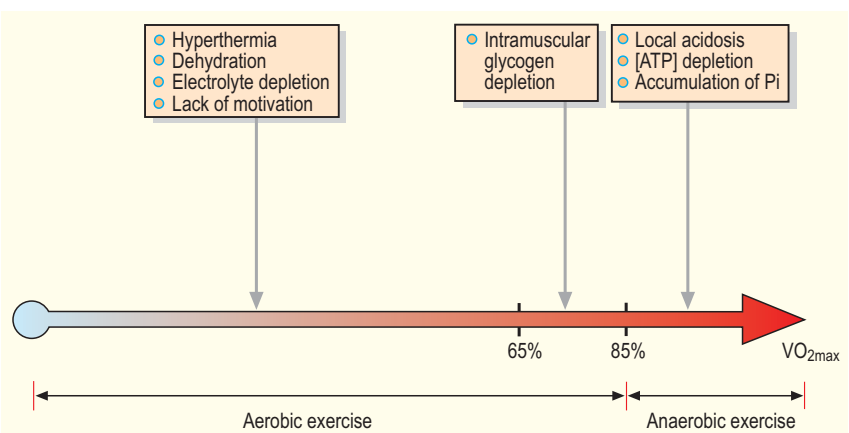


Fig. 5.30
Schematic diagram summarizing the main causes of fatigue during or after exercise of different intensity and duration. Intramuscular glycogen depletion is considered to be the main cause of fatigue during aerobic exercise (work loads between 65% and 85% of VO_{2max}). At lower exercise intensities, however, hyperthermia, fluid and electrolyte depletion and poor motivation have been suggested to be the primary factors in initiating fatigue. Causes of fatigue during supramaximal anaerobic exercise include local acidosis, ATP depletion and accumulation of pyrophosphates (Pi).

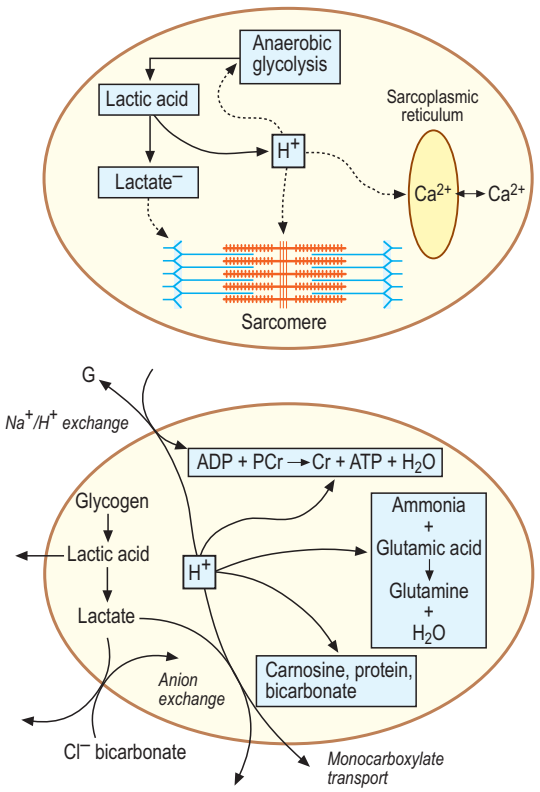


Fig. 5.31
Schematic diagrams illustrating intramuscular acidosis and buffering capacity of muscle (according to Hyyppä & Pösö).[118] (Upper) Performance inhibition (dotted arrows) caused by the accumulation of protons and lactate anions. (Lower) Diagram summarizing the major regulatory mechanisms that control intramuscular pH (explained in reference[118]).
PCr = phosphocreatine; Cr = creatine.

fatigue during maximal exercise.[121] Low pH leads to dysfunction of the excitation–contraction coupling mechanism, due to impairment of the SR calcium release channel (RYR1), together with decreased reuptake of calcium into SR during relaxation.[120] Low pH also inhibits the glycolytic enzyme phosphofructokinase, thereby diminishing ATP production.[118]

A fall in cytoplasmic pH is partially overcome by a buffering system within myofibers (Fig. 5.31). Dynamic buffering of H^+ occurs during the hydrolysis of phosphocreatine in reactions catalyzed by creatine kinase and by glutamine synthetase; static physicochemical buffering is provided by various proteins, bicarbonate, inorganic phosphate and carnosine.[118,122] Race horses have been shown to have a higher muscle buffering capacity than humans,[123] thought to be associated with their myofibers having high carnosine concentration.[76] Muscle carnosine content appears to be influenced by β-alanine bioavailability[124] and is greatest in glycolytic IIX fibers.[76,124]

Nucleotide depletion Since initial observations by Snow and co-workers,[125] numerous studies confirm a decline in muscle ATP concentration during anaerobic exercise,[17,74,89,126] suggesting that ATP regeneration can be insufficient to meet energy demands.[76] Depletion of muscle ATP concentration has also been implicated as a primary cause of fatigue during maximal effort in horses,[63] and a correlation between muscle nucleotide stores after racing and performance has recently been reported.[74] The fall in ATP occurs in parallel with a rise in IMP concentration,[74,126] the latter being a particularly prominent response in equine muscle due to high underlying AMP deaminase activity.[127] High concentrations of IMP within muscle therefore act as a marker for depletion of total nucleotide stores, given that reamination of IMP to ADP and finally restoration of ATP is a slow process, that may take up to 1 hour.[125] ATP depletion and formation of IMP within muscles working maximally are closely correlated with the production of ammonia,[90,115] uric acid[126] and allantoin,[63] all of which may be detected in the plasma. Theoretically, low levels of nucleotides in some fibers would impair the optimal functioning of all ATP-dependent muscular processes. However, because nucleotide depletion occurs concurrently with a rise in muscle lactate and free H^+ concentrations,[74] it is still unclear which of these two mechanisms plays the more significant role in the development of fatigue.

Glycogen depletion Muscle glycogen concentration declines rapidly during maximal exercise[117,126] to an extent that varies between 30% and 50% depending on the number and frequency of exercise bouts.[125] Glycogen depletion occurs most rapidly in the glycolytic low oxidative IIX fibers and occurs simultaneously with lactate formation.[3] Although glycogen depletion is not considered to be a major factor contributing to fatigue during anaerobic exercise,[63] it has recently been demonstrated that decreased muscle glycogen availability diminishes anaerobic power generation and hence the capacity for high-intensity exercise in horses.[128,129]

Other muscular changes Other factors that, though not necessarily contributing directly to fatigue, may result in reduced performance are reviewed by Snow & Valberg[63] and include increased intracellular potassium concentrations,[130] a stochiometric modification to the proportions of free carnitine and acetylcarnitine,[131] increased formation of alanine from pyruvate[132,133] and significant changes in the free intracellular amino acid pool.[134] Additional factors that are implicated include a reduction in calcium SR uptake through decreased Ca^{2+}-ATPase activity[135] and a rise in muscle temperature occurring during high-intensity exercise.[120]

Muscular response to training

Overview

Equine skeletal muscle has considerable potential to adapt during training, largely mediated by the structural and functional plasticity of myofibers. These long-term adaptations occur independently from the immediate or short-term physiologic responses to either aerobic or anaerobic exercise and are associated with altered rates and regulation of transcription of specific genes and consequently a change in the amount or isoform of proteins expressed within muscle fibers.[136]

Depending on the nature (type, frequency, intensity and duration) of the stimulus (exercise training), the adaptive

response can take the form of: (1) hypertrophy, when myofibers increase in size but otherwise retain their basal structural, physiologic and biochemical properties; or (2) remodeling without hypertrophy, where myofibers do not enlarge but acquire markedly different enzymatic and structural characteristics, often accompanied by changes in the microvasculature; or (3) a mixed response, i.e. remodeling in conjunction with hypertrophy (Fig. 5.32). Furthermore, the modality and amplitude of the response depend significantly on the basal muscle profile before training.[137] This is because the increased contractile activity that is associated with training induces a change towards slow and oxidative muscle profiles. Hence fast-twitch fibers (and therefore muscles that contain a higher proportion of glycolytic fibers) can show a relatively greater training adaptation than slow-twitch fibers. This response is particularly prominent in young inactive horses, which have a high percentage of glycolytic (low oxidative) pure IIX fibers (Fig. 5.33A,B), in contrast to active but more mature horses which have muscle fiber type profiles that are more oxidative (Fig. 5.33C,D). Although it can be hard to differentiate altered fiber properties caused by growth and training, specific training effects have been delineated in growing foals[99] and young horses.[83,84,138–141] Overall, muscular adaptations with training have important physiological implications that influence power generation, shortening velocity and resistance to fatigue.

Muscular adaptations to training

Muscle fiber size

The effects of training on equine muscle fiber size are still controversial. In general, the adaptive response of equine skeletal muscle to early and long-term exercise training takes the form of remodeling with minimal, if any, muscle fiber hypertrophy (see references[3] and [142] for reviews). However, specific muscle fiber hypertrophy can be stimulated with bursts of muscle activity against high resistance[83,143] and by prolonged stretch beyond normal resting length.[12,84] Six months of conventional jump training in competitive showjumpers also induces a selective hypertrophic growth of type II fibers, with minimal switching between myofiber phenotypes.[144] Other longitudinal studies have also reported significant and early (less than 3 months) increases in the mean cross-sectional areas of type I and/or IIA fibers after training.[72,82,145,146] This is partially explained by the simultaneous fiber type conversion in the direction IIX → IIA → I, since IIX and IIA fibers show greater cross-sectional areas than type I fibers (see Table 5.1). In contrast, in other studies of Standardbreds and Thoroughbreds, minimal changes[5,19,147,148] or a reduction in type II fiber cross-sectional area[139,149–151] have been reported. These observations are hard to reconcile with the prominent increase in muscle mass, especially in the hindquarters, that is generally observed in horses after most training programs.[3,143] When considered together, the only explanation for an increase in muscle mass, despite either no change or a reduction in fiber size, is a parallel increase in the number of muscle fibers (hyperplasia) that has previously been demonstrated in human beings.[152]

Muscle fiber type transitions

Muscle fiber type distribution and MyHC composition are strongly influenced by training (Figs 5.34, 5.35). Studies on endurance training in horses have demonstrated (by myofibrillar ATPase histochemistry) increases in the fraction of type IIA fibers, with concomitant decreases in IIX fibers[82,95,149,150,153,154] together with a relative reduction in MyHC-IIX and increase in MyHC-IIA.[84] In addition, several endurance training studies in horses have reported fiber transitions beyond type IIA fibers, i.e. an increase in hybrid I+IIA

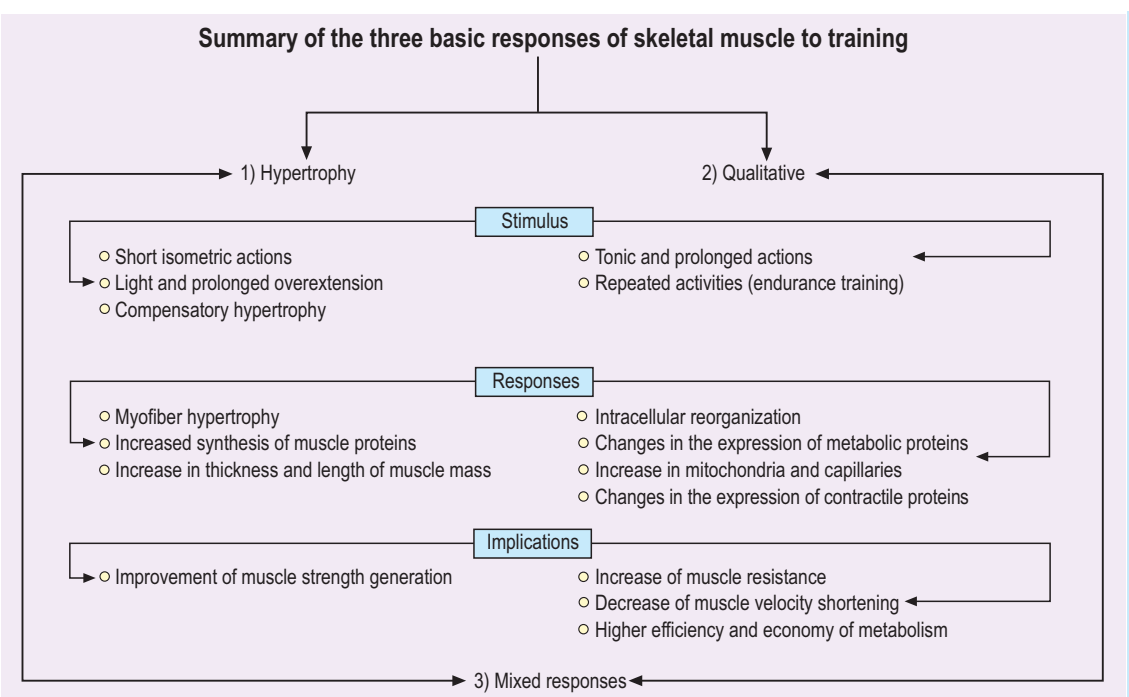


Fig. 5.32 Summary of the three basic responses of skeletal muscle to training: (1) hypertrophy, (2) remodeling without hypertrophy, and (3) remodeling with hypertrophy. Possible stimuli and the nature of the responses and physiological implications are indicated.

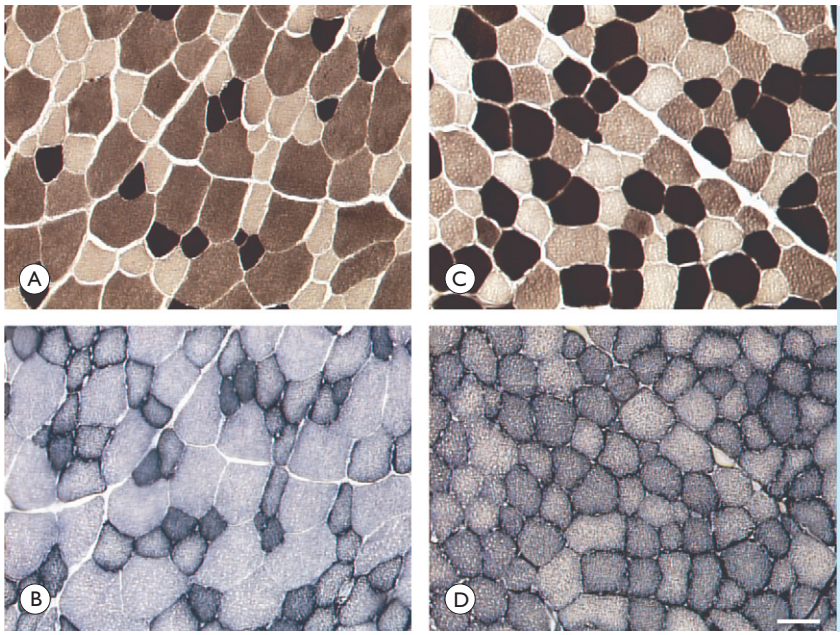


Fig. 5.33
Transverse serial sections of gluteus medius muscle biopsies stained with myofibrillar ATPase after acid preincubation at pH 4.45 (A and C) and succinate dehydrogenase (B and D) in a young adult (3 year old) and untrained Andalusian horse (A and B), and in an adult and regularly trained (10 year old) Andalusian horse (C and D). Note that the young animal has a lower proportion of type I fibers and a higher percentage of low-oxidative type IIX fibers than the adult horse; furthermore, differences in fiber size are much more pronounced in the young animal than in the adult. This therefore may explain the broader range of adaptive responses to training in young untrained horses than in adults or regularly trained animals. Bar, 50 μm.

fibers, and pure type I fibers.[5,82,84,155] Fiber type transitions during resistance training appear to resemble qualitatively those observed in endurance training. Hence, strength training in horses has been shown to result in an increase of both the IIA : IIX fiber ratio[141,145] and, when training is long enough, the I : II fiber ratio.[83] Similarly, sprint training in horses has been shown to cause increased numbers of type IIA and decreased numbers of type IIX fibers,[156] with corresponding alteration to the respective MyHC content.[72,157] In contrast to endurance and strength training, a specific decrease of type I fibers has been reported as an early, and probably transitory, response to high-intensity training.[156,157]

When these various training studies are considered in combination, it is reasonable to assume that fiber type transitions occur in a graded and orderly sequential manner and typically change from faster, more glycolytic fibers to slower and more oxidative fiber types, i.e. IIX → IIAX → IIA → IIA+I → I.[137] A dose–response relationship between the duration (in total) of the training program and the magnitude of induced changes has recently been demonstrated at the molecular level.[83,84] This relationship can be explained more readily in terms of a threshold for the type IIX → IIA transition during the early phase of training, and then a further threshold for the type IIA → type I transition. Thus, a single fiber is capable of a complete fast-to-slow transforma-

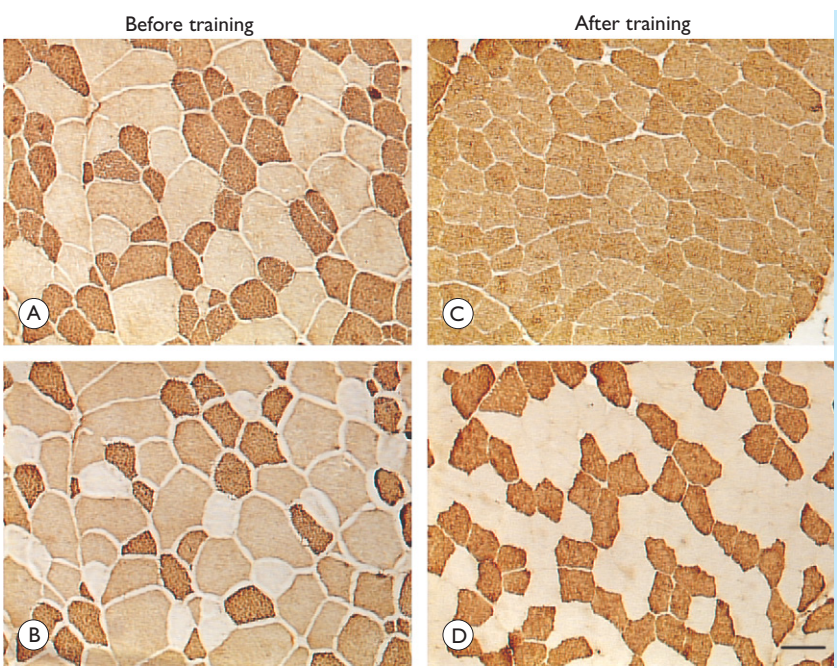


Fig. 5.34
Transverse serial sections of M. gluteus medius biopsies (depth, 6 cm) of the same horse before (A and B) and after (C and D) a long-term endurance training program (9 months in total). (A and C) Sections are stained by immunohistochemistry with a monoclonal antibody to types I or IIA myosin heavy chain isoforms; note that almost all muscle fibers express either or both of these isoforms after training. (B and D) The same sections stained by immunohistochemistry with a monoclonal antibody specific to type IIA myosin heavy chain isoform; note the significant increase in the number of fibers expressing this isoform after 9 months of training. Scale, 50 μm. Details of the training program are described in reference[84].

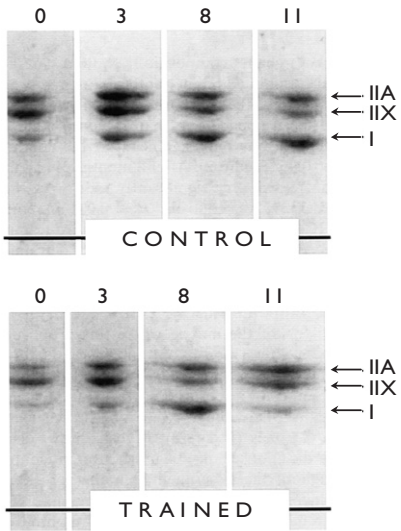


Fig. 5.35
Eight percent sodium dodecyl polyacrilamide gel electrophoresis of muscle samples from the gluteus medius muscle of a control horse (upper row) and a trained horse (bottom row) throughout an experiment to investigate the effects of prolonged endurance exercise training and detraining program. 0, pre-training; 3 and 8, after 3 and 8 months of training; 11, after 3 months of detraining. More details of the experiment in Serrano & Rivero.[83] The three myosin heavy chain isoforms are identified as I, IIA and IIX. Note the effect of training on the relative densities of the I and IIX bands, indicating a fiber type transition in the order IIX → IIA → I.

tion in response to a sufficiently long physiological training stimulus. Although many reports have investigated the training response shown by muscle fibers in terms of the MyHC component, it is important to remember that many other protein isoforms, such as the sarcomeric isoproteins, the regulatory proteins of the thin filaments and the calcium regulatory proteins of the SR, change in parallel.[158]

Metabolic changes and increased capillary density

Perhaps the most commonly detected and earliest muscular adaptation to training is an increase in the activity of enzymes of aerobic metabolism, such as selected enzymes of the TCA cycle, the electron transport chain and fat oxidation.[72,84,86,100,156] These changes are associated with increased mitochondrial and capillary densities (Fig. 5.36).[12,82,93,159,160] The latter response promotes improved oxygen diffusion and more expeditious removal of waste products (such as CO_2).

The activities of key anaerobic enzymes, such as phosphofructokinase and lactate dehydrogenase, either do not change or decrease following training.[3,72,84,86] Although training also results in an increase in the activity of AMP deaminase and other enzymes of the purine nucleotide cycle, such as creatine kinase (discussed in reference[3]), the concentration of total nucleotide stores is not affected by training.[156] Training has also been shown to result in a modest increase in muscle glycogen storage[84,148,161] that may well be associated with reduced levels of glycolytic enzymes, since the capacity to mobilize endogenous glycogen is partially influenced by the absolute activity of anaerobic enzymes expressed within muscle fibers.[64] In experimental animals, training is known to increase the sensitivity of glucose uptake across the sarcolemma, via increased GLUT-4 expression in muscle.[162] In horses however, moderate-intensity exercise training increases middle gluteal muscle GLUT-4 protein content, but this change is not reflected in an increase in sarcolemmal glucose transport activity in postexercise muscle samples.[163] Furthermore, the transfer of FFAs from the vascular to the intracellular compartment is also enhanced with

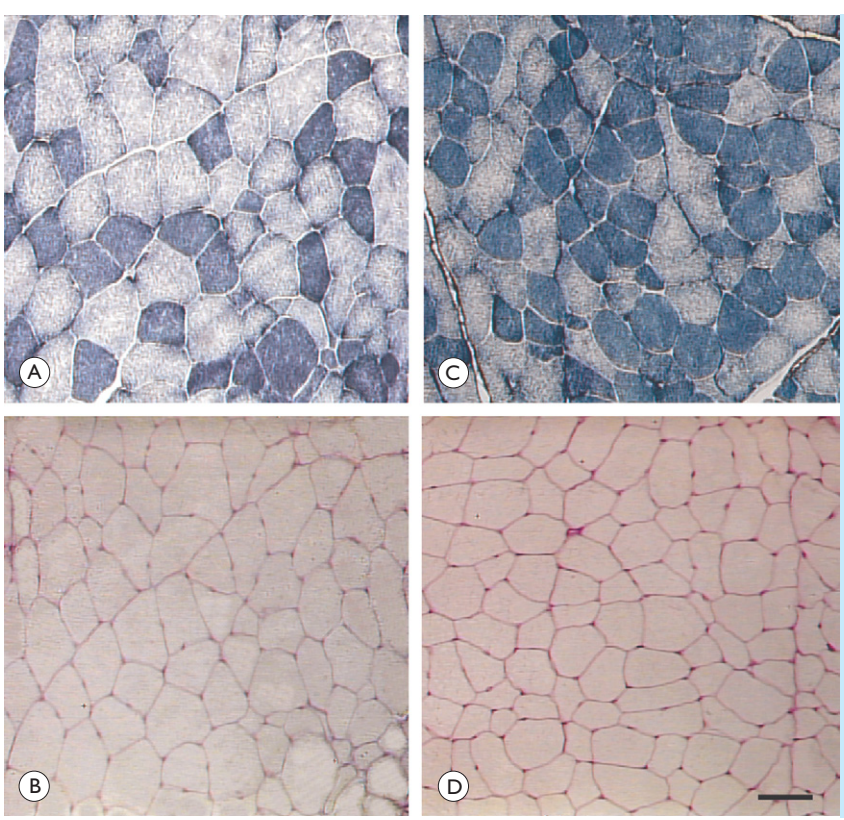


Fig. 5.36
Transverse serial sections of muscle biopsy samples of the M. gluteus medius from the same horse removed before (A and B) and after (C and D) 9 months of prolonged endurance training. (A and C) Sections are stained with succinate dehydrogenase to demonstrate the oxidative capacity of individual muscle fibers; note the increase in the number of fibers with dark staining after training. (B and D) Sections are stained with the α-amylase PAS to visualize capillaries; note the increased capillary density (e.g. number of capillaries per mm^2) after the training program. Scale, 75 μm.

endurance training, via an increase in extracellular (interstitial) albumin concentration.[164]

Physiological adaptations and buffering capacity

Significant effects of training on electrical membrane properties and ion channels have recently been reported in horse skeletal muscle.[165–167] Short-term exercise training of moderate intensity results in an increase in the density of Na^+/K^+-ATPase pumps, measured by oubain binding assays, together with an attenuation in K^+ efflux from working muscles during high-intensity exercise. Although physiologic implications of these training-induced adaptations are unclear, enhanced ionic control at the sarcolemma may result in myofibers that are better able to respond to the rate of motor neuron discharge.[168] Additional responses following physical conditioning include increased SR calcium uptake and Ca^{2+}-ATPase activity and an attenuation of the exercise-induced decline of both calcium uptake and Ca^{2+}-ATPase activity.[169]

Several studies have reported an increase in buffering capacity of equine skeletal muscle after a few weeks of sprint training.[170–172] This increase may be due to (1) increased incorporation of myofiber protein, (2) higher muscle carnosine concentrations or (3) increased creatine phosphate concentrations.[118] However, no differences in muscle carnosine concentration were found between trained and untrained Thoroughbreds.[173]

Detraining

Adaptive training responses of skeletal muscles are maintained through 5–6 weeks of inactivity,[12,148,150] but not beyond 12 weeks.[82–84,174] This maintenance of the trained phenotype during inactivity appears more prolonged in horses than other athletic species. It has been suggested that expression of the MyHC-IIX gene constitutes a default setting that may be altered (decreased) by chronic increases in contractile activity (i.e. training), and compensated for by increased expression of MyHC-IIA.[175] In line with this hypothesis is the observation reported in horses that a return to sedentary activity levels following a prolonged period of endurance training results in normalization of expression of MyHC-IIX, via a slow-to-fast fiber type transformation in the order I → IIA → IIX (Fig. 5.35).[84] These detraining-induced changes in MyHC phenotype occur in parallel with a reversion of the muscle's size and metabolic and capillary characteristics to pre-training levels.[84] Thus, fiber sizes decrease, together with a decline in mitochondrial density, aerobic enzyme activities and glycogen content, and an increase (normalization) of anaerobic enzyme activities.

Possible mechanisms underlying muscular adaptations to training

Skeletal muscle responds to altered functional demands by specific quantitative and/or qualitative alterations in gene expression (Fig. 5.37), provided that the stimuli are of sufficient magnitude and duration.[158] Repeated or persistent elevation of neuromuscular activity (i.e. during exercise and training) induces a series of concerted changes in gene expression, evoking either myofiber hypertrophy or myofiber remodeling, or both.[136] Myofiber hypertrophy is characterized by a generally co-ordinated increase in abundance, per fiber, of most protein constituents. To a limited extent, this process includes the selective and transient activation of specific genes immediately following the onset of work overload. The major events however, underlying muscle hypertrophy involve a general and non-specific augmentation of protein synthesis within cells. Remodeling of myofiber phenotype, with minimal or no hypertrophy, is the typical muscular response to prolonged training in the horse.[84] During this type of adaptation, myofibers undergo a striking reorganization, with selective activation and repression of many genes. Thus, switching among different myofibrillar isoproteins occurs in a graded and orderly sequential manner.[158] These changes occur in parallel, but not simultaneously over time, and correspond to the changes observed in enzymatic profiles, cytosolic proteins and membrane receptors and transporters.

The complexity and pleiotropic nature of the physical and metabolic stimuli presented to myofibers during contractions that ultimately result in altered gene regulation have been reviewed by Williams & Neufer.[136] Acetylcholine released from motor neurons and other signaling molecules of neural origin bind to cell surface receptors on myofibers and trigger intracellular events that may be linked to altered gene expression and hence to appropriate modifications (Fig. 5.38). Additional signals are probably derived from contracting myofibers experiencing mechanical stresses that perturb the sarcolemma and extracellular matrix, as well as exerting tension via intermediate filaments on the cytoskeleton, organelles and the nucleus.[176] Changes in the intracellular concentrations of ions and meta-

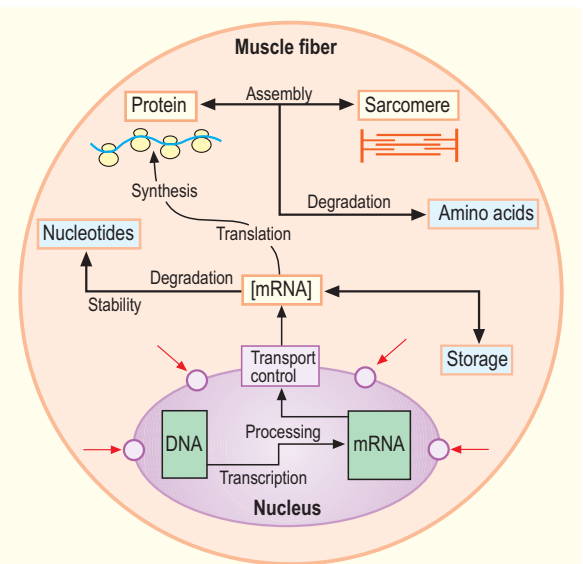


Fig. 5.37
Schematic diagram showing different steps in the regulation of gene expression in skeletal muscle associated with increased contractile activity.

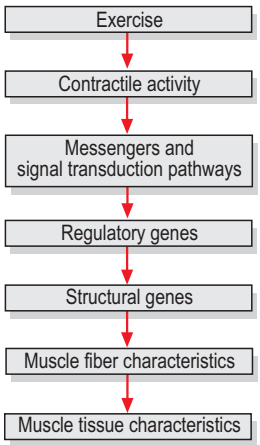


Fig. 5.38
Steps in the cascade of events by which exercise and increased neuromuscular activity lead to physiologically relevant changes in the characteristics of skeletal muscle.

bolites during chronic muscle contractions have also been implicated in the activation of signaling pathways.[64] These messengers include alterations in calcium concentration, acidosis during anaerobic exercise, the marked reduction in phosphorylation potential of the adenylate system ([ATP]/[ADP_{free}]), a depletion of the redox state (NADH/NAD), and hypoxia. Among all these factors, the imbalance between energy requirement and energy supply is perhaps the most important signal triggering an appropriate adjustment in contractile and metabolic protein expression.[177] Recent years have seen significant advances in our understanding of the signaling mechanism by which the information contained in specific action potential patterns is decoded by the transcriptional machinery of muscle fiber nuclei.[178] For example, Ras-mitogen-activated protein kinase[179] and calcineurin[180] signaling have recently been implicated in the α-motor neuron induction of slow muscle fiber phenotype, but not muscle growth. Conversely, a protein kinase B-dependent and rapamycin-sensitive pathway controls myofiber growth but not fiber type specification.[181]

Specific genes that regulate skeletal muscle following contractile activity include most genes that encode sarcomeric and cytosolic proteins, and enzymes of the glycolytic pathway, TCA cycle, the electron transport chain and fat oxidation.[136] There are, however, special signals for control of mitochondrial genes. These pathways require co-ordinated induction of some nuclear genes encoding mitochondrial proteins, as well as increased expression of genes located within mitochondrial DNA. The factors that promote angiogenesis in skeletal muscle in response to training have not been clarified although they may be related to a chronic increase in muscle capillary blood flow and the corresponding endothelial shear stress, as well as increased capillary wall tension.[182] Hudlicka and colleagues speculated that endothelial stress may disturb the luminal surface, resulting in the release of bound proteases that damage the basement membrane and contribute to an increase in basic fibroblast growth factor release.[182] Subsequently, the growth factors may enhance vascular growth and satellite cell proliferation.[183] However, much information is still unclear, including the influence of training intensity and duration on neovascularization and the mechanisms that underlie the increase seen in intramuscular substrates in response to long-term endurance training. These latter adaptations may be related to either (1) increased glucose and FFA availability (via GLUT-4 and albumin respectively), (2) a lower utilization of these substrates for energy production or (3) possible artefacts imposed by experimental design (i.e. they may be a reflection of increased dietary intake of soluble starches and fat from a parallel change in diet for horses in training).[3]

Implications of training-induced changes to the physiologic response to exercise

The main physiologic consequence of increased muscle mass in response to training is to produce a muscle with a greater peak force capacity, because force output is proportional to total cross-sectional area of the fiber mass recruited.[168] At slow speeds, this adaptation has an impact on gait, causing a marked reduction of both stance time and stride duration.[95] Additionally, such an adaptation has a significant impact on the performance of showjumpers via enhanced power output from the hindquarters.[144] Furthermore, because increased power output results in a greater ability to accelerate and may increase stride length, these training adaptations (strength rather than endurance) may be important for race horses competing over short distances.[3] However, enhanced power through training comes with the cost of a corresponding decline in aerobic potential, because the increased mass of recruited fibers and concomitant rise in ATP utilization occur simultaneously with a relative inability of oxygen to diffuse into the larger fibers.[150]

From a physiologic standpoint, remodeling of myofiber phenotype with minimal or with no hypertrophy, in response to training, produces a muscle that is much more resistant to fatigue but with an intrinsic decrease in maximal velocity of shortening. The rise in resistance to fatigue corresponds to each myofiber's increased oxidative capacity. The reduction in contractile speed is associated with the switch of muscle fiber types and the increased expression of slow MyHC and other contractile protein isoforms.[14] In a similar but reciprocal fashion to that described for strength training, some conventional training programs of young race horses produce a decrease in the size of type II fibers[151] and a corresponding decline of both speed and force of contraction.[63] Clearly a balance must be acquired at a level most appropriate for the intended use of the horse: in general, training programs in race horses should be aimed at the development of muscle properties that optimize an equilibrium between speed, stamina and strength.

Following endurance training, exercise at submaximal intensities elicits optimal delivery of oxygen and bloodborne substrates, an early activation of oxidative metabolism with a lower utilization rate of endogenous carbohydrates and an increased reliance on fat oxidation as an energy source. Muscle glycogen sparing is underlying the delay in the onset of fatigue during this type of exercise. It seems highly probable that all these metabolic adaptations are largely responsible for the increased endurance in the trained state and the lower propensity for individual muscles to fatigue as measured electromyographically following 8 weeks of aerobic conditioning.[36] The increased oxidative capacity, which is observed in skeletal muscle after training, occurs concurrently with increased maximum oxygen uptake[12] and a significant reduction in the

net rate of muscle glycogenolysis and anaerobic metabolism.[184] As a consequence, in the trained state, the speed at which a horse begins to accumulate lactate increases gradually (i.e. there is a delay in the onset of lactate accumulation, and ATP depletion).[63,140,141] This is accomplished by enhanced muscle buffering capacity and more efficient excitation–contraction coupling. Hence collectively, endurance may be enhanced by a wide variety of related factors that delay the onset of fatigue during anaerobic exercise.

References

1. Gunn HM. Muscle, bone and fat proportions and muscle distribution of thoroughbreds and quarter horses. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:253–264.
2. Armstrong RB, Essén-Gustavsson B, Hoppeler H, et al. O_2 delivery at VO_{2max} and oxidative capacity in muscles of standardbred horses. J Appl Physiol 1992; 73:2274–2282.
3. Snow DH, Valberg SJ. Muscle anatomy, physiology and adaptations to exercise and training. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: Saunders; 1994:145–179.
4. Bergström J. Muscle electrolytes in man determinated by neutron activation analysis on needle biopsy specimens: a study in normal subjects, kidney patients and patients with chronic diarrhoea. Scand J Clin Invest 1962; 14 (suppl 14): 1–110.
5. Henckel P. Training and growth induced changes in the middle gluteal muscle of young Standardbred trotters. Equine Vet J 1983; 15:134–140.
6. Lindholm A, Piehl K. Fibre composition, enzyme activity and concentrations of metabolites and electrolytes in muscles of standardbred horses. Acta Vet Scand 1974; 15:28–309.
7. Robert C, Valette JP, Degueurce C, et al. Correlation between surface electromyography and kinematics of the hindlimb of horses at trot on a treadmill. Cells Tiss Org 1999; 165:113–122.
8. Rivero JLL, Serrano AL, Diz AM, et al. Changes in cross-sectional area and capillary supply of the muscle fiber population in equine gluteus medius muscle as a function of sampling depth. Am J Vet Res 1993; 54:32–37.
9. López-Rivero JL, Serrano AL, Diz AM, et al. Variability of muscle fibre composition and fibre size in the horse gluteus medius: an enzyme-histochemical and morphometric study. J Anat 1992; 181:1–10.
10. Valette JP, Barrey E, Jouglin M, et al. Standardisation of muscular biopsy of the gluteus medius in French trotters. Equine Vet J Suppl 1999; 30:342–344.
11. Karlström K, Essén-Gustavsson B, Hoppeler H, et al. Capillary supply and fibre area in locomotor muscles of horses and steer: a comparison between histochemistry and electron microscopy. Acta Anat (Basel) 1992; 145:395–399.
12. Tyler CM, Golland LC, Evans DL, et al. Skeletal muscle adaptations to prolonged training, overtraining and detraining in horses. Pflüg Arch – Eur J Physiol 1998; 436:391–397.
13. Sosnicki AA, Lutz GJ, Rome LC, et al. Histochemical and molecular determination of fiber types in chemically skinned single equine skeletal muscle fibers. J Histochem Cytochem 1989; 37:1731–1738.
14. Rome LC, Sosnicki AA, Gobble DO. Maximum velocity of shortening of three fibre types from horse soleus muscle: implications for scaling with body size. J Physiol (Lond) 1990; 431:173–185.
15. Mlekoday JA, Mickelson JR, Valberg SJ, et al. Calcium sensitivity of force production and myofibrillar ATPase activity in muscles from Thoroughbreds with recurrent exertional rhabdomyolysis. Am J Vet Res 2001; 62:1647–1652.
16. Valberg S, Essén-Gustavsson B. Metabolic response to racing determined in pools of type I, IIA and IIB fibers. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:290–301.
17. Harris DB, Harris RC, Wilson AM, et al. ATP loss with exercise in muscle fibres of the gluteus medius of the thoroughbred horses. Res Vet Sci 1997; 63:231–237.
18. Henckel P, Ducro B, Oksbjerg N, et al. Objectivity of two methods of differentiating fibre types and repeatability of measurements by application of the TEM image analysis system. Eur J Histochem 1998; 42:49–62.
19. Rivero JLL, Talmadge RJ, Edgerton VR. Correlation between myofibrillar ATPase activity and myosin heavy chain composition in equine skeletal muscle and the influence of training. Anat Rec 1996; 246:195–207.
20. Quiroz-Rothe E, Rivero JLL. Co-ordinated expression of contractile and non-contractile features of control equine muscle fibre types characterised by immunostaining of myosin heavy chains. Histochem Cell Biol 2001; 116:299–312.
21. Snow DH, Billeter R, Jenny E. Myosin types in equine skeletal muscle. Res Vet Sci 1981; 30:381–382.
22. Sinha AK, Rose RJ, Pozgaj I, et al. Indirect myosin immunocytochemistry for the identification of fibre types in equine skeletal muscle. Res Vet Sci 1992; 53:25–31.
23. Yamaguchi M, Winnard A, Takehana K, et al. Molecular analysis of horse skeletal muscle myosin. Bull Equine Res Inst 1993; 30:15–25.
24. Hermanson J, Hegemann-Monachelli MT, Daood MJ, et al. Correlation of myosin isoforms with anatomical divisions in equine biceps brachii. Acta Anat (Basel) 1991; 141:369–376.
25. Cobb MA, Schitt Jr WA, Hermanson JW. Morphological, histochemical, and myosin isoform analysis of the diaphragm of adult horses, *Equus caballus*. Anat Rec 1994; 238:317–325.
26. Serrano AL, Petrie JL, Rivero JLL, et al. Myosin isoforms and muscle fiber characteristics in equine gluteus medius muscle. Anat Rec 1996; 244:444–451.
27. Barrey E, Valette JP, Jouglin M, et al. Enzyme-linked immunosorbent assay for myosin heavy chains in the horse. Reprod Nutr Dev 1995; 35:619–628.
28. Valette JP, Barrey E, Jouglin M. Slow myosin heavy chain content in muscles measured by ELISA. Equine Vet J Suppl 1995; 18:248–251.
29. Rivero JLL, Talmadge RJ, Edgerton VR. Myosin heavy chain isoforms in adult equine skeletal muscle: an immunohistochemical and electrophoretic study. Anat Rec 1996; 246:185–194.
30. Picard B, Lefaucheur L, Fauconneau B, et al. Dossier: caracterisation des differents types de fibers musculaires dans plusieurs espèces: production et utilisation d'anticorps monoclonaux diriges contre les chaînes lourdes de myosine rapide IIa et IIb. INRA (France) Prod Anim 1998; 1:145–163.
31. Dingboom EG, Dijkstra G, Enzerink E, et al. Postnatal muscle fibre composition of the gluteus medius muscle of Dutch warmblood foals: maturation and the influence of exercise. Equine Vet J Suppl 1999; 31:95–100.
32. Linnane L, Serrano AL, Rivero JLL. Distribution of fast myosin heavy chain-based muscle fibres in the gluteus medius of untrained horses: mismatch between antigenic and ATPase determinants. J Anat 1999; 181:363–372.
33. Rivero JLL, Talmadge RJ, Edgerton VR. A sensitive electrophoretic method for the quantification of myosin heavy chain isoforms in horse skeletal muscle: histochemical

and immunocytochemical verifications. Electrophoresis 1997; 18:1967–1972.
34. Rivero JLL, Serrano AL, Barrey E, et al. Analysis of myosin heavy chains at the protein level in horse skeletal muscle. J Muscle Res Cell Motil 1999; 20:211–221.
35. Serrano AL, Pérez M, Lucía A, et al. Immunolabelling, histochemistry and in situ hybridisation in human skeletal muscle fibres to detect myosin heavy chain expression at the protein and mRNA level. J Anat 2001; 199:329–337.
36. Cheung TK, Warren LK, Lawrence LM, et al. Electromyographic activity of the long digital extensor muscle in the exercising Thoroughbred horse. Equine Vet J 1998; 30:251–255.
37. van Wessum R, Sloet van Oldruitenborgh-Oosterbaan MM, Clayton H. Electromyography in the horse in veterinary medicine and in veterinary research – a review. Vet Quart 1999; 21:3–7.
38. Preedy DF, Colborne GR. A method to determine mechanical energy conservation and efficiency in equine gait: a preliminary study. Equine Vet J Suppl 2001; 33:94–98.
39. Büscher D, Izpisua Belmonte JC. Muscle development during vertebrate limb outgrowth. Cell Tiss Res 1999; 296:131–139.
40. Draeger A, Weeds AG, Fitzsimons RB. Primary, secondary and tertiary myotubes in developing skeletal muscle: a new approach to the analysis of human myogenesis. J Neurol Sci 1987; 81:19–43.
41. Dalin G, Jeffcott LB. Biomechanics, gait, and conformation. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: Saunders; 1994:27–48.
42. Wilson AM, McGuigan MP, Su A, et al. Horses damp the spring in their step. Nature 2001; 414:895–899.
43. Hartzel DK, Arnoczky SP, Kilfoyle SJ, et al. Myofibroblast in the accessory ligament (distal check ligament) and the deep digital flexor tendon of foals. Am J Vet Res 2001; 62:823–827.
44. Jansen MO, Raaif van JAGM, van den Bogert AJ, et al. Quantitative analysis of computer-averaged electromyographic profiles of intrinsic limb muscles in ponies at walk. Am J Vet Res 1992; 53:2343–2349.
45. Robert C, Valette JP, Denoix JM. Surface electromyographic analysis of the normal horse locomotion: a preliminary report. In: Lindner A, ed. Proceedings of the Conference on Equine Sport Medicine and Sciences. Wageningen: Wageningen Pers; 1998:80–85.
46. Hyyppä S, Hänninen O. Application of surface electromyography in horses during physical exercise. In: Lindner A, ed. Proceedings of the Conference on Equine Sport Medicine and Sciences. Wageningen: Wageningen Pers; 1998:156–162.
47. Baba K, Kawamura T, Shibata M, et al. Capillary-tissue arrangement in the skeletal muscle optimized oxygen transport in all mammals. Microvasc Res 1995; 49:163–179.
48. Hermanson JW. Architecture and the division of labor in the extensor carpi radialis muscle of horses. Acta Anat (Basel) 1997; 159:127–135.
49. Gellman KS, Bertram JEA, Hermanson JW. Morphology, histochemistry, and function of epaxial cervical musculature in the horse (*Equus caballus*). J Morphol 2002; 251:182–194.
50. Savelberg HH, Schamhardt HC. The influence of inhomogeneity in architecture on the modelled force-length relationship of muscles. J Biomech 1995; 28:187–197.
51. Monti RJ, Roy RR, Edgerton VR. Role of motor unit structure in defining function. Muscle Nerve 2001; 24:848–866.
52. Dubowitz V, Sewry C, Fitzsimons R. Muscle biopsy: a practical approach. London: Baillière Tindall; 1985.
53. Palmieri G, Panu R, Asole A, et al. Proprioceptive innervation of the external cremaster muscle of some domestic mammals. Acta Anat (Basel) 1978; 102:40–44.
54. Palmieri G, Asole A, Panu R, et al. Further observations on the innervation of the proximal sesamoidean ligament of the horse and ox. Anat Histol Embryol 1982; 65:121–133.
55. Palmieri G, Panu R, Asole A, et al. Macroscopic organization and sensitive innervation of the tendinous intersection and the lacertus fibrosus of the biceps brachii muscle in the ass and horse. Anat Histol Embryol 1986; 69:73–82.
56. Klomkleaw W, Kasashima Y, Kobayashi A, et al. Tubular aggregates observed in spindle muscle fiber of horse lumbrical muscle. Acta Neuropathol (Berl) 2001; 101:509–517.
57. Berchtold MW, Brinkmeier H, Müntener M. Calcium ion in skeletal muscle: its crucial role for muscle function, plasticity, and disease. Physiol Rev 2000; 80:1215–1265.
58. Ehmsen J, Poon E, Davies K. The dystrophin-associated protein complex. J Cell Sci 2002; 115:2801–2803.
59. Papadopoulus S, Jurgens KD, Gros G. Diffusion of myoglobin in skeletal muscle cells: dependence on fibre type, contraction and temperature. Pflüg Arch – Eur J Physiol 1995; 430:519–525.
60. Conley KE, Jones C. Myoglobin content and oxygen diffusion: model analysis of horse and steer muscle. Am J Physiol 1996; 271:C2027–C2036.
61. Schenkman KA, Marble D, Burns DH, et al. Myoglobin oxygen dissociation by multiwawe length spectroscopy. J Appl Physiol 1997; 82:86–92.
62. Grozdanovic Z. No message from muscle. Microsc Res Technol 2001; 55:148–153.
63. Valberg SJ. Muscular causes of exercise intolerance in horses. Vet Clin North Am: Equine Pract 1996; 12:495–515.
64. Booth FW, Baldwin KM. Muscle plasticity: energy demand and supply processes. In: Rowel LB, Shepherd JT, eds. Handbook of physiology. Bethesda. MD: American Physiological Society; 1996:1075–1123.
65. Eaton MD. Energetics and performance. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: Saunders; 1994:49–61.
66. Davie AJ, Evans DL, Hodgson DR, et al. Effects of muscle glycogen depletion on some metabolic and physiological responses to submaximal treadmill exercise. Can J Vet Res 1999; 63:241–247.
67. Orme CE, Harris RC, Marlin DJ, et al. Metabolic adaptation to fat-supplemented diet by the thoroughbred horse. Br J Nutr 1997; 78:443–458.
68. Geelen SN, Blazquez C, Geelen MJ, et al. High fat intake lowers hepatic fatty acid synthesis and raises fatty acid oxidation in aerobic muscle in Shetland ponies. Br J Nutr 2001; 86:31–36.
69. Geelen SN, Sloet van Oldruitenborgh-Oosterbaan MM, Beynen AC. Supplemental fat in the diet of horses: is it advantageous? Tijdschr Diergeneeskd 2001; 126:310–315.
70. Geor RJ, Hinchcliff KW, Sams RA. Glucose infusion attenuates endogenous glucose production and enhances glucose use of horses during exercise. J Appl Physiol 2000; 88:1765–1776.
71. Schiaffino S, Reggiani C. Molecular diversity of myofibrillar proteins: gene regulation and functional significance. Physiol Rev 1996; 76:371–423.
72. Miyata H, Sugiura T, Kai M, et al. Muscle adaptation of Thoroughbred racehorses trained on a flat or sloped track. Am J Vet Res 1999; 60:1536–1539.
73. Blanco CE, Sieck GC. Quantitative determination of calcium-activated myosin adenosine triphosphatase activity in rat skeletal muscle fibres. Histochem J 1992; 24:431–444.

74. Essén-Gustavsson B, Ronéus N, Pösö AR. Metabolic response in skeletal muscle fibres of standardbred trotters after racing. Comp Bioch Physiol (B) Biochem Mol Biol 1997; 117:431–436.
75. Dunnett M, Harris RC, Sewell DA. Taurine content and distribution in equine skeletal muscle. Scand J Clin Lab Invest 1992; 52:725–730.
76. Sewell DA, Harris RC, Marlin DJ, et al. Estimation of the carnosine content of different fibre types in the middle gluteal muscle of the thoroughbred horse. J Physiol (Lond) 1992; 455:447–453.
77. Dunnett M, Harris RC. Carnosine and taurine contents of type I, IIA and IIB fibres in the middle gluteal muscle. Equine Vet J Suppl 1995; 18:214–217.
78. Larsson L. Is the motor unit uniform? Acta Physiol Scand 1992; 144:143–154.
79. Snow DH, Guy PS. Muscle fibre type composition of a number of limb muscles in different types of horses. Res Vet Sci 1980; 28:137–144.
80. Ryan JM, Cobb CA, Hermanson JW. Elbow extensor muscles of the horse: postural and dynamic implications. Acta Anat (Basel) 1992; 144:71–79.
81. Sewell DA, Harris RC, Marlin DJ. Skeletal muscle characteristics in 2 year-old race-trained Thoroughbred horses. Comp Biochem Physiol Comp Physiol 1994; 108:87–96.
82. Rivero JLL, Ruz MC, Serrano A, et al. Effects of a 3 month endurance training programme on skeletal muscle histochemistry in Andalusian, Arabian and Anglo-Arabian horses. Equine Vet J 1995; 27:51–59.
83. Serrano AL, Rivero JLL. Myosin heavy chain profile of equine gluteus medius muscle following draught-exercise training and detraining. J Muscle Res Cell Motil 2000; 21:235–245.
84. Serrano AL, Quiroz-Rothe E, Rivero JLL. Early and long-term changes of equine skeletal muscle in response to endurance training and detraining. Pflüg Arch – Eur J Physiol 2000; 441:263–274.
85. Rivero JLL, Serrano AL, Henckel P, et al. Muscle fiber type composition and fiber size in successfully and unsuccessfully endurance-raced horses. J Appl Physiol 1993; 75:1758–1766.
86. Rivero JLL, Serrano AL, Henckel P. Activities of selected aerobic and anaerobic enzymes in the gluteus medius muscle of endurance horses with different performance records. Vet Rec 1995; 137:187–192.
87. Barrey B, Valette JP, Jouglin M, et al. Heritability of percentage of fast myosin heavy chains in skeletal muscles and relationship with performance. Equine Vet J Suppl 1999; 30:289–292.
88. Rivero JLL, Henckel P. Muscle biopsy index for discriminating between endurance horses with different performance records. Res Vet Sci 1996; 61:49–54.
89. Ronéus N, Essén-Gustavsson B. Skeletal muscle characteristics and metabolic response to exercise in young Standardbreds. Am J Vet Res 1997; 58:167–170.
90. Ronéus N, Essén-Gustavsson B, Lindholm A, et al. Muscle characteristics and plasma lactate and ammonia response after racing in Standardbred trotters: relation to performance. Equine Vet J 1999; 31:170–173.
91. Persson SGB, Essén-Gustavsson B, Lindholm A. Energy profile and the locomotory pattern of trotting on an inclined treadmill. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:231–238.
92. Rivero JLL, Clayton H. The potential role of the muscle in kinematic characteristics. Pferdeheilkunde 1996; 12:635–640.
93. Ronéus N, Essén-Gustavsson B, Johnston C, et al. Lactate response to maximal exercise on the track: relation to muscle characteristics and kinematic variable. Equine Vet J Suppl 1995; 18:191–194.
94. Rivero JLL, Serrano AL, Quiroz-Rothe E, et al. Co-ordinated changes of kinematics and muscle fibre properties with prolonged endurance training. Equine Vet J Suppl 2001; 33:104–108.
95. López-Rivero JL, Agüera E, Monterde JG, et al. Comparative study of muscle fiber type composition in the middle gluteal muscle of Andalusian, Thoroughbred and Arabian horses. J Equine Vet Sci 1989; 9:337–340.
96. López-Rivero JL, Agüera E, Morales-López JL, et al. Muscle fibre size in horses. Equine Ath 1990; 3:1–11.
97. Rivero JLL, Valera M, Serrano AL, et al. Variability of muscle fibre type composition in a number of genealogical bloodlines in Arabian and Andalusian horses. Pferdeheilkunde 1996; 12:661–665.
98. Rivero JLL, Barrey E. Heritabilities and genetic and phenotypic parameters for gluteus medius muscle fibre type composition, fibre size and capillaries in purebred Spanish horses. Livest Prod Sci 2001; 72:233–241.
99. Dingboom EG, Van OH, Eizema K, et al. Changes in fibre type composition of gluteus medius and semitendinosus muscles of Dutch Warmblood foals and the effect of exercise during the first year postpartum. Equine Vet J 2002; 34:177–183.
100. Ronéus M, Lindholm A, Asheim A. Muscle characteristics in Thoroughbreds of different ages and sexes. Equine Vet J 1991; 23:207–210.
101. Rivero JLL, Galisteo AM, Agüera E, et al. Skeletal muscle histochemistry in male and female Andalusian and Arabian horses of different ages. Res Vet Sci 1993; 54:160–169.
102. Ronéus M. Muscle characteristics in Standardbreds of different ages and sexes. Equine Vet J 1993; 25:143–146.
103. Gunn HM. Relative increase in areas of muscle fibre types in horses during growth. Equine Vet J Suppl 1995; 18:209–213.
104. Talmadge RJ, Roy RR, Edgerton VR. Muscle fiber types and function. Curr Opin Rheumatol 1993; 5:695–705.
105. Roy RR, Monke SR, Allen DL, et al. Modulation of myonuclear number in functionally overloaded and exercised rat plantaris fibers. J Appl Physiol 1999; 87:634–642.
106. Schiaffino S, Murgia M, Serrano AL, et al. How is muscle phenotype controlled by nerve activity? Ital J Neurol Sci 1999; 20:409–412.
107. Hyyppä S, Karvonene U, Rasanen LA, et al. Androgen receptors and muscle composition in trotters treated with nandrolone laureate. Zentralbl Veterinarmed A 1997; 44:481–491.
108. Chen J, Gollnick PD. Effect of exercise on hexokinase distribution and mitochondrial respiration in skeletal muscle. Pflüg Arch – Eur J Physiol 1994; 427:257–263.
109. Geor RJ, Hinchcliff KW, McCutcheon LJ, et al. Epinephrine inhibits exogenous glucose utilization in exercising horses. J Appl Physiol 2000; 88:1777–1790.
110. Hyyppä S, Rasanen LA, Pösö AR. Resynthesis of glycogen in skeletal muscle from Standardbred trotters after repeated bouts of exercise. Am J Vet Res 1997; 58:162–166.
111. Davie AJ, Evans DL, Hodgson DR, et al. Effects of intravenous dextrose infusion on muscle glycogen resynthesis after intense exercise. Equine Vet J Suppl 1995; 18:195–198.
112. Hyyppä S. Effects of nandrolone treatment on recovery in horses after strenuous physical exercise. J Vet Med (A) 2001; 48:343–352.
113. Essén-Gustavsson B, Gottlieb-Vedi M, Lindholm A. Muscle adenine nucleotide degradation during submaximal treadmill exercise to fatigue. Equine Vet J Suppl 1999; 30:298–302.

114. Lindinger ML. Exercise in the heat: thermoregulatory limitations to performance in humans and horses. Can J Appl Physiol 1999; 24:152–163.
115. Manohar M, Hassan AS. Diaphragmatic energetics during prolonged exhaustive exercise. Am Rev Respir Dis 1991; 144:415–418.
116. Gauvreau GM, Young SS, Staempfli H, et al. The relationship between respiratory exchanges ratio, plasma lactate and muscle lactate concentrations in exercising horses using a valve gas collection system. Can J Vet Res 1996; 60:161–171.
117. Gottlieb-Vedi M, Essén-Gustavsson B, Thornell LE, et al. A comparison of ultrastructure and metabolic response of the skeletal muscle of horses performing intense treadmill exercise at 20 and 35 degrees C. Zentralbl Veterinarmed A 1999; 46:209–218.
118. Hyyppä S, Pösö AR. Fluid, electrolyte, and acid–base responses to exercise in racehorses. Vet Clin North Am: Equine Pract 1998; 14:121–136.
119. Vaihkonen LK, Heinonen OJ, Hyyppä S, et al. Lactate-transport activity in RBCs of trained and untrained individuals from four racing species. Am J Physiol 2001; 281:R19–R24.
120. Byrd SK, McCutcheon LJ, Hodgson DR, et al. Altered sarcoplasmic function after high intensity exercise. J Appl Physiol 1989; 67:2072–2077.
121. McCutcheon LJ, Byrd SK, Hodgson DR. Ultrastructural changes in skeletal muscle after fatiguing exercise. J Appl Physiol 1992; 72:1111–1117.
122. Sewell D, Harris RC, Dunnett M. Carnosine accounts for most of the variation in physico-chemical buffering in equine muscle. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:276–280.
123. Harris RC, Marlin DJ, Dunnett M, et al. Muscle buffering capacity and dipeptide content in the Thoroughbred horse, Greyhound dog and man. Comp Biochem Physiol (A) 1990; 97:249–251.
124. Dunnett M, Harris RC. Influence of oral beta-alanine and L-histidine supplementation on the carnosine content of the gluteus medius. Equine Vet J Suppl 1999; 30:499–504.
125. Snow DH, Harris RC, Gash S. Metabolic response of equine muscle to intermittent maximal exercise. J Appl Physiol 1985; 58:1689–1697.
126. Schuback K, Essén-Gustavsson B. Muscle anaerobic response to a maximal treadmill exercise test in Standardbred trotters. Equine Vet J 1998; 30:504–510.
127. Cutmore CM, Snow DH, Newsholme AE. Effects of training on enzyme activities involved in purine nucleotide metabolism. Equine Vet J 1986; 18:72–76.
128. Lacombe VA, Hinchcliff KW, Geor RJ, et al. Exercise that induces substantial muscle glycogen depletion impairs subsequent anaerobic capacity. Equine Vet J Suppl 1999; 30:293–297.
129. Lacombe VA, Hinchcliff KW, Geor RJ, et al. Muscle glycogen depletion and subsequent replenishment affect anaerobic capacity in horses. J Appl Physiol 2001; 91:1782–1790.
130. Gottlieb-Vedi M, Dahlborn K, Jansson A, et al. Elemental composition of muscle at rest and potassium levels in muscle, plasma and sweat of horses exercising at 20 degrees C and 35 degrees C. Equine Vet J Suppl 1996; 22:35–41.
131. Foster CV, Harris RC. Total carnitine content of the middle gluteal muscle of Thoroughbred horses: normal values, variability and effect of acute exercise. Equine Vet J 1992; 24:52–57.
132. Miller-Graber PA, Lawrence LA, Kurcz E, et al. The free amino acid profile in the middle gluteal before and after fatiguing exercise. Equine Vet J 1990; 22:209–214.
133. Pösö AR, Essén-Gustavsson B, Lindholm A, et al. Exercise-induced changes in muscle and plasma amino acid levels in the Standardbred horse. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA; ICEEP Publications; 1991:202–208.
134. King N, Suleiman MS. Effect of regular training on the myocardial and plasma concentration of taurine and alpha-amino acids in Thoroughbred horses. Amino Acids 1998; 15:241–251.
135. Wilson A, Kronfeld DS, Gay L, et al. Isolating equine sarcoplasmic reticulum: its function during high intensity repeated sprints. Equine Vet J Suppl 1995; 18:252–255.
136. Williams RS, Neufer PD. Regulation of gene expression in skeletal muscle by contractile activity. In: Rowell LB, Shepherd JT, eds. Handbook of physiology: integration of motor, circulatory, respiratory and metabolic control during exercise. Bethesda, MD: American Physiological Society; 1996:1124–1150.
137. Pette D, Staron S. Mammalian skeletal muscle fiber type transitions. Int Rev Cytol 1997; 170:143–221.
138. Essén-Gustavsson B, Lindholm A, McMiken D, et al. Skeletal muscle characteristics of young Standardbreds in relation to growth and early training. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Foxton, Cambridge: Burlington Press; 1983:200–210.
139. Ronéus M, Essén-Gustavsson B, Lindholm A, et al. Skeletal muscle characteristics in young trained and untrained Standardbred trotters. Equine Vet J 1992; 24:292–294.
140. Ronéus N, Essén-Gustavsson B, Lindholm A, et al. Plasma lactate response to submaximal and maximal exercise tests with training, and its relationship to performance and muscle characteristics in standardbred trotters. Equine Vet J 1994; 26:117–121.
141. Rivero JLL, Serrano AL. Skeletal myosin heavy chain and carriage training. Equine Vet J Suppl 1999; 30:318–323.
142. Rivero JLL. Muscle variables. In: Lindner A, ed. Performance diagnosis of horses. Wageningen: Wageningen Pers; 1997:44–71.
143. Heck RW, McKeewer KH, Alway SE, et al. Resistance training-induced increases in muscle mass and performance in ponies. Med Sci Sports Exerc 1996; 28:877–883.
144. Rivero JLL, Letelier AI. Skeletal muscle profile of show jumpers: physiological and pathological considerations. In: Lindner A, ed. The elite show jumper, Conference on Equine Sports Medicine and Science 2000. Dortmund: Lensing Druck; 2000:57–76.
145. Gottlieb M, Essén-Gustavsson B, Lindholm A, et al. Effects of a draft-loaded interval-training program on skeletal muscle in the horse. J Appl Physiol 1989; 67:570–577.
146. López-Rivero JL, Agüera E, Monterde JG, et al. Skeletal muscle fiber size in untrained and endurance-trained horses. Am J Vet Res 1992; 53:847–850.
147. Lindholm A, Essén-Gustavsson B, McMiken D, et al. Muscle histochemistry and biochemistry of Thoroughbred horses during growth and training. In: Snow DH, Persson SG, Rose RJ, eds. Equine exercise physiology. Foxton, Cambridge: Burlington Press; 1983:211–217.
148. Foreman JH, Bayly WM, Allen H, et al. Muscle responses of Thoroughbreds to conventional race training and detraining. Am J Vet Res 1990; 51:909–913.
149. Essén-Gustavsson B, Lindholm A. Muscle fiber characteristics of active and inactive Standardbred horses. Equine Vet J 1985; 17:434–438.
150. Essén-Gustavsson B, McMiken D, Karlström K, et al. Muscular adaptation of horses during intensive training and detraining. Equine Vet J 1989; 21:27–33.

151. Ronéus M, Essén-Gustavsson B, Arnason T. Longitudinal changes of muscle characteristics and racing performance in Standardbred trotters. J Equine Vet Sci 1993; 13:355–359.
152. Sjoström M, Lexell J, Eriksson A, et al. Evidence of fibre hyperplasia in human skeletal muscles from healthy young men. Eur J Appl Physiol 1991; 62:301–308.
153. López-Rivero JL, Morales-López JL, Galisteo AM, et al. Muscle fibre type composition in untrained and endurance-trained Andalusian and Arab horses. Equine Vet J 1991; 23:91–93.
154. Rivero JLL. Muscle biopsy as a tool for assessing muscular adaptation to training in horses. Am J Vet Res 1996; 57:1412–1416.
155. Ronéus M, Essén-Gustavsson B, Lindholm A, et al. A field study of circulatory response and muscle characteristics in young Standardbreds. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:376–383.
156. Lovell DK, Rose RJ. Changes in skeletal muscle composition in response to interval and high intensity training. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:215–222.
157. Rivero JLL, Sporleder HP, Quiroz-Rothe E, et al. Oral L-carnitine combined with training promotes changes in skeletal muscle. Equine Vet J Suppl 2002; 34:269–274.
158. Pette D. Training effects on the contractile apparatus. Acta Physiol Scand 1998; 162:367–376.
159. Sinha AK, Ray SP, Rose RJ. Effect of constant load training on skeletal muscle histochemistry of thoroughbred horses. Res Vet Sci 1993; 54:147–159.
160. Misumi K, Skamoto H, Shimizu R. Changes in skeletal muscle composition in response to swimming training for young horses. J Vet Med Sci 1995; 57:959–961.
161. Gansen S, Lindner A, Marx S, et al. Effects of conditioning horses with lactate-guided exercise on muscle glycogen content. Equine Vet J Suppl 1999; 30:329–331.
162. Rodnick KJ, Henriksen EJ, James DE, et al. Exercise training, glucose transporters, and glucose transport in rat skeletal muscles. Am J Physiol 1992; 262:C9–C14.
163. McCutcheon LJ, Geor RJ, Hinchcliff KW. Changes in skeletal muscle Glut-4 content and sarcolemmal glucose transport following 6 weeks of exercise training. Equine Vet J Suppl 2002; 34:199–204.
164. Heilig A, Pette D. Albumin in rabbit skeletal muscle. Origin, distribution and regulation by contractile activity. Eur J Biochem 1988; 171:503–508.
165. McCutcheon LJ, Geor RJ, Shen H. Skeletal muscle Na^+-K^+-ATPase and K^+ homeostasis during exercise: effects of short-term training. Equine Vet J Suppl 1999; 30:303–310.
166. Suwannachot P, Verkleij CB, Weijs WA, et al. Effects of training on the concentration of Na^+,K^+-ATPase in foal muscle. Equine Vet J Suppl 1999; 31:101–105.
167. Suwannachot P, Verkleij CB, Kocsis S, et al. Specificity and reversibility of the training effects on the concentration of Na^+,K^+-ATPase in foal skeletal muscle. Equine Vet J 2001; 33:250–255.
168. Bottinelli R, Reggiani C. Human skeletal muscle fibres: molecular and functional diversity. Prog Biophys Mol Biol 2000; 73:195–262.
169. Wilson JA, Kronfeld DS, Gay LS, et al. Sarcoplasmic reticulum responses to repeated sprints are affected by conditioning of horses. J Anim Sci 1998; 76:3065–3071.
170. McCutcheon LJ, Kelso T, Bertocci LA, et al. Buffering and aerobic capacity in equine muscle: variation and effect of training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:348–358.
171. Fox G, Henckel P, Juel C, et al. Skeletal muscle buffer capacity changes in Standardbred horses: effects of growth and training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:341–347.
172. Sinha AK, Ray SP, Rose RJ. Effect of training intensity and detraining on adaptations in different skeletal muscles. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:223–230.
173. Marlin DJ, Harris RC, Gash SP, et al. Carnosine content of the middle gluteal muscle in Thoroughbred horses with relation to age, sex and training. Comp Biochem Physiol 1989; 93:629–635.
174. Hodgson DR, Rose RJ. Effects of a nine-month endurance training programme on muscle composition in the horse. Vet Rec 1987; 121:271–274.
175. Goldspink G, Scutt A, Loughna PT, et al. Gene expression in skeletal muscle in response to stretch and force generation. Am J Physiol 1992; 262:R356–R363.
176. Milner DJ, Taffet GE, Wang X, et al. The absence of desmin leads to cardiomyocyte hypertrophy and cardiac dilation with compromised systolic function. Mol Cell Cardiol 1999; 31:2063–2076.
177. Green HJ, Düsterhöft S, Dux L, et al. Metabolite patterns related to exhaustion, recovery, and transformation of chronically stimulated rabbit fast-twitch muscle. Pflüg Arch – Eur J Physiol 1992; 420:359–366.
178. Yan Z, Serrano AL, Schiaffino S, et al. Regulatory elements governing transcription in specialized myofiber subtypes. J Biol Chem 2001; 276:17361–17366.
179. Murgia M, Serrano AL, Calabria E, et al. Ras is involved in nerve-activity-dependent regulation of muscle genes. Nature Cell Biol 2000; 2:142–147.
180. Serrano AL, Murgia M, Pallafacchina G, et al. Calcineurin controls nerve activity-dependent specification of slow skeletal muscle fibers but not muscle growth. Proc Nat Acad Sci USA 2001; 98:13108–13113.
181. Pallafacchina G, Calabria E, Serrano AL, et al. A protein kinase B-dependent and rapamycin-sensitive pathway controls skeletal muscle growth but not fiber type specification. Proc Nat Acad Sci USA 2002; 99:9213–9218.
182. Hudlicka O, Brown M, Egginton S. Angiogenesis in skeletal and cardiac muscle. Physiol Rev 1992; 72:369–417.
183. Morrow NG, Kraus WE, Moore JW, et al. Increased expression of fibroblast growth factors in a rabbit muscle model of exercise conditioning. J Clin Invest 1990; 85:1816–1820.
184. Geor RJ, McCutcheon LJ, Shen H. Muscular and metabolic responses to moderate-intensity short-term training. Equine Vet J Suppl 1999; 30:311–317.

CHAPTER 6

Muscle disorders of equine athletes

Richard J. Piercy and José-Luis L. Rivero

Veterinarians have long recognized muscle diseases of athletic horses, but only recently have there been significant advances in our understanding of the etiopathogenesis underlying these disorders. These achievements can be attributed to various factors including: (a) recognition of similarities between human and equine muscle diseases; (b) greater awareness that muscle has a limited pathological response despite different mechanisms of injury; (c) subdivision of diseases based on breed susceptibility and histopathology; and (d) the application of molecular and cellular investigative techniques. Future developments should lead to more accurate diagnostic tests and better treatments, thereby enabling the veterinarian to provide an improved service, while benefiting from a more clinically rewarding experience.

General response of muscle to trauma and disease

Muscle tissue has a limited pathological response to different insults whether traumatic, ischemic, exercise induced or due to underlying disease. Cell membrane damage causes abnormal ion fluxes and osmotic imbalance that rapidly perturbs fiber homeostasis. Normally the resting myoplasmic Ca^{2+} concentration is maintained at a concentration that is 60–100 times lower than that of the extracellular fluid (Chapter 5). Membrane damage allows Ca^{2+} to enter the cytoplasm from the interstitium, causing activation of destructive cellular proteases and inhibition of mitochondrial respiration.[1,2] Necrotic cell death is often associated with inflammatory responses including the chemotaxis of neutrophils and macrophages and collagen deposition. However, in certain muscle diseases, fibers die without marked inflammatory responses in which case apoptosis may be responsible.[3]

Muscle's remarkable regenerative capacity is usually associated with a characteristic sequence (Fig. 6.1). Following injury, ruptured myofibers retract, forming a gap between the stumps and allowing access for inflammatory cells via capillaries.[4] 'Contraction bands', condensations of cytoskeletal and sarcomeric material, plug the myofiber stumps and prevent further damage prior to plasma membrane repair.[5,6] Satellite cells, a subpopulation of adult skeletal muscle stem cells[7] that are normally relatively undifferentiated, quiescent and located between the myofiber's sarcolemma and its basement membrane (Fig. 6.2), are responsible for regeneration. Growth factors cause satellite cell activation, division and differentiation within 24 hours.[8] The cells migrate into the damaged region and over a period of about 5 days, fuse to form multinucleated myotubes (often within the basal lamina of the damaged fiber).[9] As the proteins of the myofilaments mature, myotubes gradually differentiate into myofibers,[5] a process taking several months during which histopathology reveals immature fibers of variable sizes and with internally located nuclei (Fig. 6.3).[10] Basement membrane damage results in more extensive fibrosis that may impede reinnervation and revascularization and hence regeneration.[9] Scarring may hinder action potential proliferation; however, this is overcome by sprouts from nearby axons piercing interposed scar tissue and creating new neuromuscular junctions (Fig. 6.4).[9]

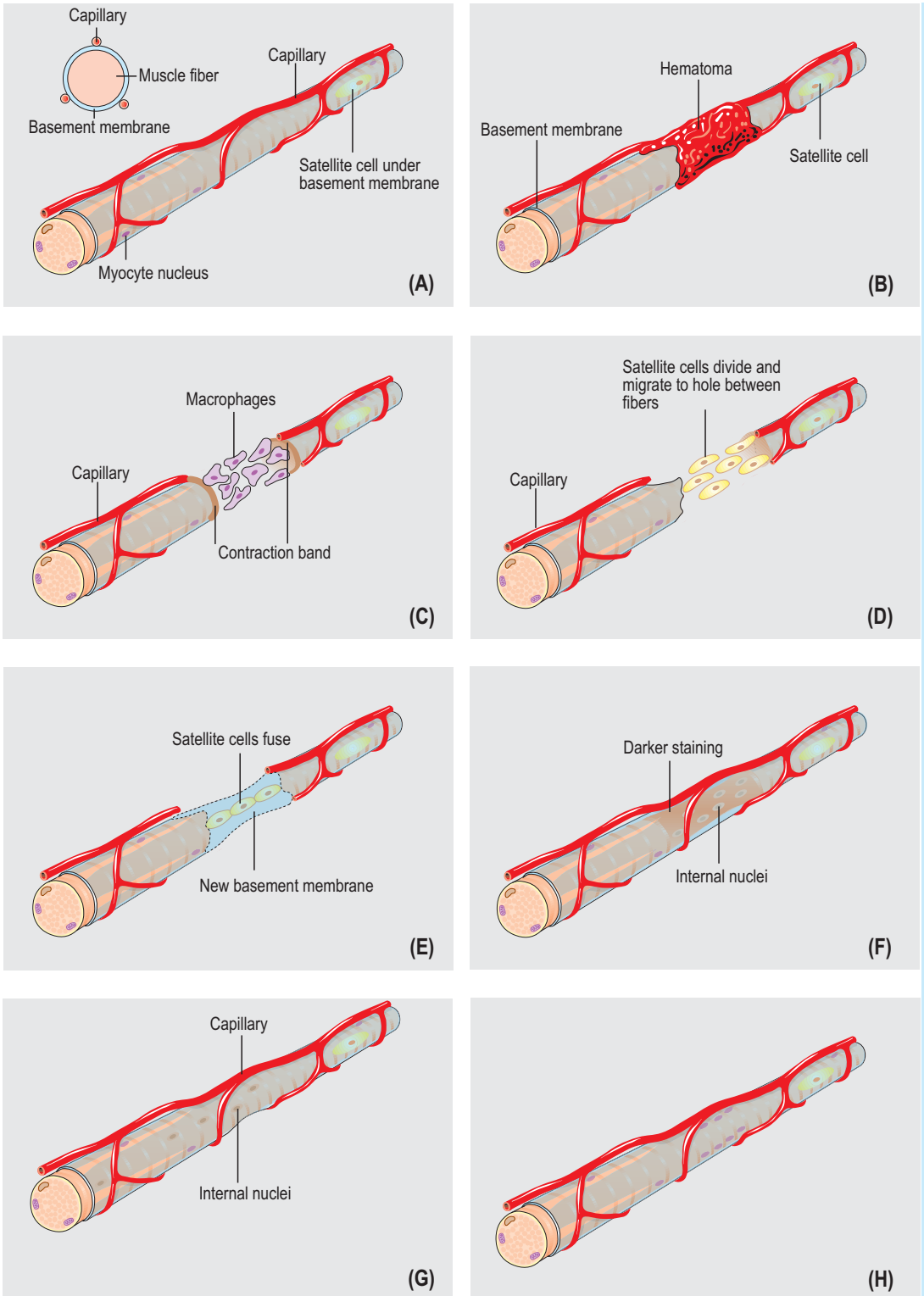


Fig. 6.1
Repair and regeneration in muscle following damage and disease. (A) Normal muscle fiber surrounded by a basement membrane that covers the occasional satellite cell together with a rich network of capillaries. (B) Damage causes myofiber disruption that may or may not involve the basement membrane and hematoma formation, depending on severity. (C) Myofiber stumps retract and the ends become plugged with the contraction band, made of sarcomeric proteins. Macrophages migrate into the (remnants of the) basement membrane cylinder within the first 24 hours and engulf and remove damaged tissue. (D) Satellite cells become activated (12–24 hours following injury), proliferate, differentiate into myoblasts and migrate to the damaged region. By days 2–3, satellite cells align and bridge the gap, fusing between the fiber stumps (E). The process continues over the next week as narrower, more differentiated myotubes with internally located nuclei form (F) followed by more mature myotubes (G). Nuclei return to the normal subsarcolemmal location over several months (H).

Muscle damage caused by trauma, strains and tears

- Muscle damage caused by strains or tears is common in athletic horses.
- The site of damage dictates the signs that may include lameness or back stiffness.
- Plasma CK and AST activities may be mildly elevated.
- Ultrasound, thermography and scintigraphy can aid diagnosis.
- Rest and non-steroidal anti-inflammatories often bring full return to function.

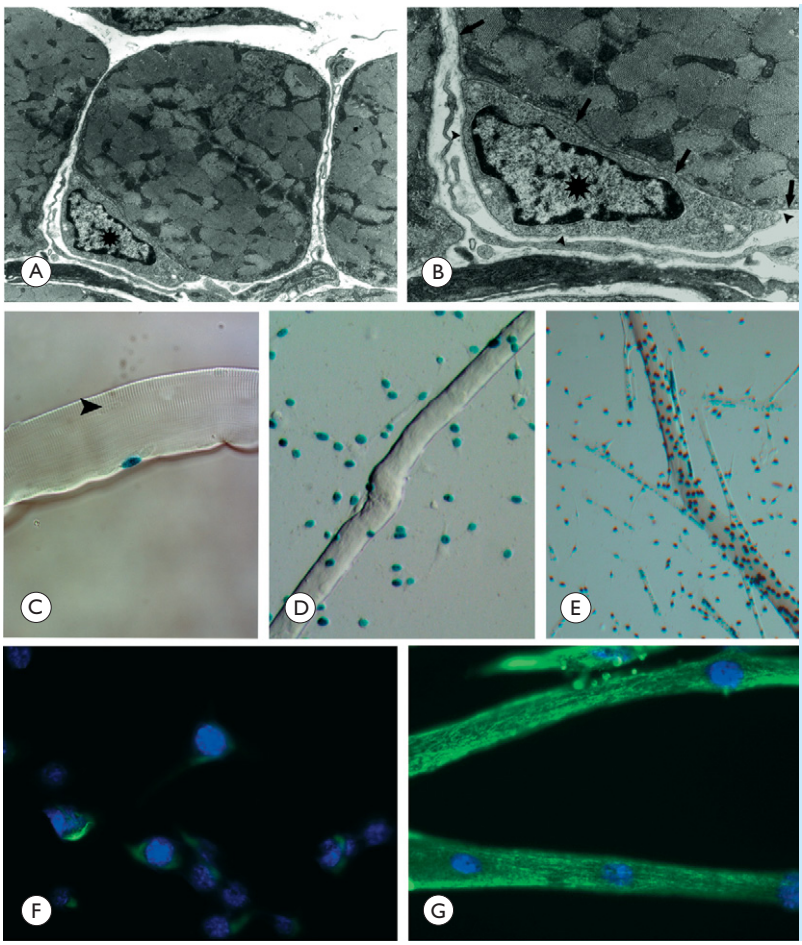


Fig. 6.2
Satellite cells in vivo and in vitro. (A) Satellite cell in situ on the sarcolemmal surface of a 9-day-old B10 mouse muscle fiber. Notice the patchwork-like distribution of myofibrils in the muscle fiber and the satellite cell nucleus marked with an asterisk. (B) Higher power view of the satellite cell from (A) showing the sarcolemma (arrows) and the basement membrane (arrowheads). (C) Single muscle fiber in culture following its isolation from a transgenic mouse that expresses lacZ (blue staining) in satellite cell nuclei in response to Myf5 transcription factor expression;[231] notice the fiber striations and the unlabeled subsarcolemmal myonuclei (arrowhead). (D) Single fiber from a transgenic mouse (as in C) following several days in culture. Notice the proliferation of satellite cells. (E) Following several further days in culture, satellite cells begin to fuse into myotubes. (F) H2K myoblasts in culture labeled with a monoclonal antibody to the muscle-specific protein, desmin (green); nuclei are stained blue with the chromosomal DNA marker 4,6-diamidino-2-phenylindoledihydrochloride hydrate (DAPI). (G) H2K cells as in (F) following their differentiation and fusion into myotubes.
(A & B courtesy of Dr Susan Brown, C, D & E courtesy of Dr Peter Zammit, Imperial College of Science Technology and Medicine, UK.)

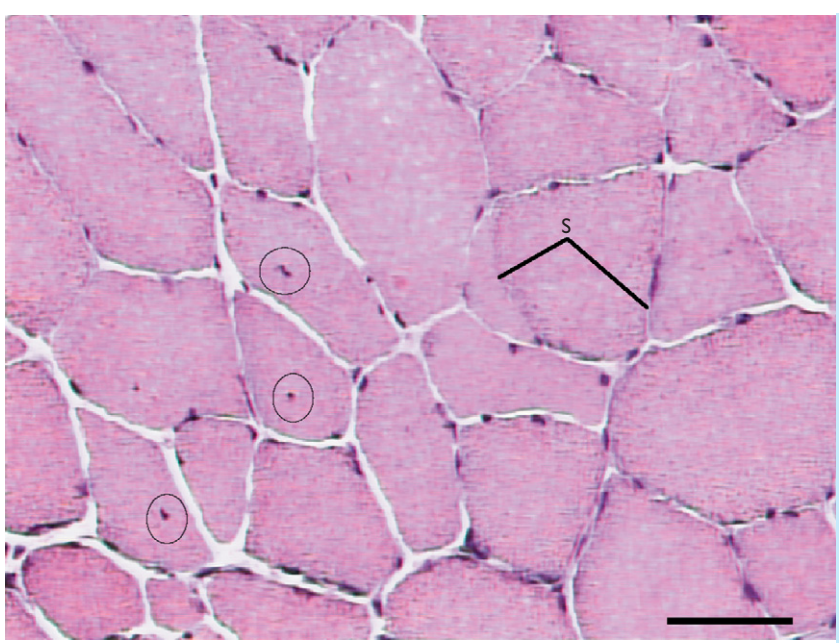


Fig. 6.3
Hematoxylin and eosin transverse section from a M. gluteus medius biopsy from a horse with idiopathic recurrent exertional rhabdomyolysis. A few fibers have internalized nuclei (circled), and signs of fiber splitting (S) are evident.

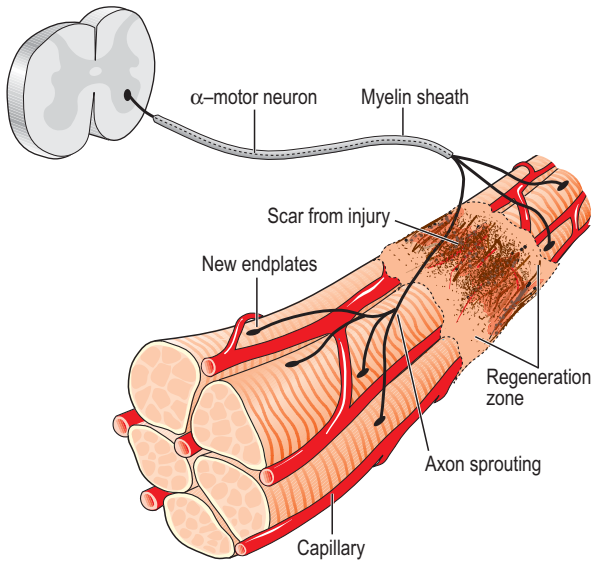


Fig. 6.4
Diagrammatic representation of resprouting of an α-motor neuron following injury to a group of myofibers. Axon sprouts penetrate interposed scar tissue forming new end-plates, thereby reinnervating the myofiber stumps.

Recognition

History and presenting complaint

Delay in the onset of inflammation after trauma may complicate the history, but pain may be evident in showjumpers and eventers (both prone to lumbar and gluteal strain) as unwillingness to jump or turn sharply[11] or in other animals as mild to moderate lameness or stiffness. Generally injuries occur during exercise but severe muscle damage can follow prolonged recumbency[12] or direct trauma.[13,14]

Physical examination

In acute stages, palpation reveals painful muscles with focal heat, swelling and edema. Trauma, secondary to impact injury, may be associated with overlying skin damage. In more chronic cases an organizing hematoma and/or a scar may be palpable. Certain lacerations and muscle tears may manifest as an abnormally held limb, unusual gait or an inability to bear weight.[14,15]

Special examination

Radiography may rule out bony abnormalities such as avulsion fractures. Thermography, scintigraphy and ultrasound can aid diagnosis and lesion localization and help assess healing.[16–18]

Laboratory examination

Plasma muscle enzyme activities may be increased in the early stages.

Diagnostic confirmation

In some cases establishing a definitive diagnosis may be difficult, but confirmation is aided by ruling out skeletal injury.

Treatment and prognosis

Therapeutic aims

Minimizing further damage while allowing for repair and regeneration of the damaged muscle and providing analgesia are critical.

Therapy

Adequate rest followed by gradual return to exercise is essential. Severe injuries may require immobilization in casts or splints. Non-steroidal anti-inflammatory drugs (NSAIDs) (e.g. phenylbutazone 4.4 mg/kg i.v. or p.o. q 12 h for one day followed by 2.2 mg/kg p.o. q 12 h for several days; or flunixin meglumine 0.5–1.1 mg/kg i.v. or p.o. q 12 h or q 24 h) provide analgesia and may reduce fibrosis. Massage, electrical stimulation and swimming may speed recovery.

Prognosis

The prognosis for most muscle strains and tears is good, although fibrosis may cause mechanical lameness.[19] When severe, or where tearing occurs near the myotendinous junction, the prognosis for return to full function becomes guarded.

Prevention

Although traumatic injuries are hard to prevent, exercise-induced injuries are less likely when horses are warmed up before work and exercise schedules are intensified gradually.

Exertional rhabdomyolysis syndromes (during acute and between intermittent episodes; acquired, idiopathic, defective calcium regulation, polysaccharide storage myopathy)

- Both acquired and inherited forms of exertional rhabdomyolysis exist.
- Overexertion is a common acquired cause.
- Likely inherited causes include a disorder of defective myofiber calcium regulation and another associated with abnormal muscle polysaccharide accumulation.
- Environmental effects probably modify the phenotype in genetically susceptible animals.

- Severity ranges from subclinical to life threatening.
- Pain may be severe.
- Plasma CK and AST activities are moderately to markedly elevated.
- Myoglobinuria may cause renal tubular damage and acute renal failure.
- Muscle biopsy is indicated in animals with histories of multiple episodes.
- In acute cases, rest and intravenously administered isotonic fluids and analgesics form the mainstays of treatment.
- Dietary management can prevent episodes recurring in some horses.

There are many historical, somewhat speculative reports suggesting different possible causes of equine exertional rhabdomyolysis (ER).[20] A large number of causes is unsurprising given the numerous acquired and inherited forms in humans.[21] However, since certain types of equine ER appear to have underlying genetic causes, the intermittent and varying severity of phenotype in these animals may be explained by the influence of modifying genes and environmental factors, factors that in the past were determined to be the primary etiology. Episodes of rhabdomyolysis not generally associated with exercise may be of toxic, infectious, immune-mediated or iatrogenic origin and are not included in this chapter but are discussed in detail in general medicine texts.[12,22]

The recent identification of certain specific forms of ER means that classification can now be based on the underlying etiopathogenesis. In the text that follows, the clinical sections have been written in a manner aimed at the investigation of a case with unknown etiology, when there are generally two presentations. The first is that of an animal with acute signs requiring emergency medical treatment. The second scenario is a clinically normal horse with a history of several episodes of ER or a history of poor performance. The clinical investigation and management for each situation differ, even though the underlying cause may be the same and for this reason they are considered separately.

Acute exertional rhabdomyolysis

Recognition

History and presenting complaint

Often the history includes training or management changes. The complaint may vary from a mild stilted gait to severe stiffness, sweating or recumbency.[23] However, most animals are mildly or moderately affected.

Physical examination

During an attack, horses with ER show varying clinical signs. Mildly or moderately affected animals are tachycardic, with firm painful hindlimb, epaxial and gluteal musculature causing gait stiffness.[23] In some, pain localization may be difficult or pain may be manifest in other ways: male horses, for example, may frequently posture to urinate[24] and other horses exhibit colic. Pigmenturia may be evident, especially in more severe cases (Fig. 6.5). These animals are often extremely painful, tachycardic, hyperthermic and tachypneic; they sweat profusely and may be totally unwilling or unable to move.[23] These horses have widespread muscle involvement and may become recumbent. The worst affected animals may show signs compatible with underlying shock and disseminated intravascular coagulation.

Fig. 6.5 Urine containing myoglobin (brown discoloration) from a horse with severe rhabdomyolysis (plasma CK activity > 700 000 IU/L).

Special examination

The history, clinical signs and clinicopathologic investigation (see below) are usually sufficient to establish a diagnosis of ER but scintigraphy may be helpful to localize and quantify muscle involvement in certain cases.[16]

Laboratory examination

Blood samples Routine clinicopathologic changes in mild cases usually consist solely of elevations in the activities of the muscle-derived enzymes CK and AST. CK is the most convenient and specific marker of acute muscle damage and peaks at 4–6 hours following muscle damage and (unless the damage continues) starts to decline, with a half-life of approximately 12 hours (Fig. 6.6).[25] AST activity peaks about 24 hours after an episode and may remain elevated for several days to weeks.[12,24] Although both CK and AST activities rise in proportion to the degree of muscle damage, they do not always reflect the severity as assessed clinically[12] or the prognosis. Other markers, sometimes used experimentally to assess muscle damage, such as serum myoglobin concentration or aldolase, LDH and carbonic anhydrase III activities, offer few if any clinical advantages over the measurement of CK and AST.

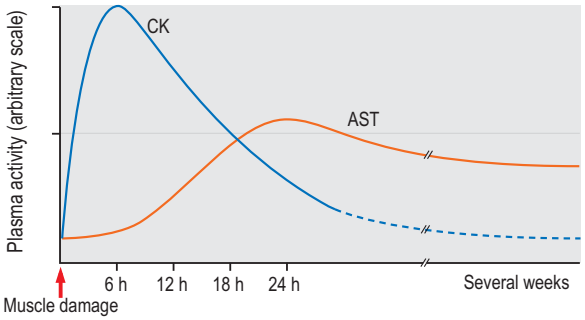


Fig. 6.6
Diagrammatic representation of changes to serum CK and AST activity following an acute brief episode of rhabdomyolysis.

More severe cases have additional less-specific abnormalities. Hyperkalemia may reflect the release of potassium from damaged muscle fibers. The hematocrit and total protein may rise due to intracompartmental fluid shifts. High serum creatinine concentration suggests the possibility of acute renal failure. Complex acid–base abnormalities are sometimes present as the usual hypochloremic metabolic alkalosis[26] shifts to metabolic acidosis if shock ensues. Widespread hematological and biochemical abnormalities are evident in terminal cases.

Urinalysis A urine sample collected early during treatment may, with microscopic examination, reveal urinary casts, a useful indicator of tubular necrosis and impending acute renal failure, prior to the plasma creatinine concentration rising.

Reagent strip analysis of urine does not differentiate myoglobin from hemoglobin, so specific assays are required to determine the cause of any pigmenturia.[12] However, measurement of urinary myoglobin concentration is not usually necessary in an animal with significantly elevated serum muscle enzyme activities. Mild pigmenturia is a normal finding in some horses following high-intensity exercise.[27]

The calculation of electrolyte clearance ratios (see below) during an episode of ER may help evaluate renal function,[28] but should not be used to determine whether electrolyte imbalances were responsible for precipitating the attack.

Necropsy examination

Histopathological assessment often reveals widespread muscle involvement, even in non-locomotor muscles. Occasionally there may be focal muscle involvement so a wide selection of muscles should be sampled, including several epaxial muscles, forelimb and hindlimb locomotor muscles and psoas.

Diagnostic confirmation

In the acute form the disease may be confused with colic, laminitis, tetanus, hyperkalemic periodic paralysis and some cardiac arrhythmias. However, usually these diseases are readily distinguishable by additional signs, specific tests and the lack of significantly elevated serum muscle enzyme activities. Occasionally sedentary horses may present with classic signs of rhabdomyolysis with markedly elevated serum muscle enzyme activities. In these animals underlying genetic susceptibility, more usually associated with exertional forms of the disease, is possible because other events such as stress may precipitate attacks. Toxic, infectious or immune-mediated causes should also be considered.[12,22,29]

Treatment and prognosis

Therapeutic aims

The therapeutic goals are to minimize further muscle damage, establish and maintain diuresis, correct underlying systemic abnormalities and provide analgesia. Early treatment is essential.[30]

Therapy

Management Exercise should be stopped and the horse rested in a deep-bedded stall. In very mildly affected animals gentle hand walking is sometimes recommended.

Fluid therapy Mildly affected animals, in which vital signs are close to normal, can recover without intravenous fluid therapy. However, they should be monitored for signs of deterioration. In moderate to more severe cases, however (even in those without clear pigmenturia), establishing diuresis and preventing or treating hypovolemia is the priority because myoglobin is nephrotoxic. Large volumes of isotonic fluids are usually effective (0.9% NaCl or lactated Ringer's solution infused intravenously at 100–150 mL/kg/24 h). The addition of sodium bicarbonate to fluids, though rarely necessary,[26] is generally only indicated in a horse with metabolic acidosis when the urine remains acidic despite fluid therapy, because myoglobin is significantly more nephrotoxic when in acidic urine.[31]

In rare cases, isotonic electrolyte solutions, even when administered rapidly, cannot compensate for the worsening hypovolemia. This state is reflected by a climbing heart rate and hematocrit, accompanied by a steady or occasionally falling total plasma protein and serum albumin concentrations as widespread muscle lysis and inflammation allow water and proteins to leave the vasculature and enter the interstitium and damaged muscle fibers. These animals often die despite intensive therapy.

Diuretics If there is little or no urine production during appropriate intravenous administration of fluids, attempts should be made to invoke diuresis. Furosemide (frusemide) is generally effective (0.5–1 mg/kg i.v. or i.m. q 12 h). Careful monitoring and adjustment of fluid rates are essential to ensure that diuresis does not cause or exacerbate hypovolemia. Diuretics are not recommended in animals not receiving fluids.

Absence of urination for several hours despite fluid therapy and furosemide (frusemide) suggests oliguric renal failure, in which case renal blood flow may be increased with dopamine (3–5 μg/kg/min diluted in 5% dextrose intravenously) to promote diuresis. Close monitoring of heart rate and the ECG is required because of the risk of tachyarrhythmias.

Analgesia In mild to moderate cases NSAIDs (e.g. phenylbutazone 4.4 mg/kg i.v. or p.o. q 12 h for one day followed by 2.2 mg/kg p.o. q 12 h for several days; or flunixin meglumine 0.5–1.1 mg/kg i.v. or p.o. q 12–24 h) medication

is all that is necessary; however, clinicians should monitor renal function given the drugs' nephrotoxicity. In severe cases more potent analgesics such as butorphanol (0.1 mg/kg i.v. or i.m. q 4–6 h) may be required. In the worst cases the pain is very difficult to relieve.

Other therapy Acepromazine (0.04–0.11 mg/kg i.v. or i.m. q 8 h) has been advocated for its vasodilatory effects within the musculature; however, it should be used with caution in hypovolemic animals. Corticosteroids (e.g. dexamethasone 0.02 mg/kg i.v. q 24 h for 1–2 days) are sometimes used to stabilize membranes, but their efficacy is unproven.

Dantrolene, a drug that limits release of Ca^{2+} from the sarcoplasmic reticulum (SR) via the skeletal muscle ryanodine receptor (RYR1),[32] has been used in the acute stages of idiopathic rhabdomyolysis[33] but pharmacokinetics[34] suggest that the dose and the frequency of administration were unlikely to have resulted in beneficial drug concentrations (when compared with those required to effect a response in humans).[35] Although dantrolene administration has been associated with causing weakness in some horses,[36] emerging experimental evidence suggests that it may be indicated in the prophylaxis or treatment of the acute stages of the form of ER associated with abnormal calcium regulation. As yet, however, the dose required to limit RYR1 release of Ca^{2+} in horses is unknown, as the drug has not been tested. We therefore recommended that clinicians await efficacy trials, particularly given the high cost of the drug.

Prognosis

The prognosis for most horses with mild to moderate acute episodes of ER is good for recovery, but horses with an underlying genetic susceptibility will always be prone to future episodes. For horses in shock, the prognosis is poor. Many horses that develop acute renal failure, if treated early, recover.

Prevention

Refer to the section below that covers investigation and management of horses between episodes.

Exertional rhabdomyolysis (between intermittent episodes)

Recognition

History and presenting complaint

Histories are often compatible with recurring episodes of rhabdomyolysis as described above. Often, a horse is presented because there is no good explanation for the rhabdomyolysis and owners believe that some underlying factor is responsible. Some horses may present with histories of poor performance.[37]

Physical examination

Often animals appear normal when examined.

Special examinations

Exercise testing An exercise test may be helpful in horses with no evidence of ongoing muscle damage (by measuring serum CK and AST activities), but is potentially dangerous in ER-susceptible animals so sound clinical judgment is critical. Exercise testing is contraindicated in animals with evidence of recent muscle damage. The sensitivity and specificity of exercise tests have not been evaluated and the intermittent nature of the disease may result in a negative test in a susceptible animal.[12]

Ideally, a positive test should provoke a subclinical episode of rhabdomyolysis that can be detected via a rise in CK activity between pre- and 4-h post-exercise serum samples. Titrating the amount and type of exercise can be difficult, but should be based on the horse's history and level of fitness. Bouts of maximal exercise appear less likely to precipitate episodes[38,39] and are therefore not recommended. Generally, 10–20 minutes of moderate exercise (trot and canter) on a lunge line or a treadmill is appropriate. Ideally, a normal horse should be evaluated in a similar manner for direct comparison, because some normal animals show a rise in CK activity post exercise; a rise in plasma CK activity of less than 250% has been regarded as normal.[12]

Laboratory examinations

Blood samples Despite a normal physical examination, elevations in plasma CK and AST activities suggest recent muscle damage. A high plasma AST activity without a concomitant elevation in plasma CK activity may indicate that muscle damage has occurred within preceding weeks. However, given that AST is not a specific marker for muscle disease, careful evaluation of the hemogram and biochemistry profile, and if necessary further tests, are indicated to rule out hepatocellular disease.

Electrolyte clearance ratios Clearance ratios are calculated to assess whole-body electrolyte status. Electrolytes and creatinine concentrations are measured in a urine (free catch or catheterized) and serum sample from the same animal. Ratios determined following collection of a single urine sample give similar results to those obtained with a 24-hour pooled (volumetric) urine sample, except for magnesium,[40] but accurate measurement requires urinary acidification (e.g. addition of concentrated nitric or hydrochloric acid)[40,41] to dissolve any suspended crystals. Horses should not eat between collection of the samples.[42]

The fractional clearance for each electrolyte ($FC_{(electrolyte)}$), is calculated as follows.[28]

$$FC_{(electrolyte)}\% = \frac{[electrolyte]_{urine}}{[electrolyte]_{plasma}} \times \frac{[creatinine]_{plasma}}{[creatinine]_{urine}} \times 100$$

where the square brackets represent the concentration (the acidification dilution factor should be factored in). There are wide variations for normal values in veterinary literature,[28,40,41,43,44] probably from differences in management,

sampling and analysis. Normal ranges for FC(sodium) have been reported as 0.04–0.52%; for potassium, 35–80%; for chloride, 0.7–2.1%; and for phosphate, 0–0.2%.[45] However, the identification of wide daily fluctuations in clearance ratios in the same horse, despite standardized management, casts doubt on the test's relevance.[44,46]

Plasma vitamin E and selenium Most ER-susceptible horses are not deficient in vitamin E or selenium, but measuring plasma vitamin E and selenium concentrations may demonstrate deficiencies in animals on poor planes of nutrition or from selenium-deficient areas.

Muscle biopsy A muscle biopsy is indicated in an animal with several unexplained episodes of ER. The technique is described in Chapter 5. The biopsy site is based on the physical examination, but epaxial, gluteal and semimembranosus muscles are most commonly chosen.[29] Ideally, a fresh muscle sample should be snap-frozen in isopentane cooled in liquid nitrogen,[10] but since this is not usually practical, a compromise is necessary. Good results can be obtained when a sample is sent overnight to a suitable laboratory, wrapped in moist but not dripping gauzes (0.9% saline), and chilled (not frozen) on icepacks.[29] Formalin fixation, though more convenient, is unsuitable for histochemical investigation and leads to more artefact; it does allow morphological assessment, however, and has enabled a diagnosis to be reached in cases of polysaccharide storage myopathy (PSSM).[47]

Histopathological lesions of idiopathic cases and ER associated with defective calcium regulation are highly variable and depend on severity and the time between the biopsy and the last bout of rhabdomyolysis (Figs 6.7, 6.8). Mild inflammation with hypercontracted and swollen fibers, interstitial edema and occasionally hemorrhage is seen in single episodes of acute rhabdomyolysis and during the first 24–48 hours following a new episode in animals with histories of recurring episodes (Fig. 6.7A). In this latter group, there may be hyaline degeneration, edema, scattered swollen fibers, fiber fragmentation, necrosis and macrophage infiltration and signs of regeneration (occasional fibroblasts with large nuclei and prominent nucleoli, myotubes and mature fibers with centrally located nuclei) within the same section.

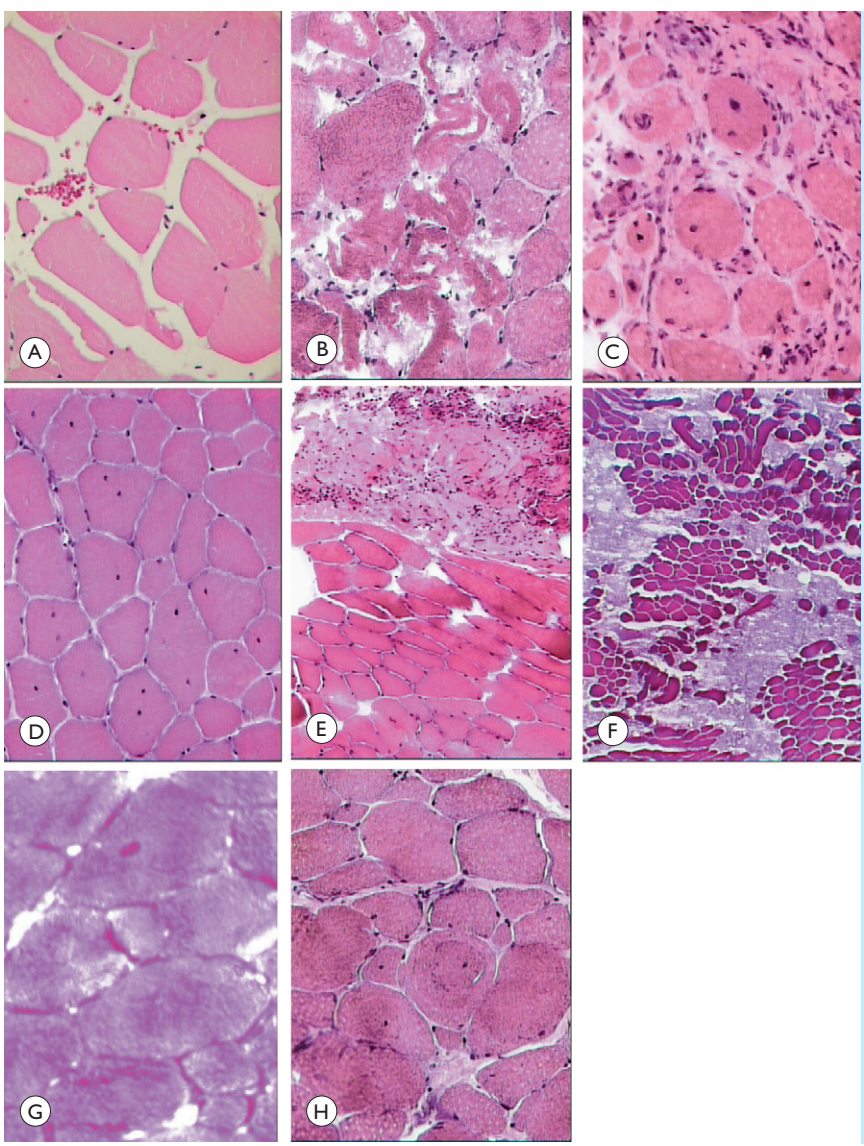


Fig. 6.7
Transverse sections stained with hematoxylin and eosin of the hindlimb and epaxial musculature of horses with idiopathic recurrent ER. (A) Several large, rounded and hypercontracted fibers are shown with diffuse interstitial edema and abundant hemorrhage. (B) Focal hyaline degeneration of type II fibers. (C) Severe myopathic changes characterized by increased fiber size variability, hypercontraction and degeneration, macrophage infiltration and abundant fibroblasts with large nuclei and prominent nucleoli. (D) Mature fibers with internalized nuclei that have regenerated following damage within the previous 1–2 months. (E) A scar is shown in the top of this frame, indicating ineffective muscle repair in an animal after recurrent rhabdomyolytic episodes. (F) Extensive ineffective muscle repair with massive loss of myofibers and replacement by connective tissue. (G) A fiber (top) with an intracytoplasmic mass, probably an aggregate of intracellular calcium. (H) Signs of regeneration including a whorled fiber towards the center.

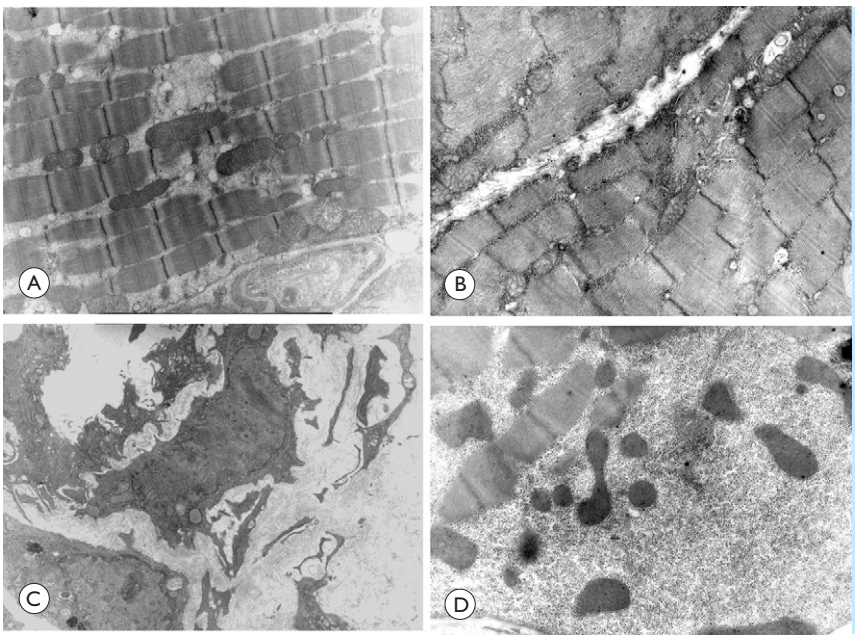


Fig. 6.8
Electron micrographs of muscle from horses with idiopathic recurrent ER. (A) Myofibrillar degeneration with loss of contractile material, dilated terminal cisternae and swollen mitochondria with different electrodensities and abnormal cristae; × 16 800. (B) Loss of myofibrillar architecture with abundant Z-line streaming; × 22 400. (C) Macrophage infiltration; × 11 200. (D) Loss of contractile material with abundant glycogen; × 25 200. (Courtesy of Drs Sucre and Finol from the Universidad Central de Venezuela.)

Additionally, in severe cases, fibrosis, scars and fat infiltration and/or substitution are common (Fig. 6.7E,F).[23,48–50] Fast-twitch (type II) fibers are usually more severely affected than type I. Scattered fibers with subsarcolemmal and/or intracytoplasmic masses, possibly of calcium, are occasionally present (Fig. 6.7G).[51] Other signs of regeneration, such as whorled fibers (Fig. 6.7H), may be observed.

Common electron microscopic lesions found in idiopathic recurrent cases of rhabdomyolysis include myofibrillar disruption with loss of contractile material, streaming of Z disks, dilated SR, enlarged and rounded mitochondria with dilated matrices and degenerated cristae, macrophage infiltration and increased granular deposits of glycogen (Fig. 6.8).[39]

The changes described above are non-specific and reflect the general pathologic processes explained at the beginning of this chapter. Additional histopathologic changes associated with PSSM[47,52,53] include: (a) a heterogeneous distribution of periodic acid-Schiff (PAS) stained intrafibrillar glycogen with subsarcolemmal vacuoles; (b) PAS-positive inclusions; and (c) α-amylase-resistant PAS-positive inclusions (i.e. consistent with abnormal polysaccharide) (Fig. 6.9). The PAS-positive and α-amylase-resistant inclusions are observed in type II fibers, do not stain with ATPase and SDH histochemistry, and have a slight eosinophilic light blue appearance with hematoxylin and eosin stains, magenta to dark blue with PAS and magenta with α-amylase-PAS.[52,54,55] The morphology of these inclusions, as multiple intracytoplasmic 'lakes' and/or as larger or more confluent accumulations totally or partially replacing the fiber in transverse section, is consistent with similar changes recognized in formalin-fixed, paraffin-embedded muscle from affected animals.[56]

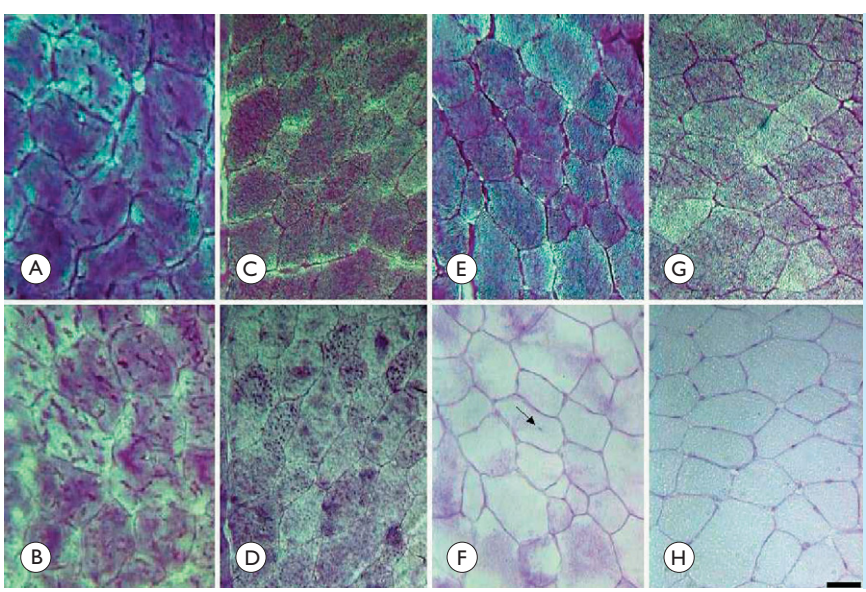


Fig. 6.9
Serial sections stained with PAS (A, C, E and G) and α-amylase-PAS (B, D, F and H) of longissimus lumborum muscle (A and B) and gluteus medius (C and D) muscle from the same horse with PSSM, of gluteus medius muscle from a Standardbred with idiopathic recurrent ER (E and F), and of gluteus muscle from a normal control Standardbred (G and H). Note the high glycogen content and the dark PAS-positive inclusions in muscle from the horse with PSSM (A–D), the lack of PAS-positive material after amylase digestion in idiopathic ER (F) and control (H) horses, as well as the low intensity of the PAS stain in the control (G). An internalized nucleus is present in (F) (arrow). Bar = 25 μm.

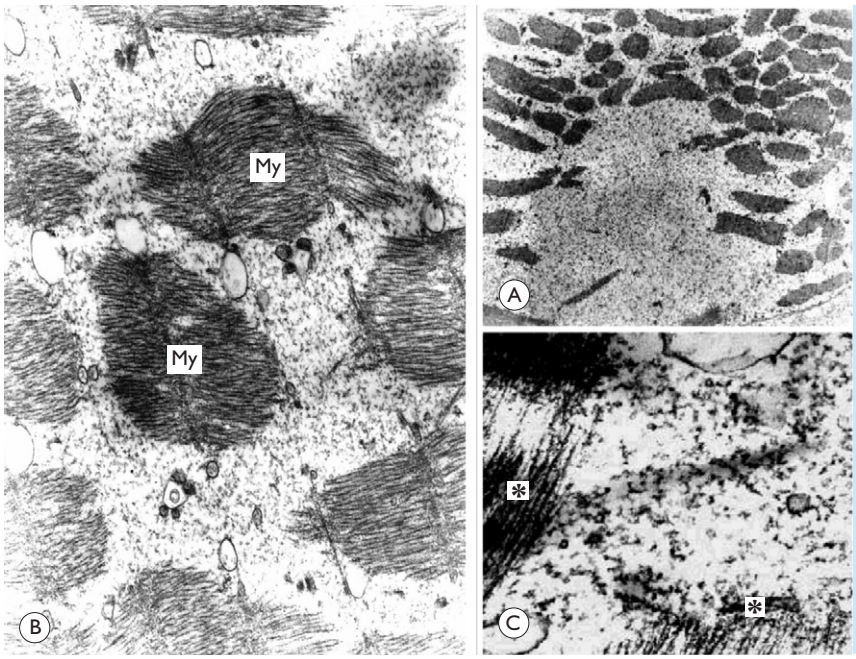


Fig. 6.10
Transmission electron micrographs of M. longissimus lumborum biopsies from horses with polysaccharide storage myopathy (PSSM). (A) A large intracytoplasmic irregular aggregate of granular material is distributed between myofibrils with massive disruption of their normal arrangement (× 20 000). At higher magnifications (B, × 37 000) the inclusions appear to consist of β-particles of glycogen disrupting myofibrils (My) and (C, × 65 000) large aggregates of filamentous material (asterisks).

Pathological features of PSSM may also be observed by electron microscopy (Fig. 6.10). Muscle damage is usually extensive and consists of numerous fibers containing varying degrees of myofibrillar disruption and both loss and disruption of contractile material, characterized by irregular myofibrils and striation patterns. Filamentous material consisting of disrupted contractile proteins and probably abnormal polysaccharide are present amongst excessive granular glycogen.

Although PSSM was originally identified in Quarter Horses,[52] it has also been described in other breeds.[54–58] Even though PAS-staining accumulations that remain following amylase digestion are regarded as a specific feature of PSSM and the disease's hallmark[29,53] they are sometimes absent.[56] Some investigators have overcome this lack of sensitivity by making the same diagnosis based on histopathologic evidence of *myopathy* in combination with excessive deposits of glycogen.[57] Excessive glycogen accumulation occurring prior to the deposition of abnormal polysaccharide is representative of milder and earlier pathologic changes in certain human polysaccharide storage diseases,[59] so there is some justification for this approach. Characteristic PAS-positive, amylase-resistant inclusions are only detectable in (genetically susceptible) PSSM Quarter Horse foals at 3 years of age, some time after their enhanced insulin sensitivity is detectable.[60] However, care must be exercised, given that the PAS staining intensity as quantified by photometry (and hence glycogen content) of muscle from horses with other (idiopathic) causes of ER is higher than in normal controls (Fig. 6.9).[54]

Additional tests Additional experimental tests used further to differentiate etiologies include glucose tolerance testing for diagnosis of PSSM and contracture testing of muscle and calcium fluorescence testing of cultured muscle for the diagnosis of recurrent ER due to disordered calcium regulation.[61–64] However, with the exception of glucose tolerance, these tests require specialist facilities and the expertise of a dedicated laboratory. Further study may result in some of these tests becoming clinically useful in the future.

Diagnostic confirmation

Reaching a diagnosis of ER is not usually difficult but categorizing the disease according to the etiology may be much harder. Both acquired and inherited causes should be considered in an animal with acute signs; in a horse that presents following multiple episodes, underlying genetic predisposition is more likely, although acquired forms should not be overlooked. Certain acquired causes may be obvious from the history (e.g. overexertion) and specific testing may identify other forms.[35,53] Of the disorders that are probably inherited, definitive diagnosis for PSSM can now be made by muscle biopsy. Unfortunately, other cases (away from the research setting) continue to contribute to a large idiopathic category, a situation in common with the diagnosis of human ER.[65] Identification of specific genetic abnormalities responsible for familial forms of ER should provide the means for definitive genetic testing in the future.

Prevention

The association of a disease with a considerable number of anecdotal treatments usually reflects current and historical inability to establish the precise etiology and the treatments' questionable or limited efficacies. Such is the case for the prophylactic treatment of ER where a wide variety of preventive treatments exist,[66] with only a few having been scrutinized objectively.

Diet Despite apparent differences in etiology and pathogenesis[64] the substitution of a proportion of dietary calories derived from soluble carbohydrate, with additional fat, reduces the severity of episodes of ER via poorly understood

mechanisms in both Thoroughbreds with dysfunctional calcium regulation[67] and horses with PSSM.[68,69]

High-fat diets have a calming effect on horses[70] and are associated with lower plasma cortisol concentrations during exercise;[71] since stress has been associated with ER in Thoroughbreds[66] the calming effect may explain the rapid prophylactic efficacy of high-fat diets in recurrent ER caused by abnormal calcium regulation.[67] There is currently conflicting evidence as to whether high-fat (low-carbohydrate) diets reduce the excessive glycogen accumulation in muscle in horses with PSSM[72,73] so further work is required to clarify the attractive hypothesis that the beneficial effect of fat in PSSM is a shift of energy metabolism from the assumed dysfunctional glucose uptake/glycogen synthesis pathways towards β-oxidation.

Most studies have investigated the beneficial effect of a diet that contains approximately 20% fat, together with a reduction in soluble carbohydrate (grain) intake.[67] Increased fat in the diet can be achieved by the addition of vegetable oil (up to approximately 1 g/kg bodyweight per day or 1.1 mL/kg bodyweight per day). Rice bran (15–20% fat) can also be used as a substitute source in animals that find the oil unpalatable[74] or a combination may be suitable in some animals. Forage intake should be at least 1% of bodyweight, but some authors recommend that fast-growing lush pastures and high-quality sweet hays should be avoided.[74] Alfalfa pellets and beet pulp may also be used. Horses should be introduced to higher fat diets over several weeks and the dietary intake of minerals and vitamins should meet recommendations. In particular, owners should ensure that the calcium : phosphorus ratio in the diet is adequate, as rice bran and high-fiber products such as beet pulp contain excessive phosphorus relative to calcium. There are several high-fat, low soluble carbohydrate feeds commercially available.

Exercise Evidence suggests that a regular daily exercise program with changes introduced gradually, and preferably daily access to pasture, may help horses that are susceptible to intermittent episodes of ER.[66,68]

Electrolyte therapy Electrolyte supplementation is appropriate in animals that have been identified as deficient by specific testing. There is no rationale for the once popular administration of sodium bicarbonate to horses to prevent episodes, because most affected animals do not have underlying acid–base disorders prior to exercise and become alkalotic during exercise.[26,67]

Antioxidant supplementation Vitamin E (1–6 IU/kg/day α-tocopherol) and selenium (1–2 mg/day) supplementation in food are indicated when deficiencies have been confirmed.[35,74]

Prophylaxis Numerous drugs are administered prophylactically, but most are used with unproven efficacy. The recent identification of separate disease etiologies may result in properly controlled drugs' trials in the near future (see comments on the use of dantrolene in the section on treatment of acutely affected horses, above). One group has reported the use of phenytoin[35] but it is expensive, it interacts with other drugs and may cause sedation, ataxia, focal seizures and recumbency.[35] Therefore, until further studies prove the drug's efficacy in horses with a well-established underlying etiology, the authors suggest its use only as last resort.

Etiology and pathophysiology

Acquired causes

Although important as specific causes in normal horses, some apparently acquired causes may be associated with underlying genetic predisposition to ER.

Overexertion Extreme or unaccustomed exercise predisposes horses to rhabdomyolytic attacks. Muscle damage in such cases may include a combination of physical damage incurred during excessive eccentric contractions, metabolic exhaustion and oxidative injury.

Eccentric contraction Delayed-onset muscle soreness in humans is associated with damage caused by excessive eccentric contractions (contraction during muscle lengthening).[75] Stiffness and pain, usually experienced 1–2 days following such exercise, is initially most evident at the myotendinous junction and then spreads throughout the muscle. Although the mechanism is poorly understood, there are prominent signs of damage within a muscle following eccentric contractions that include disruption of sarcomeres and damage to the excitation–contraction coupling mechanism and the sarcolemma.[76] This damage is reflected by (sometimes considerable) elevations in serum muscle enzyme activities[77,78] and triggers a local inflammatory response accompanied by edema and the sensitization of nociceptors.[75]

Whether horses experience this syndrome is unknown. Exercising horses are most likely to encounter eccentric contractions during downhill exercise and jumping. Given that muscle damage in humans generally occurs when the type or extent of eccentric contractions are unaccustomed and that adaptation occurs with training,[76] it seems sensible to introduce horses gradually to these types of exercise.

Metabolic exhaustion Exceeding the level of training either by excessive endurance exercise or overexertion when galloping is a common cause of acute ER in horses.[24] Exhaustion during endurance exercise results in heat retention, fluid and electrolyte loss, acid–base imbalance and intramuscular glycogen depletion.[79] Although the causes are numerous and likely involve electrolyte imbalances and hyperthermia, in certain cases a presumed underlying factor is the deficiency of ATP, which results in an inability to maintain ion homeostasis. In turn, a corresponding rise in intracellular calcium concentration precedes the final common pathways, leading to muscle fiber death described at the beginning of this chapter.

Oxidative injury Increased oxygen utilized during exercise leads to proportionate increases in free radical production (Fig. 6.11).[80] Free radicals are widely believed to cause post-exercise stiffness and fatigue in muscle, through several deleterious mechanisms that include the peroxidation of lipid membranes. Cell damage is normally minimized by the action of a complex cascade of free radical scavengers and antioxidants, including vitamin E and the selenium-dependent enzyme, glutathione peroxidase. When antioxidants fail to quench free radicals sufficiently, the body is subjected to so-called 'oxidative stress'.[80]

Although evidence suggests that exercise-induced oxidative stress occurs in horses, particularly when ambient

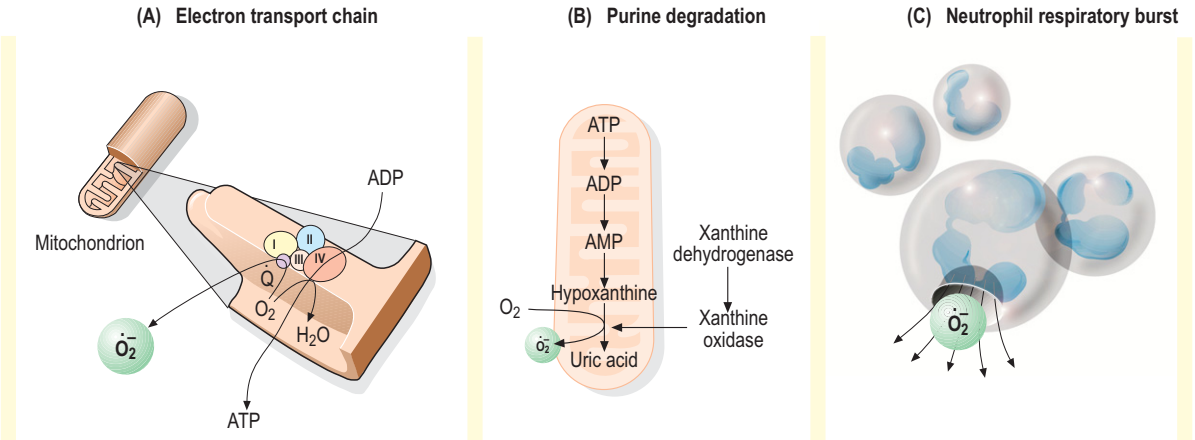


Fig. 6.11
Diagrammatic representation of free radical formation via the electron transport chain in mitochondria (A), via hypoxanthine degradation after ischemia (B) and during the neutrophil respiratory burst (C).

temperature and humidity are high,[81] there is no clear association with muscle damage.[82] This is corroborated by studies demonstrating that antioxidant supplementation fails to attenuate exercise-induced elevations in plasma CK activity,[83–85] and a lack of studies demonstrating antioxidant deficiencies in horses prone to ER. Instead, higher serum and muscle vitamin E concentrations and serum glutathione peroxidase activity were detected in ER-susceptible Standardbreds compared with controls (although prior supplementation could not be ruled out as a potential cause).[86]

In adult horses, vitamin E or selenium deficiency has been associated with nutritional myodegeneration (white muscle disease) of the masseter muscle[87] and was implicated in horses with rhabdomyolysis, colic and myocardial disease.[88] In growing foals, nutritional myodegeneration is characterized histopathologically by changes that are sometimes seen in horses with ER.[89] However, such changes likely reflect the general response of muscle to cycles of degeneration and regeneration, rather than damage caused specifically by oxidative stress.

There is therefore no good evidence that oxidative stress plays a primary role in ER, particularly given the apparent high incidence of the disorder in horses on excellent planes of nutrition.[35] Despite this, during conditions likely to result in significant oxidative stress, such as very strenuous or prolonged exercise, antioxidant deficiencies may exacerbate muscle damage caused by other mechanisms. Horses from selenium-deficient regions or animals on poor diets that are denied access to green pasture are most at risk.

Electrolyte imbalance Published and anecdotal reports of improvement following correction of electrolyte clearance ratios[45] underlie continued interest in this area.[35] In a group of 38 ER-susceptible Thoroughbreds, about a third had potassium clearance ratios of less than 30% or low chloride clearance.[90] These differences could potentially reflect differences in the handling of electrolytes by ER-susceptible animals but horses prone to ER exhibit the same dietary-induced alterations to electrolyte clearance ratios as normal animals.[40] Much attention has been directed at potassium, because low muscle potassium concentrations can precipitate rhabdomyolysis in other species.[91] Erythrocyte potassium concentration has been measured in attempts to investigate whole-body potassium stores: results indicate both low[92] and normal[90] erythrocyte potassium in horses with ER. However, the significance of either study is questionable given that erythrocyte potassium concentrations do not correlate with muscle or plasma potassium concentrations in horses.[90,93,94] Compared with normal animals, lower dry weight muscle potassium concentrations were detected in ER-susceptible horses.[90] However, characteristic muscle histopathological changes, seen in humans with potassium deficiency,[91] are generally not observed in muscle from horses with ER[90] so it is hard to draw conclusions.

The primary influence of altered electrolyte status as a cause of ER is better studied prospectively in normal horses, rather than retrospectively in horses known to be susceptible to the disorder. In comparison with controls, normal Thoroughbreds administered furosemide (frusemide) and sodium bicarbonate developed lower plasma calcium, chloride, magnesium and potassium concentrations. Following exercise, serum CK activity was found to be significantly higher in the treated group.[95] Some evidence therefore suggests that electrolyte imbalance may play a role in the development of certain forms of the disorder.

Hormonal influence In experimental animal models sex hormones influence the degree of disruption and post-damage inflammatory response in skeletal muscle. For instance, estrogen is known to have a protective effect following eccentric contraction and ischemia reperfusion injury.[96] It is intriguing therefore that many studies report a higher incidence of ER in female horses compared with males.[66,97–102] No correlation has been found between the stage of the estrus cycle and plasma CK activities in Thoroughbreds in training,[103] suggesting that a direct association of female sex hormones with ER is unlikely. As yet, therefore, the higher incidence of ER in females remains unexplained.

Hypothyroidism is associated with subclinical elevations of serum CK activity[104] and rarely causes ER in humans.[105] Although a cause of poor performance in horses,[106] hypo-

thyroidism has not been associated with ER in horses.[39,64,103,107–109] Other signs associated with hypothyroidism in horses, such as alopecia, lethargy and excessive fat accumulation,[110,111] are not frequently seen in ER-susceptible horses. Furthermore, given its rarity, it is unlikely that hypothyroidism is associated with ER in most animals.

Infectious causes Equine herpes virus 1 (EHV1) infection was proposed as causing an outbreak of ER in a training yard, where several horses seroconverted to the virus.[112] Equine influenza virus (EIV) has also been diagnosed by seroconversion as the potential cause of certain equine myopathies.[98] Both EIV and EHV1 infections are common in groups of young race horses and although the acute-phase response to viral infection may cause transient arthralgia and myalgia, and therefore stiffness, rhabdomyolysis is not a common feature of these diseases. As with other acquired causes, viral infection may modify the phenotype of genetically susceptible horses.

Inherited causes

Recurrent exertional rhabdomyolysis due to defective calcium regulation The term 'recurrent exertional rhabdomyolysis' (RER) has recently evolved to define a disease reported in Thoroughbreds with aberrant myofiber calcium regulation and caffeine-hypersensitive muscle.[38,113,114] Although possible, it should not be assumed that this syndrome is common to all Thoroughbreds with intermittent bouts of ER. It is also unclear whether this disease is unique to Thoroughbreds: certain similarities in vivo and in vitro suggest that other breeds, such as Standardbreds,[99] may share a similar, if not identical disorder, particularly if the suspected autosomal dominant inheritance, reported in families of Thoroughbreds with uncharacterized ER,[115] is confirmed in horses with defective calcium regulation. Use of the word 'recurrent' leads to further confusion given that recurring episodes are a prominent feature of several ER disorders. Until a more practical diagnostic test becomes widely available and the disease's etiology is understood, it may be safer to qualify the diagnosis.

In the remainder of this section, the abbreviation RER(c) is used for horses in which caffeine hypersensitivity has been established; RER refers to the broader group of horses, mostly Thoroughbreds but including some other breeds, in which there is reasonable evidence for the same etiology.

Defective calcium regulation Speculation that ER may be related to a defect in calcium regulation[116–118] was strengthened by a report of elevated resting intracellular calcium concentrations in muscle from ER-susceptible horses by Lopez et al.[33] However, recent calcium fluorescence experiments using cultured equine myotubes from Thoroughbreds with RER(c) found no difference in resting calcium concentration when compared with controls.[63] This disparity may reflect differences in case selection, active disease processes in the former study or the less differentiated nature of myotubes in culture compared to mature muscle.

Muscle from some Standardbreds and Thoroughbreds that are susceptible to RER is, however, hypersensitive to agents that induce calcium release from the SR (Fig. 6.12) such as caffeine, a potent activator of RYR1.[99,119] Caffeine can be used to identify humans, pigs and dogs that are susceptible to malignant hyperthermia (MH) when stressed or under halothane anesthesia, because lower caffeine concentrations elicit contraction in biop-

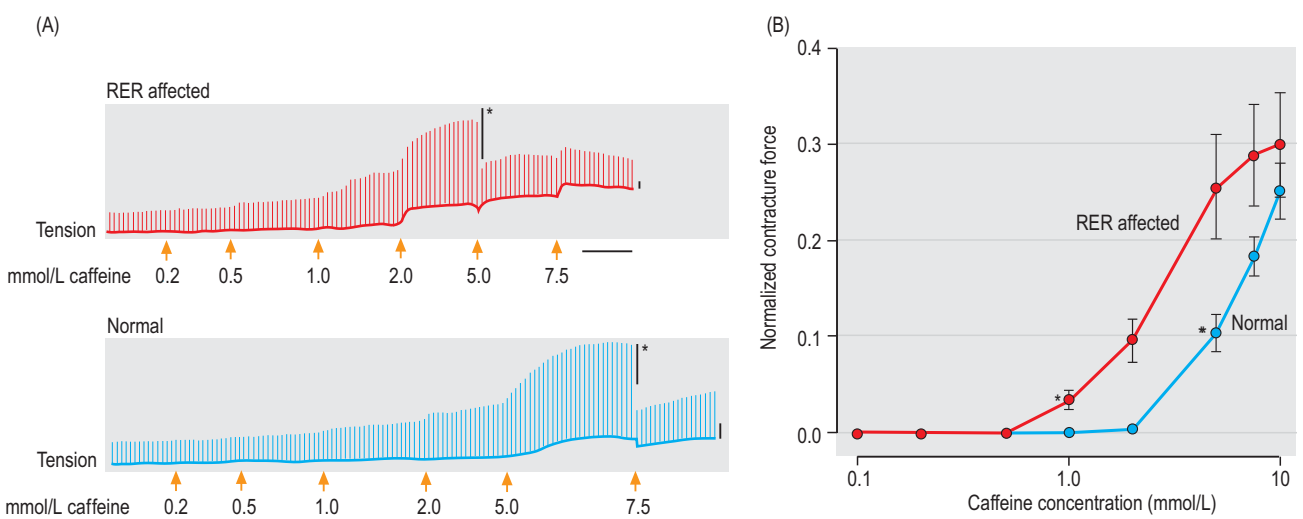


Fig. 6.12
(A) Tension (baseline) record for a caffeine contracture experiment performed on isolated intercostal muscle preparations from a normal horse and a Thoroughbred with RER(c). Twitches (vertical deflections) were elicited via electrical stimulation at 0.05 Hz and caffeine was added to the bathing solution as indicated by the arrows to obtain the final concentration as noted. Horizontal bar = 5 min; heavy left vertical bar = 0.5 N/cm;^{2} heavy right vertical bar = 1.0 N/cm.^{2} Asterisk = recorder gain change. Notice that caffeine elicits a change in baseline tension in muscle from the RER(c)-affected horse at between 1 and 2 mmol/L caffeine, whereas the baseline does not change until the bathing solution contains 5.0 mmol/L caffeine for the control muscle. (B) Contracture force versus caffeine concentration for muscle bundles from clinically normal horses (n = 12; blue line) and RER(c)-affected horses (n = 10; red line). Contracture force was normalized to the preceding tetanus for both groups. Asterisks show force of contracture thresholds > 0 at 1.0 mmol/L and 5.0 mmol/L caffeine for RER(c)-affected and clinically normal horses respectively. (Reproduced from Lentz et al[113] with permission.)

sied strips of muscle from subjects with MH compared to that of normal subjects.[120–122] Humans and pigs with MH are also susceptible to exercise- or stress-induced rhabdomyolysis;[123,124] conversely, MH-like reactions have been reported in several breeds of horse during or following anesthesia.[117,125–127] Some, but not all studies report ER-susceptible horses with muscle that tests positive for MH, perhaps because case selection included horses with different types of ER:[116,117,127] recent evidence now confirms that caffeine hypersensitivity is not a feature of muscle from horses with PSSM.[64,119]

In pigs, dogs and in most humans, MH is associated with mutations in the gene encoding RYR1,[122,128,129] but abnormal RYR1 ligand binding, characterized in vesicles prepared from the muscle of MH pigs,[130] is not a feature of similar vesicles from horses with RER(c).[131] Furthermore, whereas lower concentrations of caffeine elicit calcium release from the SR of RER(c)-susceptible Thoroughbreds when compared with normal horses, the same is not true for 4chloro-m-cresol, a RYR1 agonist with higher specificity.[63] Finally, characteristic clinical and histopathologic features seen in other human myopathies caused by RYR1 mutations are not seen in muscle from horses with RER(c).[29,132] Hence a mutation in the gene encoding RYR1, though not ruled out, appears less likely.

Caffeine-hypersensitive muscle is not exclusively found in human MH patients with RYR1 mutations: the same abnormality is reported in MH patients with mutations in other genes, such as the gene that encodes the α1-subunit of the L-type voltage-sensitive calcium channel (dihydropyridine receptor).[133] At least three more genes are implicated in human MH, based on linkage mapping;[129] furthermore, given that other proteins regulate calcium release from the SR (Fig. 5.12)[134] another, as yet unidentified gene may be the cause. Alternatively, since MH-like attacks and caffeine-hypersensitive muscle are reported in humans with other diseases,[135] horses with RER(c) may have an unrelated defect.

Defective kinetics of contraction/relaxation Muscle from RER-susceptible Thoroughbreds contracts more rapidly than normal muscle in vitro.[99] Furthermore, authors have detected abnormal relaxation, though they disagree as to whether relaxation is hastened or slowed.[99,113] The SR Ca^{2+}- ATPase pump is a major determinant of relaxation following contraction, but SR Ca^{2+}-ATPase pump activity is normal in extracted SR vesicles from horses with RER(c).[131] Abnormalities of the contractile apparatus could also explain some of the experimental findings in horses with RER(c). However, when compared with normal horses, there was no difference in its calcium sensitivity or in the myofibrillar ATPase activity.[114]

Diet and temperament High carbohydrate diets lead to more severe muscle damage in horses with RER(c),[38,67] while high-fat diets are protective.[67] Though unexplained, one possibility is that a high-fat diet may result in the stabilization of sarcolemmal membranes but the rapidity of the protective response[67] suggests that this is less likely. As stress is known to instigate MH in other species,[124] evidence suggests that the protective response may relate to dietary-induced alteration in temperament[70,71] (see section on prevention above).

Polysaccharide storage myopathy Since the first detailed report of PSSM in Quarter Horses,[52] a comparable disease has been recognized in other breeds.[54–58] Although similar histopathologically and sometimes associated with ER, some affected non-Quarter Horse breeds have neuromuscular weakness, muscle atrophy and abnormal hindlimb gaits characteristic of 'shivers'.[136] Abnormal muscle polysaccharide is also identified as an incidental finding.[56,57] Phenotypic variation caused by the effects of modifying genes and the environment is frequently encountered in human muscle diseases, so these may well be allelic disorders. Most work on pathophysiology has been in Quarter Horses, so here they are considered separately.

Quarter Horses Glycogen and abnormal polysaccharide accumulation are seen in several human muscle diseases known as glycogenoses, many of which are caused by abnormal regulation or deficiencies of glycolytic or glycogenolytic enzymes; others are idiopathic or caused by lysosomal dysfunction.[59] Early experiments suggested that Quarter Horses with PSSM displayed impaired lactate production[52,137] similar to humans with glycogenolytic or glycolytic enzyme deficiencies.[138] However, recent experiments using more stringent exercise tests demonstrated normal or exaggerated lactate production.[139] Affected Quarter Horses do not have detectable abnormalities in either glycolytic enzyme activities or their regulation,[52,140] and their oxidative metabolism appears functional since they can maintain low plasma lactate concentrations during long-term submaximal exercise.[139]

Glycogen is a branched three-dimensional molecule formed by glycogen synthase that adds straight 1,4 glucose linkages, and branching enzyme, that adds 1,6 linkages after every seventh glucose molecule (Fig. 6.13). The formation of abnormal polysaccharide, though not well understood, may be related to an abnormal increase in the glycogen synthase: branching enzyme ratio.[59] High muscle glucose-6-phosphate concentrations (found in PSSM muscle both before and after exercise[139]) may stimulate glycogen synthase activity[141] without a corresponding rise in branching enzyme activity, thereby altering their ratio and causing filamentous abnormal polysaccharide to form. Abnormal polyglucosan accumulates in tissues of humans with branching enzyme deficiency,[142] a fatal disease identified in a group of Quarter Horse foals,[143] but branching enzyme activities are normal in Quarter Horses with PSSM.[144]

Excessive muscle glycogen and polysaccharide may be associated with abnormal increased glucose uptake rather than diminished utilization.[61] Muscle's glucose uptake is controlled primarily by insulin in a process of facilitated diffusion via GLUT-4 receptors (Fig. 6.14A).[145] A separate, but poorly understood mechanism recycles GLUT-4 receptors when insulin concentrations diminish.[146] Compared with normal animals, Quarter Horses with PSSM clear glucose from plasma more rapidly following its intravenous injection (Fig. 6.15) and have reduced peak plasma glucose concentrations after oral carbohydrate intake.[62] Affected horses have lower resting serum insulin concentrations and lower insulin : glucose ratios than controls both before and after glucose infusion.[61] Enhanced insulin sensitivity in affected animals is demonstrated by a more rapid decline in plasma glucose concentration and prolonged hypoglycemia following intravenous insulin administration compared with controls.[61] Hence, although glucose uptake specifically into muscle has not been investigated, because skeletal muscle is the greatest insulin-sensitive tissue, horses with PSSM probably have enhanced skeletal muscle glucose uptake, a hypothesis strengthened by similar observations in transgenic mice

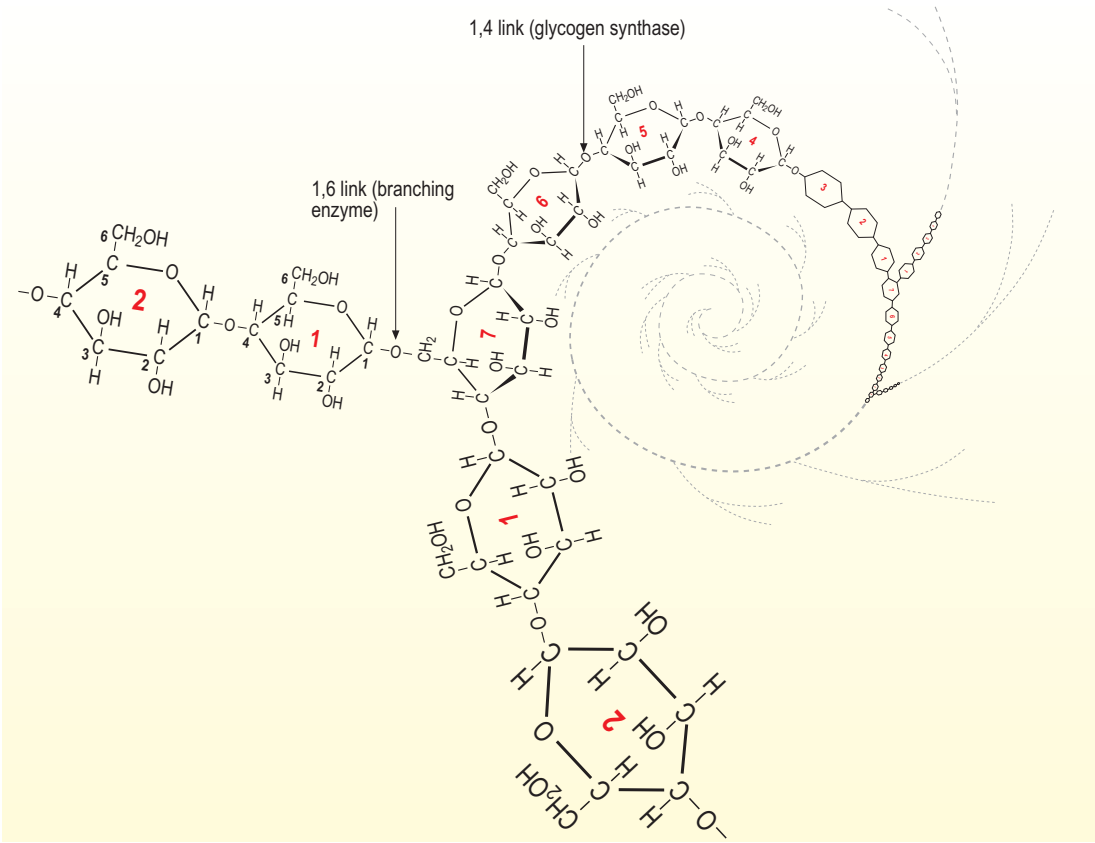


Fig. 6.13 Diagrammatic representation of the three-dimensional structure of glycogen. Note that glycogen is composed of chains of glucose molecules joined enzymatically via 1-4 linkages (glycogen synthase) and 1-6 linkages (branching enzyme).

that overexpress GLUT-4 receptors.[147] Whether muscle from horses with PSSM has greater numbers of sarcolemmal GLUT-4 receptors or whether they persist for longer within the sarcolemma following their translocation from the cytoplasm remains to be determined.

Exercise results in insulin-independent translocation of a separate pool of GLUT-4 receptors to the sarcolemma via poorly understood pathways (Fig. 6.14B).[148–150] After exercise, enhanced insulin-independent glucose uptake is maintained for several hours due to delayed GLUT-4 transporter recycling.[151] A second phase of increased glucose uptake results from enhanced insulin sensitivity in a mechanism that may be modulated by glycogen.[150,151] Normal horses fed grain following exercise show enhanced glucose clearance compared to non-exercised horses; a similar, but diminished enhancement occurs in horses with PSSM together with a relative decline in their insulin sensitivity.[62] One possible explanation is that glycogen's control over the regulation of insulin sensitivity is defective in affected horses. Alternatively, because horses with PSSM have greater post-exercise muscle

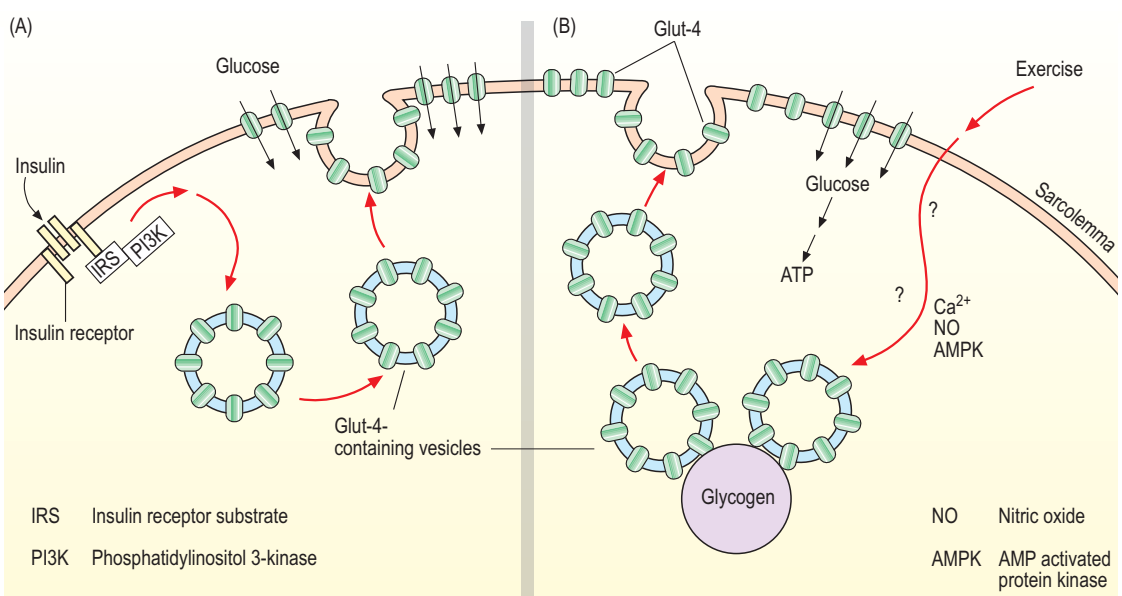


Fig. 6.14 Diagrammatic representation of insulin-dependent translocation of vesicle-bound GLUT-4 receptors from the cytoplasm to the sarcolemma (A) and the similar translocation of GLUT-4 receptors in response to exercise (B). Either way, GLUT-4 receptors at the sarcolemma result in increased rates of glucose uptake.

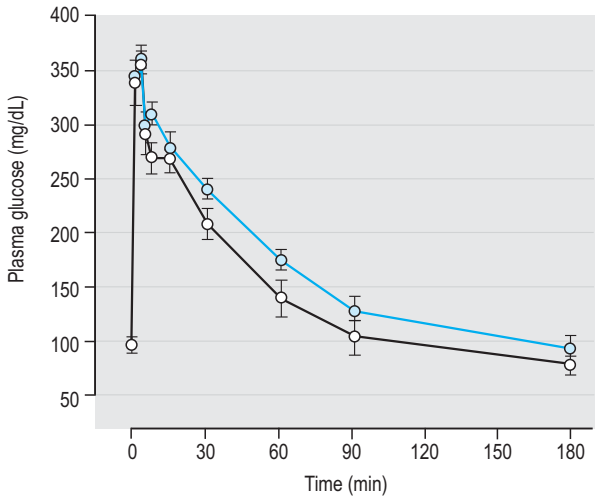


Fig. 6.15
Mean plasma glucose concentrations in six horses with PSSM (black line) and 10 healthy control horses (blue line) immediately before (time 0) and at various times after i.v. glucose injection. Glucose concentration from 0 to 180 minutes was significantly ($P < 0.001$) lower in horses with PSSM than in controls. Bars represent SEM. (Reproduced from de la Corte et al[61] with permission.)

glycogen stores than normal horses,[139] their stimulus for glucose reuptake may be less intense.

Other breeds In 1931 Carlström noted high glycogen concentrations in draft horses that developed rhabdomyolysis following a day of inactivity, proposing that the myopathy was related to a build-up of lactic acid.[152] Subsequent analysis does not support this hypothesis[139,153] and it seems most likely that this disease was probably PSSM[55,57] that, like in Quarter Horses, has been associated with excessive glycogen accumulation and amylase-resistant polysaccharide in muscle.[55,154] As with Quarter Horses, researchers have not identified glycolytic enzyme deficiencies in other affected breeds;[72] plasma glucose clearance and insulin sensitivity have yet to be investigated.

Various human glycogenoses affect tissues other than skeletal muscle, including the heart.[59,155] PSSM has been diagnosed as an incidental finding in a number of draft horses with seemingly unrelated diseases and in a few with sudden (perhaps cardiac-related) death. However, of nine draft horses examined, amylase-resistant polysaccharide was identified in the (otherwise histologically normal) myocardium of only one Belgian.[57] Quarter Horses with PSSM do not have overt cardiac disease[52] although histopathological assessment is lacking.

Epidemiology of exertional rhabdomyolysis syndromes

Characterizing horses as susceptible to ER by measuring serum CK activity is practical but cannot distinguish groups based on the underlying etiology. This drawback is partially overcome by grouping horses by breed or type, a method used in several studies.

Idiopathic cases Idiopathic ER has a worldwide distribution. Studies indicate that between 4.9% and 6.7% of racing Thoroughbreds can be affected during a single season[66,102] with the disorder probably inherited as an autosomal dominant trait with variable expression.[115] Subjective impression that ER occurs more frequently in young fillies has been confirmed by several studies.[66,102,109] Additionally, it was found that Thoroughbreds that were nervous or lame were more likely to develop episodes of rhabdomyolysis.[66,102] Another study that examined ER in polo ponies in the UK and the US also found a high incidence,[156] particularly in animals with an excitable temperament. In both Thoroughbreds and polo horses, the disease resulted in significant time away from training or competing.[66,102,156] Evidence suggests that ER also has a genetic component in Swedish Standardbreds.[101]

Polysaccharide storage myopathy The familial basis of PSSM in Quarter Horses may be autosomal recessive.[157] A retrospective epidemiological study of Quarter Horses with PSSM (diagnosed histopathologically) found that horses were prone to rhabdomyolysis when affected by respiratory disease. The age of onset varied between 3 months and 14 years and unlike in Thoroughbreds, there was no association with either gender or temperament.[68]

In a group of 37 draft-related horses (referred to a veterinary teaching hospital in the US with various diseases), when examined at necropsy, between 45% and 66% had signs compatible with PSSM (depending on diagnostic criteria).[57] The growing number of breeds diagnosed with PSSM now includes Quarter Horses,[52] Warmbloods, Morgans, Standardbreds and Arabians,[56] Haflingers,[58] Anglo-Arabians and Andalusians.[54] In addition, if the classification criteria for diagnosis of PSSM are relaxed, the list includes Thoroughbreds and ponies.[69] PSSM has been reported in North America and Europe.[54,57,68]

Hyperkalemic periodic paralysis

- Genetic disorder seen in Quarter Horses and related breeds descended from the stallion Impressive.
- Caused by a mutation in the α subunit of the skeletal muscle sodium channel.
- Autosomal dominant inheritance.
- Homozygotes are more severely affected than heterozygotes.
- Signs vary from subclinical to severe.
- Weakness is the predominant physical sign, although muscle spasm and fasciculation may occur.
- Life-threatening complications include cardiac arrhythmias secondary to hyperkalemia and asphyxiation due to laryngospasm.
- Prophylactic dietary and therapeutic management can reduce the frequency and severity of attacks.

Recognition

History and presenting complaint

Hyperkalemic periodic paralysis (HYPP) episodes occur intermittently, last several minutes to hours, and are more

common in young adults or foals. Affected horses are well muscled, particularly over the hindquarters, and appear normal between episodes. Episodes often follow sleep or may be precipitated by stress, cold weather and sometimes exercise.[158] Evidence suggests that the condition is more common in young males[159–162] although this has not been confirmed experimentally.

Physical examination

Clinical signs vary, with homozygotes being more severely affected than heterozygotes. Myotonia is often brief or unapparent; however, third eyelid protrusion is sometimes seen along with spasm of certain facial muscles and, more commonly, muscle fasciculation.[163] Laryngeal or pharyngeal spasm may occur, causing pharyngitis, dysphagia and occasionally severe dyspnea.[164] These signs are more common in young homozygous foals,[164] but in adults may present as abnormal respiratory noise during exercise.[165] More characteristic, especially in older horses, are signs of weakness, such as swaying or buckling, a stilted gait, dog sitting, collapse or recumbency.[160] Respiratory muscle weakness and increased muscular effort may be manifest as shallow tachypnea and sweating. Horses remain alert, responsive and unpainful.[158,163] Death, when it occurs, may be the result of the dyspnea associated with laryngospasm or, more commonly, cardiac arrhythmia (ventricular fibrillation) due to underlying hyperkalemia;[166,167] horses that are under or recovering from anesthesia appear particularly at risk.[168,169]

Special examinations

Electrocardiography Consistent with hyperkalemia, during episodes the ECG reveals smaller, wider P waves, increased amplitude of T waves and widening of QRS complexes.[162,170–173] Between episodes the ECG is normal.[162]

Endoscopy Endoscopy may reveal pharyngeal collapse and edema, dorsal displacement of the soft palate, bilateral laryngeal paresis and persistent opening of the guttural pouch ostia.[158,165]

Electromyography Electromyography reveals abnormalities such as doublets and characteristic myotonic discharges (Fig. 6.16).[174]

Laboratory examination

Serum biochemistry During an episode, clinical pathological changes usually, but not always,[159,169,175] include hyperkalemia (5.5–12 mEq/L).[162,176] Elevated total serum protein concentration (7.0–9.0 mg/dL) suggests fluid compartmental shifts.[162,177] Serum CK and AST activities are normal to moderately elevated.[162,178]

Muscle biopsy Muscle histopathology is not normally indicated and often appears normal, but may reveal centrally located vacuoles in type II fibers, excessive fiber size variation, occasional internal nuclei, moth-eaten fibers, connective tissue proliferation and fiber degeneration.[51,161,162] Electron microscopy reveals distension and proliferation of the SR and copious networks of transverse tubules.[158]

Diagnostic confirmation

The differential diagnosis includes colic, ER, laminitis, cardiac disease, tetanus, botulism, seizures and upper airway obstruction. Myotonic discharges, observed during EMG examination, are also seen in the rare disorders known as myotonic dystrophy and myotonia (see later sections).[179–181] Recognition of weakness and muscle fasciculations in

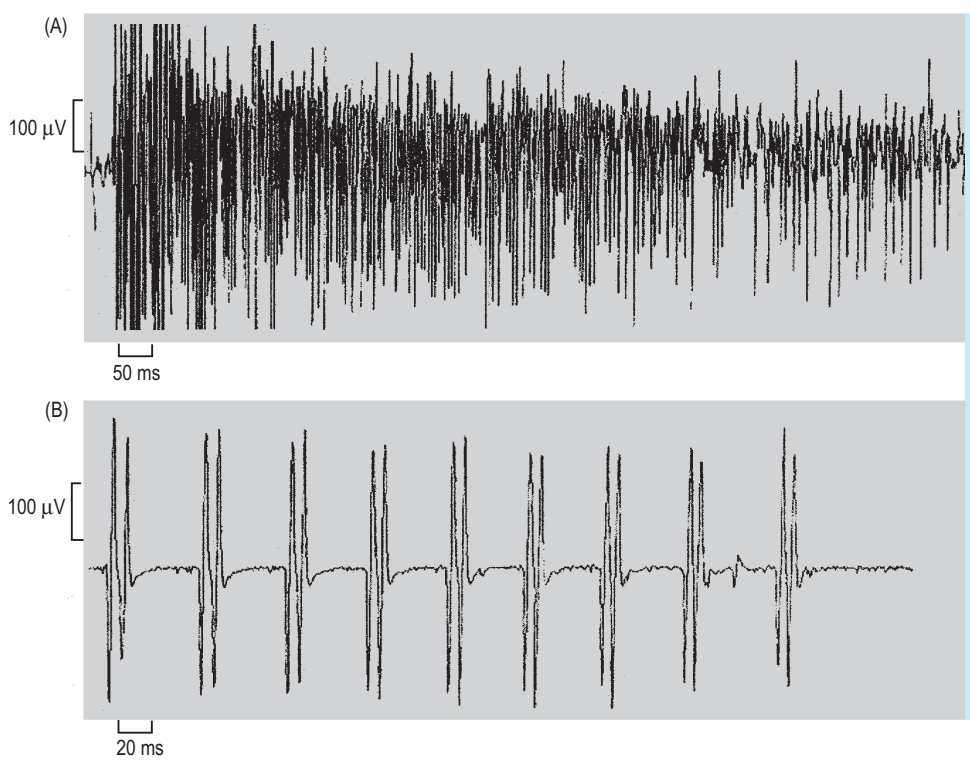


Fig. 6.16
Electromyographic features of HYPP-affected muscle. (A) Myotonic discharges and (B) trains of doublets recorded in an HYPP-affected horse while clinically normal. (Copyright of Jonathan M Naylor BSc PhD, Saskatoon, Canada. Reproduced with permission.)

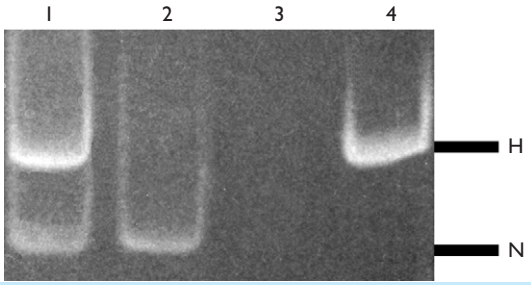


Fig. 6.17
Restriction fragment length polymorphism analysis for the testing of HYPP. Complementary DNA primers are used to amplify by polymerase chain reaction (PCR) a portion of extracted genomic DNA that contains the HYPP mutation. The PCR product is digested with a specific (restriction endonuclease) enzyme and is loaded into separate lanes of an agarose gel, containing ethidium bromide, which fluorescently labels the DNA. The enzyme cuts the DNA into a shorter fragment (which migrates more quickly and hence further down the gel) only if the sequence is normal (N). DNA from mutated alleles remains uncut, and therefore migrates more slowly in the gel (H). In lane 1 the extracted DNA contains both mutated (H) and normal (N) sequences, hence the animal is a heterozygote (H/N). In lane 2, all the DNA has been cut by the enzyme, hence both alleles must be normal (N/N). Lane 3 is a PCR control with no added DNA. In lane 4 none of the PCR-amplified DNA has been cut by the enzyme, hence both alleles must be mutated and the animal is homozygous (H/H). (Image courtesy of Dr Glen Byrns, University of California, Davis.) Postal address for HYPP gene testing: Veterinary Genetics Laboratory HYPP Testing, University of California, Davis, Davis, CA 95616-8744, USA. Downloadable forms and further details are available at the laboratory's website address: http://www.vgl.ucdavis.edu/horse/tsthypp.htm.

combination with hyperkalemia in an Impressive-related Quarter Horse should leave little doubt that the animal has HYPP. Hyperkalemia itself, though not always present, may be due to other causes such as recent exercise, a hemolyzed blood sample or, more rarely, renal failure.

Diagnostic confirmation via the potentially fatal potassium chloride challenge test[158,162,176,182] has been rendered obsolete with the advent of genotyping. Electromyography, a useful ancillary test with a reported sensitivity of 90%,[183] can support the diagnosis before DNA test results are available. Abnormal EMG signals can be detected both during and between episodes and in HYPP-positive horses undergoing treatment.[183,184]

Definitive diagnosis can only be achieved by mutational analysis of the sodium channel α subunit gene, which determines an animal as heterozygous or homozygous (Fig. 6.17). Any sample containing DNA (for example, tissues removed at necropsy) could be used but whole blood (in EDTA) or a plucked hair sample (containing roots) is preferred. The American Quarter Horse Association recommends testing foals born to unclassified parents; those related to Impressive are identified with their established genotype on registration certificates. Note that a horse may be heterozygous for HYPP but display weakness and collapse for some other reason and that the test only identifies the single specific mutation seen in all horses to date with HYPP.[185]

Treatment and prognosis

Therapeutic aims

Therapy is aimed at systemic abnormalities, specifically the life-threatening hyperkalemia and, if present, the dyspnea.

Therapy

Mild cases require stall rest or hand walking together with grain or a sweet-feed meal or orally administered corn syrup.[163] Horses should be observed closely for worsening signs. More severely affected animals with prominent weakness or auscultable cardiac arrhythmia require aggressive medical therapy. Severe dyspnea may require emergency tracheotomy.

Emergency treatment during an attack Intravenous calcium gluconate given slowly, diluted in isotonic fluids (0.2–0.4 mL/kg of 23% calcium gluconate in 2 liters of 5% dextrose) raises membrane threshold potential, reducing the likelihood of an action potential despite the muscle cells' relatively depolarized state.[158] Cardiomyocytes are also protected.[186]

Intravenous administration of potassium-free fluids containing dextrose triggers insulin release and hence glucose movement followed by potassium, intracellularly. Intravenous administration of insulin has been advocated but should be done with dextrose-containing fluids to avoid hypoglycemia; doses are not well established.[158] A mild alkalosis from sodium bicarbonate administration should also promote intracellular potassium movement. One author recommends 0.9% NaCl containing 0.5–1 mL/kg 1.3% $NaHCO_3$ and 0.5–1 mL/kg 50% dextrose.[163] Other treatments aimed at reducing hyperkalemia include β-adrenergic agonists[158,187] to stimulate the Na/K ATPase pump, which reduces the resting membrane potential. These drugs are rarely necessary, though, and may increase the risk of cardiac arrhythmia.[169]

Phenytoin ameliorates skeletal muscle signs probably by altering sodium channel activity through the influence of cytoplasmic free fatty acids;[188,189] however, serum phenytoin concentrations should be monitored. Note that phenytoin does not reduce serum potassium levels[166] and is not usually required.

Prognosis

Most mildly to moderately affected animals will respond well but if hyperkalemia is severe and not treated promptly, sudden cardiac death may occur. Asphyxiation is possible in cases with laryngospasm as is aspiration pneumonia, particularly in nursing foals. Evidence suggests that in many animals the signs can be controlled successfully but given the underlying genetic abnormality, horses remain susceptible for life.

Prevention

Management and dietary changes Horses that suffer repeated attacks often benefit from long-term management

changes and prophylaxis. In some cases a change in diet and avoidance of the cold and stressful events, such as transportation, may suffice.

Feed modification reduces the number of attacks.[159] Many horses do well when maintained principally at pasture but when not practical, they should always have access to hay and concentrate feed should be divided and given several times daily. High potassium-containing forages such as brome hay and alfalfa should be avoided, as should canola and soybean oil, molasses and certain potassium-containing mineral supplements. Late bloom timothy hay, sugar beet pulp and barley or oats are suitable alternatives, although calcium supplementation may be required to ensure appropriate calcium : phosphorus ratios.[190]

Prophylaxis

Acetazolamide (2–4 mg/kg q 12–14 h p.o.), a carbonic anhydrase inhibitor, is widely used in horses. It prevents attacks induced by experimental potassium challenge[191] and anecdotal evidence suggests that the drug is useful in the field.[163,178] Carbonic anhydrase inhibition in renal proximal convoluted tubules decreases reabsorption of sodium ions via an indirect inactivation of luminal H^+-Na^+ antiporters, thereby enhancing sodium for potassium exchange in the distal tubules and promoting potassium excretion.[186] However, some have doubted this explanation for acetazolamide's efficacy, suggesting that other mechanisms, such as the stimulation of insulin secretion, may be involved.[158,192,193] Other potassium-wasting diuretics such as hydrochlorothiazide have also been tried in horses but experience is limited.[194]

Etiology and pathophysiology

Etiology

A disease resembling human HYPP was reported in Quarter Horses in the mid 1980s[160,195] but the etiology of human HYPP was then unknown. In the early 1990s, several groups confirmed that human HYPP is caused by mutations in a gene encoding the α subunit of a sodium channel expressed only in skeletal muscle.[196,197] Linkage of equine HYPP to a single locus[198] and identification of a single base pair substitution in the equine sodium channel α subunit gene quickly followed.[199] Unlike in humans, in equine HYPP all identified cases have the same mutation,[185] the substitution of a cytosine for a guanine residue, causing the amino acid phenylalanine to be replaced by leucine in the cytoplasmic end of the IVS3 transmembrane domain (Figs 6.18, 6.19) of the encoded 260 kDa protein.[199]

As in the human disorder, equine HYPP is inherited in autosomal dominant fashion.[177,200] The different severity of homozygotes compared to heterozygotes is a reflection of the codominance of the mutated and wild-type alleles. As with many diseases, phenotypic severity varies between heterozygotes, perhaps due to the modifying influence of other genes or environmental effects. One group has reported a correlation of disease severity with the ratio of mRNA from affected: wild-type (unaffected) alleles,[201] although this finding has not been confirmed at the protein level.

Pathophysiology

Transient myotonia The skeletal muscle sodium channel associated with HYPP lies in the sarcolemmal (and T-tubule) membrane and allows sodium to enter the fiber during action

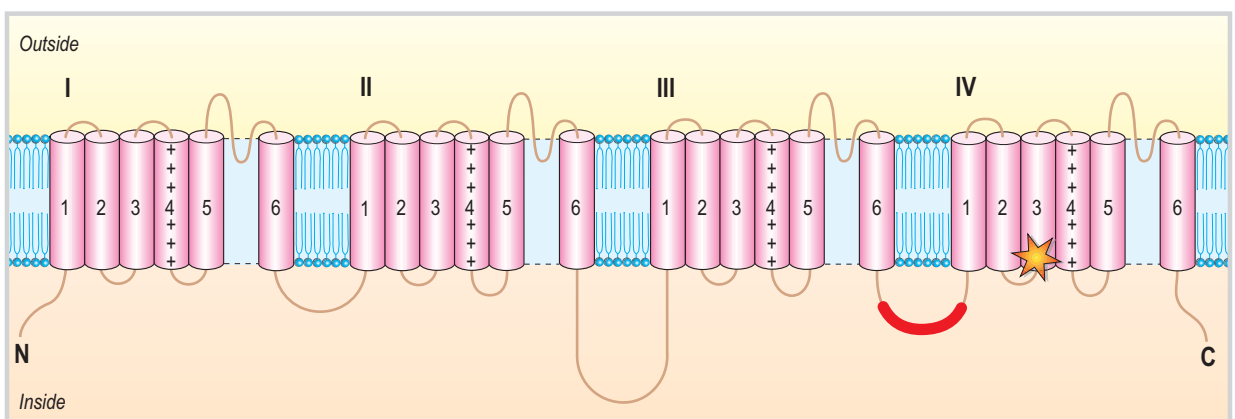


Fig. 6.18
Diagrammatic representation of the equine sodium channel α subunit. The protein contains four domains (I–IV), each containing six transmembrane hydrophobic segments (1–6) that combine to form a channel in the sarcolemma. Segment 4 in each domain contains a high density of charged amino acids that participate in sensing voltage changes across the sarcolemma. The phenylalanine to leucine mutation is located close to the cytoplasmic surface of segment 3 in domain IV (asterisk). The spanning region between III-S6 and IV-S1 is believed to participate in channel inactivation (colored red).

Human	V G W N I F D F V V V I L S I V G L A L S D L I	*Homo sapiens*
Horse	V G W N I F D F V V V I L S I V G L A L S D L I	*Equus caballus*
Horse HYPP	V G W N I L D F V V V I L S I V G L A L S D L I	*Equus caballus* (HYPP)
Rabbit	I G W N I F D F V V V I L S I V G M F L A E L I	*Oryctolagus cuniculus*
Mouse	I G W N I F D F V V V I L S I V G L A L S D L I	*Mus musculus*
Rat	I G W N I F D F V V V I L S I V G L A L S D L I	*Rattus norvegicus*
Boney fish	N G W N I F D F I V V I L S I A G T M L S D I I	*Takifugu pardalis*
Tunicate	N P W N V F D F I V V I L S V V G S T M N E V I	*Halocynthia roretzi*
Mosquito	E P W N L F D F V V V I L S I L G L V L S D I I	*Anopheles gambiae*
Mollusc	E P W N I F D F V V V V L S I L G I A L S D I I	*Loligo opalescens*
Newt	I G W N V F D F V V V I L S I V G M F L S E I I	*Cynops pyrrhogaster*

Fig. 6.19
Comparison of IVS3 amino acid sequences of various species. Standard single letter codes for each amino acid are used and amino acids with similar properties are shown with the same background color; hence polar-negative amino acids are red, polar-neutral amino acids are green, non-polar aliphatic amino acids are white and non-polar aromatic amino acids are purple. Glycine and proline tend to have structural properties in biological membranes and are colored brown. Note the significant conservation of either amino acid sequence or amino acid type within the structural domain between species. Such conservation usually reflects the functional and structural importance of the region to the protein. Also note the replacement of phenylalanine (F) by leucine (L) (circled in red), in horses with HYPP.

potential conduction (see Chapter 5). In vitro studies demonstrate dysfunctional inactivation of the mutant channel and an increased open probability, hence abnormal influx of sodium while at rest (Fig. 6.20).[202,203] Although individual fibers vary, in HYPP-affected fibers, the resting potential is higher (less negative) than normal.[145] Blocking sodium channels in HYPP muscle with tetrodotoxin returns the membrane potential towards normal (more polarized) but has no effect on the resting potential in normal muscle.[145] The closer proximity to the threshold potential in HYPP muscle results in more readily elicited action

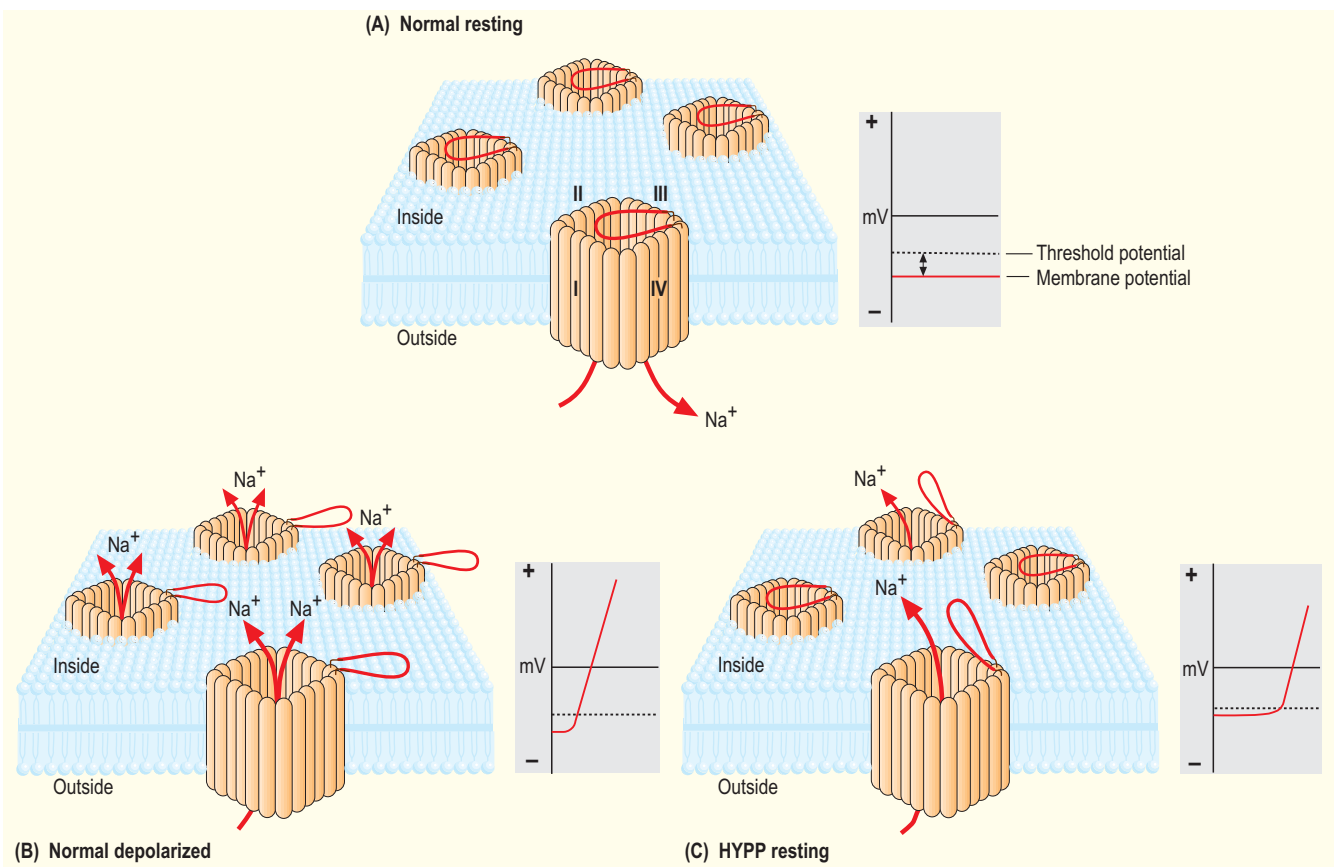


Fig. 6.20
Diagrammatic explanation for the pathophysiology of HYPP. In a normal resting muscle cell, sodium channels are inactive and closed and the resting potential lies some way below the threshold potential (A). A regional change in voltage activates sodium channels, causing them to open, allowing sodium to enter the fiber (the upswing of the action potential) (B). In muscle fibers from horses with HYPP, some sodium channels have abnormal inactivation and remain open, despite the fiber's resting state. Sodium can enter the fiber down its concentration gradient. This results in the fiber's resting potential being close to the threshold potential (C) and hence more readily elicited action potentials.

potentials, explaining the transient myotonia and muscle fasciculations. Fibers from younger horses with HYPP have higher resting potentials than older horses and muscle cooling raises the resting potential. These observations explain the higher incidence of HYPP episodes in young horses and during cold weather.[145]

Weakness Following rapid depolarization of the action potential, sodium channels normally close in response to the now positive membrane potential. In addition, voltage-gated potassium channels open, allowing potassium to leave the muscle fiber and return it to its resting potential. Failure of mutant sodium channels to inactivate prevents repetitive trains of action potentials[203,204] (required for Ca^{2+} release), causing the weakness that is the predominant sign in affected horses.

Hyperkalemia can be both the consequence and the cause of an attack Most horses are hyperkalemic during or immediately following an episode, probably due to voltage-gated potassium channels remaining open, allowing continual potassium efflux. Hyperkalemia itself raises the fiber resting potential and promotes an open sodium channel configuration, thereby exacerbating the condition[205,206] or, as demonstrated by the formerly used potassium challenge test,

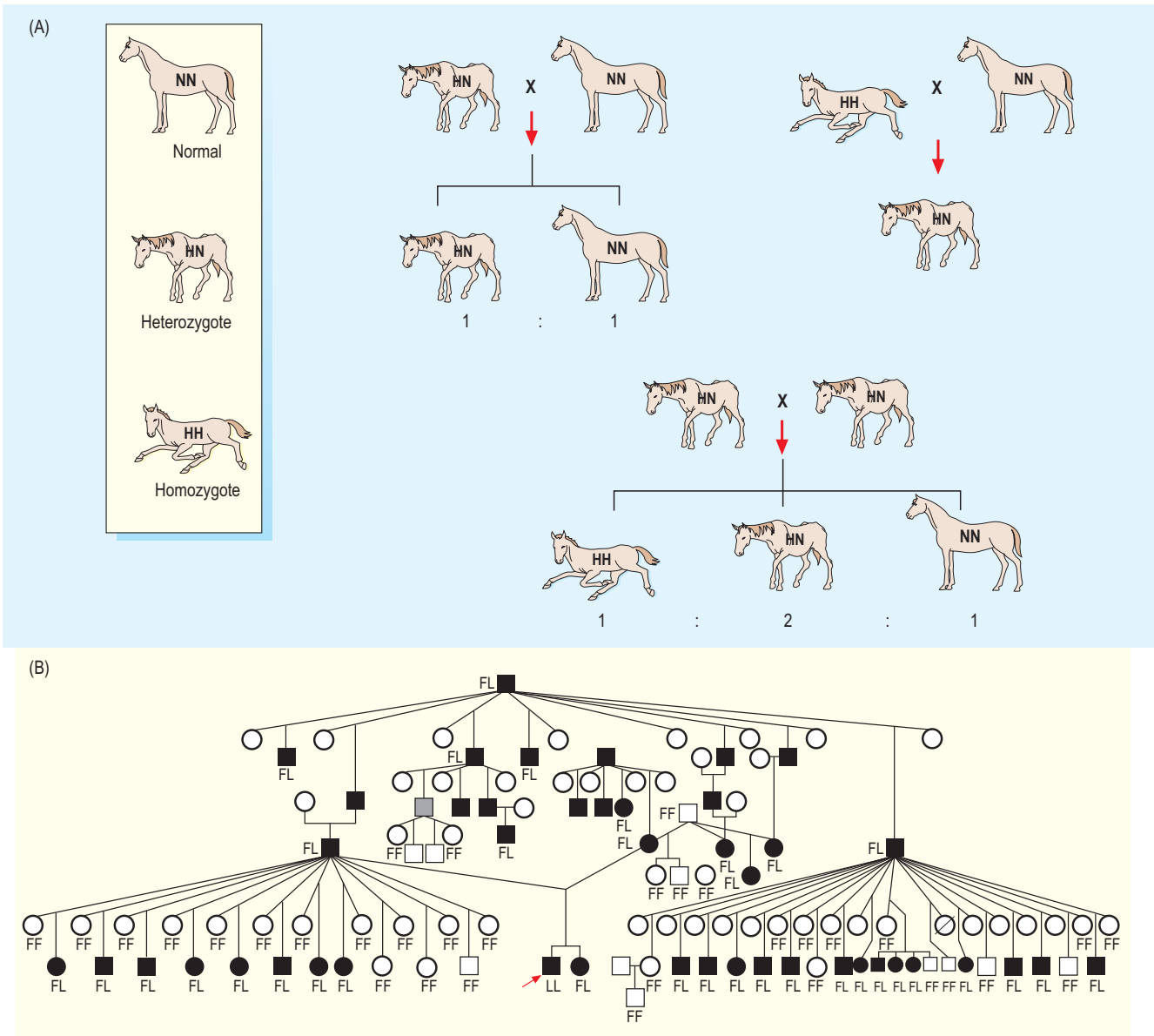


Fig. 6.21
(A) Diagrammatic representation of matings between horses with HYPP and normal animals. (B) HYPP Quarter Horse pedigree. Horses are shown typed for the normal allele of the sodium channel (phenylalanine (F)) and the allele that causes HYPP (leucine (L)) in the sodium channel region IVS3. A homozygous affected horse is indicated by an arrow. The horse represented by a gray symbol has an unknown status. Squares represent males and circles represent females. Black symbols represent horses with the HYPP phenotype and open symbols represent normal horses. (Reproduced from Rudolph et al[199] with permission.)

precipitating an attack. Spontaneous recovery often follows attacks, perhaps as a result of the kidneys' correcting the hyperkalemia or a local rise in muscle temperature.[163]

Muscle hypertrophy Horses with HYPP typically have hypertrophied muscles and this favorable trait in halter classes likely resulted in the maintenance and propagation of the mutation in the gene pool until a rule change by the American Quarter Horse Association.[184] The mechanism causing the hypertrophy is not understood, but may relate to myotonia-induced gene expression.

Exercise intolerance Experiments show that despite the hypertrophic muscles, horses with HYPP have reduced exercise tolerance compared with normal animals and produce relatively more lactate during exercise.[207] Even when weakness or muscle fasciculations are absent, exercised homozygotes exhibit intermittent laryngospasm, pharyngeal collapse, hypoxia, hypercapnia and ventricular premature contractions.[208]

Epidemiology

The spontaneous mutation that first occurred in Impressive (born 1969) spread via line breeding throughout the Quarter Horse population (Fig. 6.21). Within the US the frequency of affected heterozygotes in 1996 was believed to be 4.4%.[185] Dominant inheritance has led to cases in Quarter Horse-related breeds such as Appaloosas, American Paint horses and crosses. Although seen predominantly in North America, HYPP has also been reported in Impressive-descended Quarter Horses in Australia.[171]

Myotonia

- Equine myotonia is very rare and likely has a genetic cause: the sarcolemmal chloride channel has been implicated.
- Percussion dimpling and prolonged muscle contractions are present from an early age.
- Electromyography reveals frequent myotonic discharges.
- No successful treatment or prophylaxis has been reported.
- The prognosis for life in myotonia is fair to good, though athletic potential is likely to be poor.

Although horses with HYPP may exhibit (usually transient) myotonia, several case reports describe more prolonged myotonia. As in HYPP, some cases are probably associated with mutations in genes encoding sarcolemmal ion channels.[181] In humans, the phenotype varies depending on the channel involved and the mutation, but there is considerable overlap. Early literature combined equine myotonia with myotonic dystrophy but on close evaluation of the disease descriptions, it is clear that at least two myotonia-causing disorders exist.

Recognition

History and presenting complaint

Gait abnormalities and stiffness that are worst following a period of rest may be apparent early in life.[181]

Physical examination

Examination reveals symmetrical muscle hypertrophy and percussion causes localized muscle spasm and prolonged dimpling.[181,209] Animals with myotonia are not expected to deteriorate significantly with time.

Special examinations

Electromyography Changes are similar to those observed in HYPP (Fig. 6.16).[181]

Muscle biopsy Histopathology will likely be normal or show mild myopathic changes including excessive fiber size variation and internally located nuclei.[209]

Diagnostic confirmation

The main differential is myotonic dystrophy, which is characterized by severe muscle histopathological changes, endocrine abnormalities and progressive clinical signs. Affected horses share similarities with the prolonged myotonia of humans with chloride channel disorders[196] but the equine chloride channel gene has not been identified. Certain mutations in the human sarcolemmal sodium channel α subunit gene are manifest as myotonia rather than periodic paralysis: direct sequencing, rather than the routine HYPP DNA test would be required for definitive diagnosis of a sodium channel disorder in affected horses.

Treatment and prognosis

There are no reports of successful treatment. The prognosis for athletic function is poor but the prognosis for life may be good.[181]

Etiology and pathophysiology

Although the etiology is unknown, clinical descriptions and comparison with human diseases suggest that a sarcolemmal chloride channel mutation probably causes equine myotonia.[181,196] In human chloride channelopathies, reduced muscle chloride conductance causes membrane potential to rise, resulting in membrane hyperexcitability and hence myotonia.[197]

Epidemiology

The disease, which may be inherited, has been reported in a Thoroughbred filly in the US.[181]

Myotonic dystrophy

- Myotonic dystrophy is rare and probably has an underlying genetic cause.

- Percussion dimpling and prolonged muscle contractions are early signs.
- Horses with myotonic dystrophy may develop tendon contractures, kyphoscoliosis and testicular atrophy.
- Electromyography reveals myotonic discharges in certain muscles.
- Muscle histopathology reveals moderate to severe dystrophic changes.
- Successful treatment has not been reported and euthanasia may be necessary.

Recognition

History and presenting complaint

Horses are usually presented early in life with stiff gaits and prolonged contraction of certain muscles.

Physical examination

Animals are alert and responsive, with marked muscular hypertrophy particularly in the gluteal region and hindlimbs. Percussion dimpling is readily elicited in many animals and prolonged contraction may follow spontaneous or induced movements (Fig. 6.22). Weakness, manifest as knuckling or stumbling, may also be seen. Signs may progress to include tendon contractures, kyphoscoliosis, a pendulous abdomen, colic and testicular atrophy.[179,180]

Special examination

Electromyography Myotonic discharges are common in some but not all muscles, as are high-frequency electrical bursts during needle insertion, movement or following percussion.[179,180] Motor unit potentials in the thoracic paraspinal muscles of one animal were polyphasic and reduced in amplitude, but normal in the gastrocnemius.[180]

Laboratory examination

Hematology and biochemistry Hematology and biochemistry values may become abnormal with age.[210] CK and AST activities have been reported to be both normal and raised in affected horses. Some animals have endocrine abnormalities.[179,180]

Muscle biopsy Mild to severe dystrophic changes such as fiber-size variation and fiber-type grouping, increased perimyseal and endomyseal connective tissue, necrosis with inflammatory cell infiltration, internally located nuclei and whorled fibers may be seen (Fig. 6.23). There may be selective type I muscle fiber hypertrophy with moth-eaten fibers and ring bands.[51,179,180,210–214]

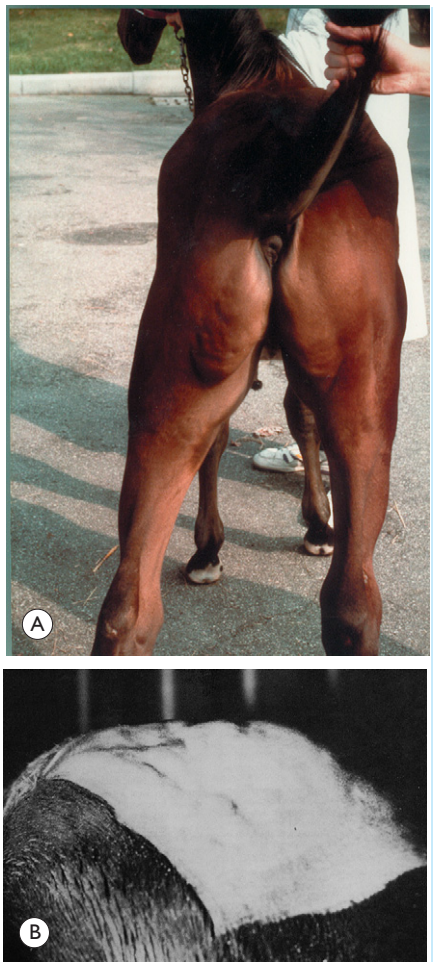


Fig. 6.22
(A) Spontaneous contraction and dimpling of hindlimb muscles of a 5-month-old colt of Anglo-Arab-Sardinian descent with myotonic dystrophy (courtesy of Prof Pascale Montagna, University of Bologna, Italy).
(B) Percussion dimpling following clipping in the gluteal musculature of a 1-month-old Quarter Horse colt with myotonic dystrophy. (From Reed et al[179]. Reproduced by permission of John Wiley & Sons Inc.)

Diagnostic confirmation

The main differential is equine myotonia. Additional clinical signs and muscle biopsy will aid in the diseases' differentiation.

Treatment and prognosis

There are no reports of successful treatment.

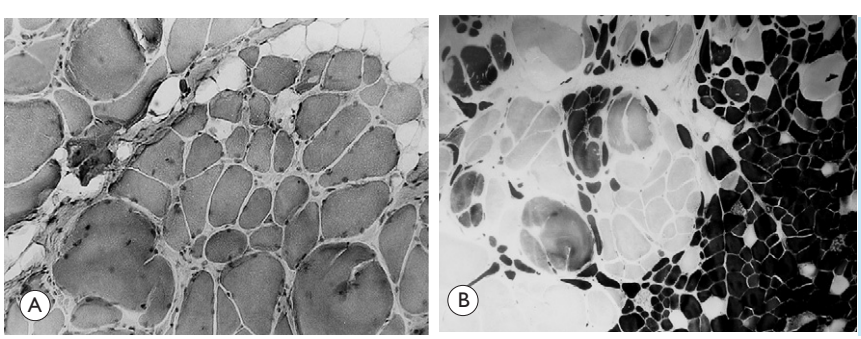


Fig. 6.23
(A) Transverse section of gluteus medius muscle from a horse with myotonic dystrophy stained with hematoxylin and eosin. Note the fiber size variability, extensive perimysial connective tissue and internalized nuclei.
(B) ATPase staining at alkaline pH. Compare with Fig. 5.20F, p. 60). Note the marked variation in fiber size with type I hypertrophy and fiber type grouping. (Courtesy of Prof Mario Cipone, University of Bologna, Italy.)

Prevention

Owners should be advised with regard to breeding affected or related animals, as the disorder may be genetic in origin.

Etiology and pathogenesis

The etiology and pathogenesis have not been established. There are several inherited forms of myotonic dystrophy in people, one of which is caused by mutations in a gene encoding a protein kinase,[215,216] although other genes are also implicated.[217] In humans, endocrine disorders including hyperinsulinemia and hypogonadism are common.[218,219]

Epidemiology

The condition has been reported in Quarter Horses and in a horse of Anglo-Arab-Sardinian descent.[179,180,210]

Mitochondrial myopathy

- Rare cause of severe exercise intolerance.
- Light exercise causes pronounced lactic acidemia.
- Diagnosis is achieved via muscle biopsy and measurement of mitochondrial enzyme activities.
- Reduced activity of mitochondrial enzyme complexes are probably associated with mitochondrial or genomic DNA mutations.
- There is no treatment and prognosis is poor.

Recognition

History and presenting complaint

The most likely history will include severe exercise intolerance. Mitochondrial myopathies in people are associated with exercise-induced myalgia and cramps.[220]

Physical examination

In the reported case, the Arabian appeared normal at rest.[221] However, human patients frequently have additional cardiac and central nervous system involvement.[222]

Special examination

Exercise test Light exercise resulted in stiff, short strides, profuse sweating and metabolic acidosis due to marked lactic acidemia (Fig. 6.24). Oxygen consumption was reduced, but PVO_2 increased. The horse was unable to exercise for more than 6 minutes and recovery was prolonged.[221]

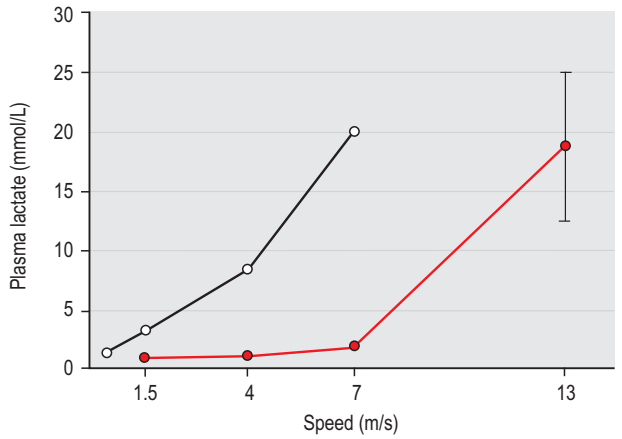


Fig. 6.24
Graph showing rise in plasma lactate concentration in a control horse (red line) and in a horse with a mitochondrial myopathy (black line) according to the speed of the treadmill. Notice that the affected horse produces large amounts of lactate even at slow treadmill speeds. (From Valberg et al.[221] Reproduced by permission of John Wiley & Sons Inc.)

Laboratory examinations

Hematology and biochemistry Routine hematology and biochemistry analysis, including CK activity, was normal in the reported horse at rest.[221] However, given the multiple systems involvement in humans,[222] other cases may have variable abnormalities.

Muscle biopsy Mild myopathic changes may be evident. In humans, classic findings include intense red-staining subsarcolemmal deposits of mitochondria in a few fibers with modified Gomori's trichrome stain – so-called 'ragged

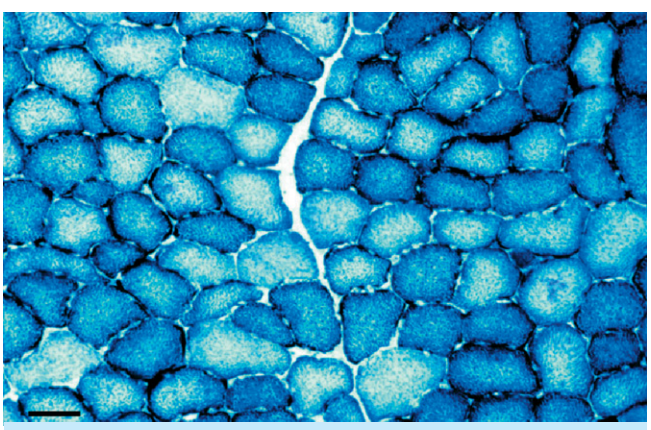


Fig. 6.25
Light microscopic transverse section of gluteus medius muscle stained with nicotinamide adenine dinucleotide tetrazolium reductase from an Arabian horse with suspected mitochondrial myopathy. Note the dark staining (mitochondria), particularly towards the rim of many myofibers, including the paler glycolytic fibers.

red fibers'. However, normal trained horses have abundant subsarcolemmal mitochondria, which can appear similar. Histochemical staining of NADH-dehydrogenase (complex I), succinate dehydrogenase (complex II) and cytochrome oxidase (complex IV)[10] may be abnormal, suggesting respiratory chain enzyme dysfunction (Fig. 6.25). Electron microscopy may reveal extensive subsarcolemmal and intermyofibrillar mitochondria with distorted or concentric cristae.[221]

Biochemical analysis of mitochondrial oxidative enzymes Mitochondrial respiratory chain enzyme activities are analyzed in mitochondrial preparations from affected muscle. The following enzyme activities should be measured by a specialist laboratory and compared with controls; in the reported horse, complex I enzyme activities were significantly reduced.[221]

Citrate synthase	(matrix enzyme)
NADH-dehydrogenase	(complex I)
Rotenone-sensitive NADH – cytochrome-c-reductase	(complex I and III)
Succinate – cytochrome-c-reductase	(complex II and III)
Succinate dehydrogenase	(complex II)
Cytochrome oxidase	(complex IV)
ATP-synthase	(complex V)

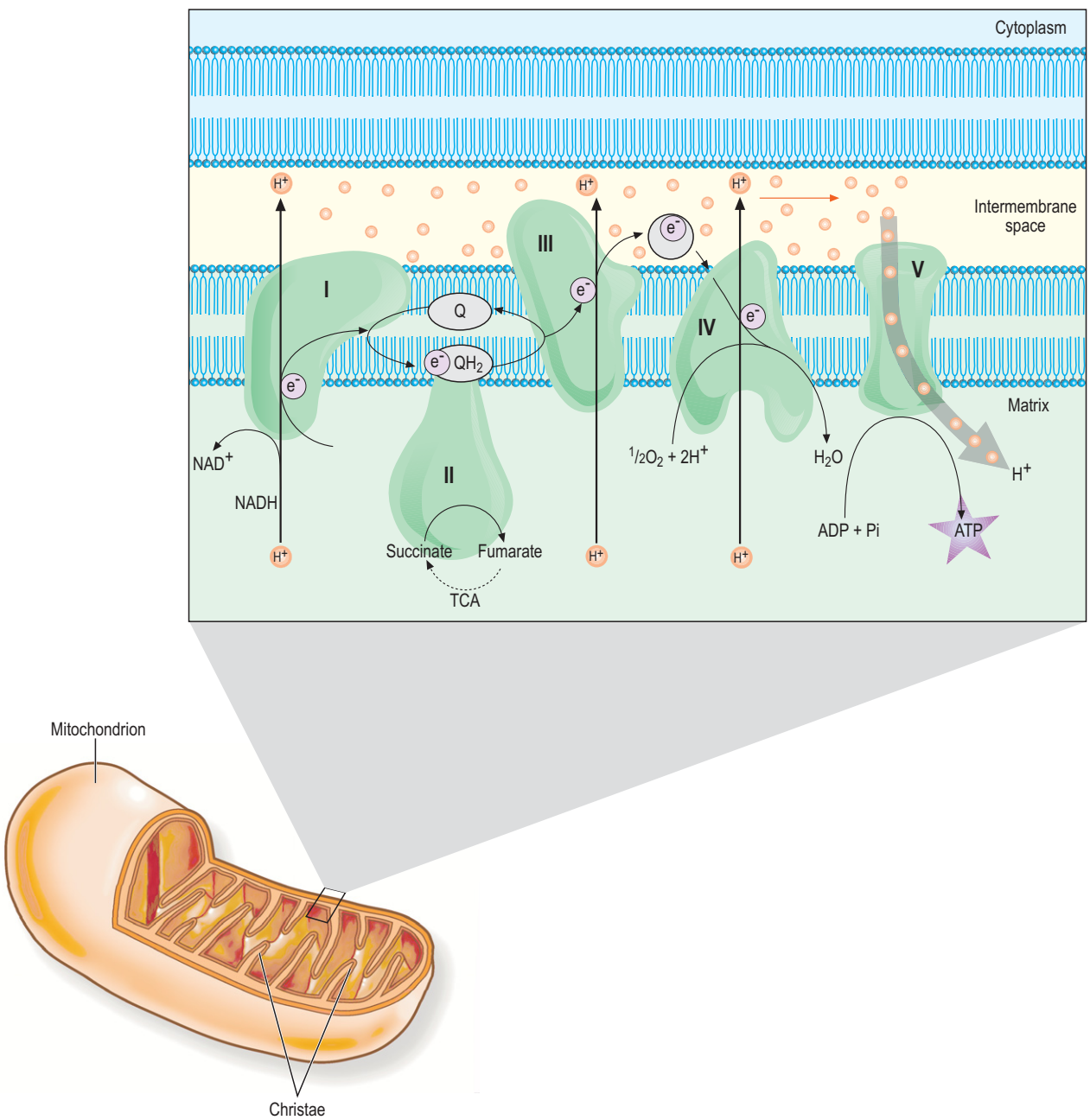


Fig. 6.26
Diagrammatic representation of the mitochondrial respiratory chain in mitochondria. The enzyme components of each complex are located in the inner membrane. Protons accumulate in the intermembrane space and their energy is harnessed to regenerate ATP (via ATP synthase). Q = ubiquinone.

Diagnostic confirmation

Other much more common causes of exercise intolerance should be ruled out before diagnosing mitochondrial myopathy. In their absence, severe exercise intolerance and unusually pronounced exercise-induced lactic acidemia should prompt muscle histopathological investigation and measurement of mitochondrial enzyme activities. Mutational analysis of mitochondrial or genomic DNA enables definitive diagnosis in humans; the complete equine mtDNA sequence is now available.[223]

Treatment and prognosis

The prognosis depends on the degree of respiratory chain compromise, but is likely to be poor as there is no treatment. Affected animals are very unlikely to be athletic.[221]

Etiology and pathophysiology

Etiology

The respiratory chain enzyme complexes that produce ATP during oxidative phosphorylation are located in the folded cristae of the inner mitochondrial membranes (Fig. 6.26). In humans, the proteins that make up complex II are encoded by genomic DNA, whereas the other complexes are encoded by genes in both genomic DNA and mtDNA,[222] hence mitochondrial myopathies may be caused by mutations in either.

Pathophysiology

Mutations in mtDNA occur spontaneously or are inherited from the mother, because mitochondria are maternally derived. Within individuals, different tissues may contain normal and mutated mitochondria in varying amounts (heteroplasmy). If sufficient normal mitochondria exist, oxidative phosphorylation defects go unrecognized, but become evident in tissues when mutated mtDNA predominates, especially when ATP requirements are high, as in muscle. In muscle, defective oxidative phosphorylation results in greater emphasis on anaerobic glycolysis for energy production and correspondingly, a rise in lactate production. In humans, mitochondrial diseases often affect multiple systems, although postmitotic tissues, such as the central nervous system and muscle, are over-represented, probably because of inability to select against abnormal mitochondria in affected cells.[222]

Fibrotic myopathy

- Mechanical hindlimb lameness characterized by the foot abruptly slapping the ground at the end of the anterior phase.
- Congenital and acquired forms have been recognized.
- Most horses have a history of trauma to the affected limb.
- A fibrotic mass may be palpable in the semitendinosus or other hamstring muscles.
- Transection of the mass or tibial insertion tenotomy results in return to normal function in some horses.

Recognition

History and presenting complaint

Horses present with unilateral or occasionally bilateral hindlimb lameness. There may be a history of injury, trauma or intramuscular injection in the affected limb.[224]

Physical examination

The mechanical lameness, which does not respond to analgesics, is most obvious at the walk or slow trot and is characterized by a sudden cessation of the anterior phase of the stride, with the hoof abruptly slapping the ground. At faster gaits the lameness may disappear. Taut muscles containing a firm, fibrous mass may be palpable in the bellies or myotendinous junctions of the semitendinosus (most commonly), but also the semimembranosus, biceps femoris and gracilis muscles (Fig. 6.27).[19,224–226]

Special examination

Ultrasound may help locate sites of fibrosis[227] and radiography can identify ossification.[19,224] Electromyography may suggest denervation that can be confirmed by muscle biopsy.[228]

Diagnostic confirmation

Other causes of hindlimb lameness should be considered. Mild stringhalt is sometimes confused with fibrotic myopathy

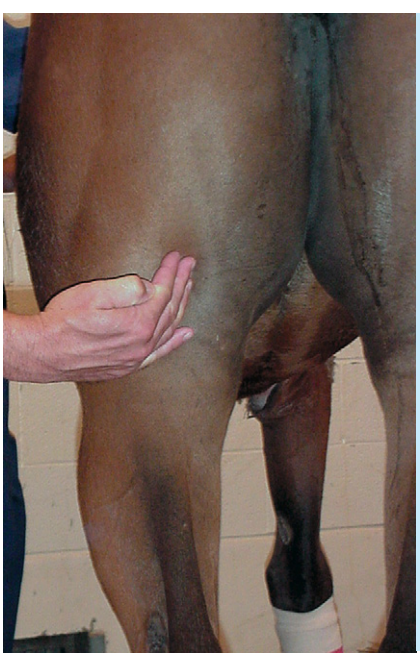


Fig. 6.27 Palpating the hamstring musculature for evidence of fibrotic myopathy. (Photograph courtesy of Dr Kenneth Hinchcliff, Ohio State University, USA.)

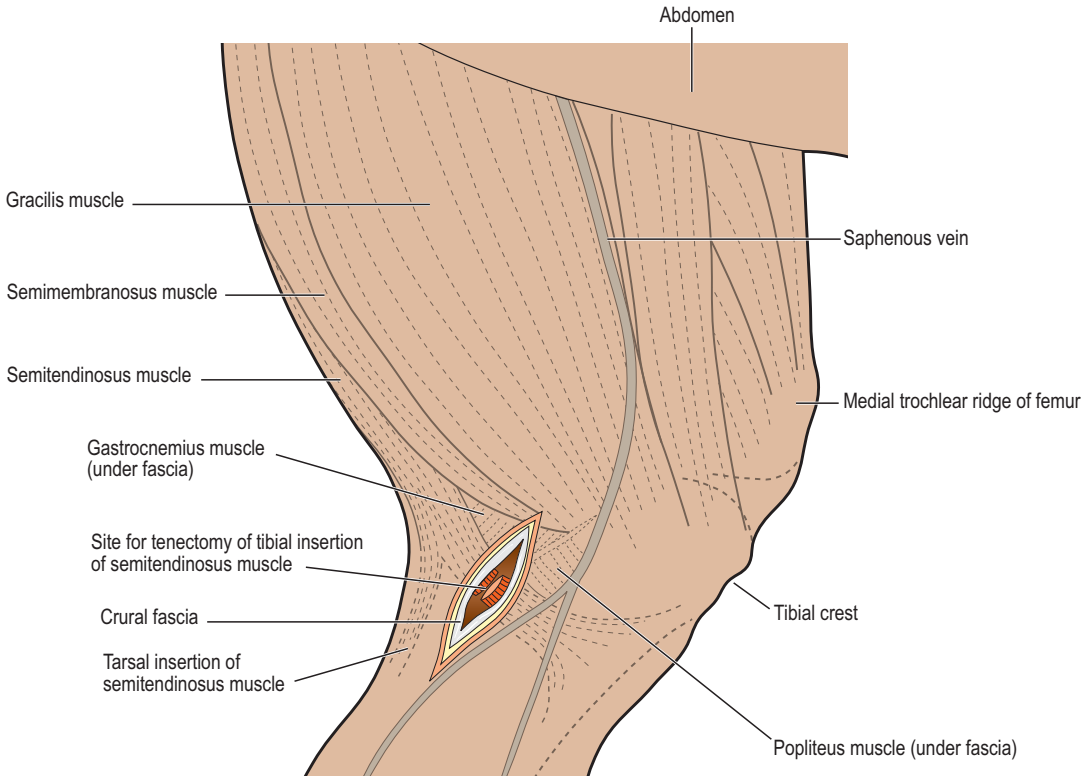


Fig. 6.28 Diagrammatic representation of the medial aspect of the hindlimb showing the semitendinosus tibial insertion tenotomy site with regional anatomy.

but stringhalt is associated with abnormal sudden upward flexion of the limb. In most cases of fibrotic myopathy the gait is pathognomonic.

Treatment and prognosis

Therapeutic aims

The main aim is to restore the normal mechanical function of the limb.

Surgery Transection[226] or excision[224] of the fibrotic mass or tenotomy of the tibial insertion of the semitendinosus muscle are described.[19,229]

Muscle transection Although usually performed under general anesthesia, transection of the fibrotic mass using a bistoury knife has been performed in the standing horse under local anesthesia. Postsurgical drainage is maintained with a Penrose drain inserted through a second incision, ventral to the first, and healing occurs via second intention. Light exercise is resumed the day after surgery.[22,226]

Tibial insertion tenotomy under general anesthesia The tendon of insertion of the semitendinosus muscle is palpated medially (with the horse in lateral recumbency and the affected limb down), caudodistal to the femorotibial joint (Fig. 6.28). The tendon is exposed and transected following vertical skin incision caudal to the medial saphenous vein. Closure is routine and tension sutures are placed in the skin. Residual healing occurs via second intention if dehiscence occurs. Mild exercise is recommended 2 weeks postoperatively with full exercise allowed after 6 weeks.[19,230]

Analgesia Treatment consists of NSAIDs (e.g. 2–3 mg/kg phenylbutazone i.v., q 12 h p.o.) postoperatively for 2–3 days.

Prognosis

Tenotomy is reported to result in fewer complications and have greater success.[19,224] Results depend on which muscles are affected and are better when only the semitendinosus muscle is involved.[229]

Etiology and pathophysiology

This disorder is seen worldwide in athletic horses and is often associated with trauma during work (particularly Quarter Horses) or from fences or ropes. Fibrosis following intramuscular injection has also been described[224] as has denervation atrophy (e.g. sciatic nerve entrapment following fracture of the greater trochanter).[228] In young animals, the disorder may be congenital.[19]

The hamstring musculature supports the stifle during the early stance phase of the gait cycle, enhances propulsion in the late phase and controls the limb's momentum during the swing phase of the stride. Limited range of movement imposed by fibrotic muscle causes an abrupt termination of the swing phase.

References

1. Belcastro AN, Shewchuk LD, Raj DA. Exercise-induced muscle injury: a calpain hypothesis. Mol Cell Biochem 1998; 179:135–145.
2. Gissel H, Clausen T. Excitation-induced Ca^{2+} influx and skeletal muscle cell damage. Acta Physiol Scand 2001; 171:327–334.
3. Sandri M, Carraro U. Apoptosis of skeletal muscles during development and disease. Int J Biochem Cell Biol 1999; 31:1373–1390.
4. Tidball JG. Inflammatory cell response to acute muscle injury. Med Sci Sports Exerc 1995; 27:1022–1032.
5. Hurme T, Kalimo H, Lehto M, Jarvinen M. Healing of skeletal muscle injury: an ultrastructural and immunohistochemical study. Med Sci Sports Exerc 1991; 23:801–810.
6. Grounds MD. Muscle regeneration: molecular aspects and therapeutic implications. Curr Opin Neurol 1999; 12:535–543.
7. Zammit P, Beauchamp J. The skeletal muscle satellite cell: stem cell or son of stem cell? Differentiation 2001; 68:193–204.
8. Rantanen J, Hurme T, Lukka R, Heino J, Kalimo H. Satellite cell proliferation and the expression of myogenin and desmin in regenerating skeletal muscle: evidence for two different populations of satellite cells. Lab Invest 1995; 72:341–347.
9. Kaariainen M, Jarvinen T, Jarvinen M, Rantanen J, Kalimo H. Relation between myofibers and connective tissue during muscle injury repair. Scand J Med Sci Sports 2000; 10:332–337.
10. Dubowitz V, Sewry C, Fitzsimons R. Muscle biospy: a practical approach. London: Baillière Tindall; 1985.
11. Rivero JL, Letelier AI. Skeletal muscle profile of show jumpers: physiological and pathological considerations. Conference on Equine Sports Medicine and Science, Dortmund, 2000. Gestalt manufaktur GmbH.
12. Harris P, Mayhew I. Musculoskeletal disease. In: Reed S, Bayley W, eds. Equine internal medicine. Philadelphia: Saunders; 1998:384–385.
13. Sprinkle F, Swerczek T, Ward Crowe M. Gastrocnemius muscle rupture and hemorrhage in foals. Equine Pract 1985; 7:10–17.
14. Schneider J, Guffy M, Leipold H. Ruptured flexor muscles in a neonatal foal. Equine Pract 1986; 8:11–15.
15. Stashak T. Serratus ventralis rupture. In: Stashak T, ed. Adams' lameness in horses. Philadelphia: Lea and Febiger; 1987:693–694.
16. Morris E, Seeherman HJ, O'Callaghan MW, Schelling SH, Paradis MR, Steckel RS. Scintigraphic identification of skeletal muscle damage in horses 24 hours after strenuous exercise. Equine Vet J 1991; 23:347–352.
17. Eddy AL, van Hoogmoed LM, Snyder JR. The role of thermography in the management of equine lameness. Vet J 2001; 162:172–181.
18. Reef VB. Equine diagnostic ultrasound. Philadelphia: Saunders; 1998:143–149.
19. Bramlage LR, Reed SM, Embertson RM. Semitendinosus tenotomy for treatment of fibrotic myopathy in the horse. J Am Vet Med Assoc 1985; 186:565–567.
20. Gibson JS, Ellory JC. More theories than facts: equine rhabdomyolysis. Equine Vet J 1993; 25:327–328.
21. Warren JD, Blumbergs PC, Thompson PD. Rhabdomyolysis: a review. Muscle Nerve 2002; 25:332–347.
22. Hodgson DR. Diseases of muscle. In: Colahan P, ed. Equine medicine and surgery. St Louis, Missouri: Mosby; 1999:1489–1490.
23. McEwen SA, Hulland TJ. Histochemical and morphometric evaluation of skeletal muscle from horses with exertional rhabdomyolysis (tying-up). Vet Pathol 1986; 23:400–410.
24. Snow DH, Valberg SJ. Muscle anatomy, physiology, and adaptions to exercise and training. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: Saunders; 1994:169.
25. Toutain PL, Lassourd V, Costes G, et al. A non-invasive and quantitative method for the study of tissue injury caused by intramuscular injection of drugs in horses. J Vet Pharmacol Ther 1995; 18:226–235.
26. Koterba A, Carlson GP. Acid–base and electrolyte alterations in horses with exertional rhabdomyolysis. J Am Vet Med Assoc 1982; 180:303–306.
27. Schott HC 2nd, Hodgson DR, Bayly WM. Haematuria, pigmenturia and proteinuria in exercising horses. Equine Vet J 1995; 27:67–72.
28. Kohn CW, Chew DJ. Laboratory diagnosis and characterization of renal disease in horses. Vet Clin North Am Equine Pract 1987; 3:585–615.
29. Valberg SJ. Spinal muscle pathology. Vet Clin North Am Equine Pract 1999; 15:87–96, vi–vii.
30. Andrews FM. Acute rhabdomyolysis. Vet Clin North Am Equine Pract 1994; 10:567–573.
31. Moore KP, Holt SG, Patel RP, et al. A causative role for redox cycling of myoglobin and its inhibition by alkalinization in the pathogenesis and treatment of rhabdomyolysis-induced renal failure. J Biol Chem 1998; 273:31731–31737.
32. Fruen BR, Mickelson JR, Louis CF. Dantrolene inhibition of sarcoplasmic reticulum Ca^{2+} release by direct and specific action at skeletal muscle ryanodine receptors. J Biol Chem 1997; 272:26965–26971.
33. Lopez JR, Linares N, Cordovez G, Terzic A. Elevated myoplasmic calcium in exercise-induced equine rhabdomyolysis. Pflugers Arch 1995; 430:293–295.
34. Court MH, Engelking LR, Dodman NH, Anwer MS, Seeler DC, Clark M. Pharmacokinetics of dantrolene sodium in horses. J Vet Pharmacol Ther 1987; 10:218–226.
35. Beech J. Chronic exertional rhabdomyolysis. Vet Clin North Am Equine Pract 1997; 13:145–168.
36. Valverde A, Boyd CJ, Dyson DH, Pascoe PJ. Prophylactic use of dantrolene associated with prolonged postanesthetic recumbency in a horse. J Am Vet Med Assoc 1990; 197:1051–1053.
37. Martin BB Jr, Reef VB, Parente EJ, Sage AD. Causes of poor performance of horses during training, racing, or showing: 348 cases (1992–1996). J Am Vet Med Assoc 2000; 216:554–558.
38. MacLeay JM, Valberg SJ, Pagan JD, Xue JL, de la Corte FD, Roberts J. Effect of ration and exercise on plasma creatine kinase activity and lactate concentration in Thoroughbred horses with recurrent exertional rhabdomyolysis. Am J Vet Res 2000; 61:1390–1395.
39. Valberg S, Jonsson L, Lindholm A, Holmgren N. Muscle histopathology and plasma aspartate aminotransferase, creatine kinase and myoglobin changes with exercise in horses with recurrent exertional rhabdomyolysis. Equine Vet J 1993; 25:11–16.
40. McKenzie EC, Valberg SJ, Godden SM, et al. Plasma and urine electrolyte and mineral concentrations in Thoroughbred horses with recurrent exertional

rhabdomyolysis after consumption of diets varying in cation–anion balance. Am J Vet Res 2002; 63:1053–1060.
41. Toribio RE, Kohn CW, Chew DJ, Sams RA, Rosol TJ. Comparison of serum parathyroid hormone and ionized calcium and magnesium concentrations and fractional urinary clearance of calcium and phosphorus in healthy horses and horses with enterocolitis. Am J Vet Res 2001; 62:938–947.
42. Clarke LL, Argenzio RA, Roberts MC. Effect of meal feeding on plasma volume and urinary electrolyte clearance in ponies. Am J Vet Res 1990; 51:571–576.
43. Kohn CW, Strasser SL. 24-hour renal clearance and excretion of endogenous substances in the mare. Am J Vet Res 1986; 47:1332–1337.
44. Morris DD, Divers TJ, Whitlock RH. Renal clearance and fractional excretion of electrolytes over a 24-hour period in horses. Am J Vet Res 1984; 45:2431–2435.
45. Harris P, Colles C. The use of creatinine clearance ratios in the prevention of equine rhabdomyolysis: a report of four cases. Equine Vet J 1988; 20:459–463.
46. McKenzie DC, Valberg SJ, Godden S, et al. Volumetric urine collection versus single sample collection in horses consuming diets varying in dietary cation–anion balance. 20th Annual ACVIM Forum, Dallas, TX, 2002.
47. Valentine B, Divers TJ, Murphy DJ, Todhunter P. Muscle biopsy diagnosis of equine motor neuron disease and equine polysaccharide storage myopathy. Equine Vet Educ 1998; 10:42–50.
48. Lindholm A, Johansson HE, Kjaersgaard P. Acute rhabdomyolysis ('tying-up') in standardbred horses. A morphological and biochemical study. Acta Vet Scand 1974; 15:325–339.
49. Meijer AE, van den Hoven R, Wensing T, Breukink HJ. [Histochemical changes in skeletal muscles of racehorses susceptible to rhabdomyolysis after exertion. II. Later myopathological and regeneration phenomena]. Acta Histochem 1989; 87:13–21.
50. Meijer AE, van den Hoven R, Wensing T, Breukink HJ. [Histochemical changes in skeletal muscles of racehorses susceptible to rhabdomyolysis after exertion. I. Early myopathological changes]. Acta Histochem 1989; 87:1–11.
51. Andrews FM, Reed SM, Johnson GC. Muscle biopsy in the horse: its indications, techniques and complications. Vet Med US Equine Pract 1993:357–365.
52. Valberg SJ, Cardinet GH 3rd, Carlson GP, DiMauro S. Polysaccharide storage myopathy associated with recurrent exertional rhabdomyolysis in horses. Neuromuscul Disord 1992; 2:351–359.
53. Rivero JL, Glitz F. Equine polysaccharide storage myopathy: differential diagnosis with unspecific exertional rhabdomyolysis. Conference on Equine Sports Medicine and Science, Dortmund, 2000. Gestalt manufaktur.
54. Quiroz-Rothe E, Novales M, Aguilera-Tejero E, Rivero JL. Polysaccharide storage myopathy in the M. longissimus lumborum of showjumpers and dressage horses with back pain. Equine Vet J 2002; 34:171–176.
55. Valentine BA, Credille KM, Lavoie JP, et al. Severe polysaccharide storage myopathy in Belgian and Percheron draught horses. Equine Vet J 1997; 29:220–225.
56. Valentine BA, McDonough SP, Chang YF, Vonderchek AJ. Polysaccharide storage myopathy in Morgan, Arabian, and Standardbred related horses and Welsh-cross ponies. Vet Pathol 2000; 37:193–196.
57. Valentine BA, Habecker PL, Patterson JS, et al. Incidence of polysaccharide storage myopathy in draft horse-related breeds: a necropsy study of 37 horses and a mule. J Vet Diagn Invest 2001; 13:63–68.
58. Gerber V, Glitz F, Welle M. Discussion of four cases of polysaccharide storage myopathy (PSSM). Pferdehelkubde 2001; 17:11–20.
59. DiMauro S, Lamperti C. Muscle glycogenoses. Muscle Nerve 2001; 24:984–999.
60. de la Corte FD, Valberg SJ, MacLeay JM, Mickelson JR. Developmental onset of polysaccharide storage myopathy in 4 quarter horse foals. J Vet Intern Med 2002; 16:581–587.
61. de la Corte FD, Valberg SJ, MacLeay JM, Williamson SE, Mickelson JR. Glucose uptake in horses with polysaccharide storage myopathy. Am J Vet Res 1999; 60:458–462.
62. de la Corte FD, Valberg SJ, Mickelson JR, Hower-Moritz M. Blood glucose clearance after feeding and exercise in polysaccharide storage myopathy. Equine Vet J 1999; 30(suppl):324–328.
63. Lentz L, Valberg S, Herold L, Onan G, Mickelson J, Gallant E. Myoplasmic calcium regulation in myotubes from horses with recurrent exertional rhabdomyolysis. Am J Vet Res 2002; 63(12):1724–1731.
64. Valberg SJ, Mickelson JR, Gallant EM, MacLeay JM, Lentz L, de la Corte F. Exertional rhabdomyolysis in quarter horses and thoroughbreds: one syndrome, multiple aetiologies. Equine Vet J 1999; 30(suppl):533–538.
65. Poels PJ, Gabreels FJ. Rhabdomyolysis: a review of the literature. Clin Neurol Neurosurg 1993; 95:175–192.
66. MacLeay JM, Sorum SA, Valberg SJ, Marsh WE, Sorum MD. Epidemiologic analysis of factors influencing exertional rhabdomyolysis in Thoroughbreds. Am J Vet Res 1999; 60:1562–1566.
67. McKenzie EC, Valberg SJ, Godden SM, et al. Effect of dietary starch, fat and bicarbonate content on exercise responses and serum creatine kinase activity in equine recurrent exertional rhabdomyolysis. J Vet Intern Med 2003; 17:693–701.
68. Firshman A, Valberg SJ, Finno C, Bender, JB. Epidemiological aspects of polysaccharide storage myopathy (PSSM) in Quarter Horses (QH). 20th Annual ACVIM Forum, Dallas, TX, 2002.
69. Valentine B, Reynolds A, Ducharme N, et al. Dietary therapy of equine polysaccharide storage myopathy. Equine Pract 1997; 19:30–37.
70. Holland JL, Kronfeld DS, Meacham TN. Behavior of horses is affected by soy lecithin and corn oil in the diet. J Anim Sci 1996; 74:1252–1255.
71. Crandell KG, Pagan JD, Harris P, Duren SE. A comparison of grain, oil and beet pulp as energy sources for the exercised horse. Equine Vet J 1999; 30(suppl): 485–489.
72. Valentine B, Reynolds A, Wakshlag J, Ducharme N. Muscle glycogen, myopathy, and diet. World Equine Vet Rev 1997; 2:27–31.
73. de la Corte F, Valberg SJ, MacLeay JM. The effect of feeding a fat supplement to horses with polysaccharide storage myopathy. World Equine Vet Rev 1999; 4:12–19.
74. Valentine BA, van Saun RJ, Thompson KN, Hintz HF. Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. J Am Vet Med Assoc 2001; 219:1537–1544.
75. MacIntyre DL, Reid WD, McKenzie DC. Delayed muscle soreness. The inflammatory response to muscle injury and its clinical implications. Sports Med 1995; 20:24–40.

76. Proske U, Morgan DL. Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. J Physiol 2001; 537:333–345.
77. Sayers SP, Clarkson PM, Rouzier PA, Kamen G. Adverse events associated with eccentric exercise protocols: six case studies. Med Sci Sports Exerc 1999; 31:1697–1702.
78. Sayers SP, Clarkson P, Patel JJ. Metabolic response to light exercise after exercise-induced rhabdomyolysis. Eur J Appl Physiol 2002; 86:280–282.
79. Foreman JH. The exhausted horse syndrome. Vet Clin North Am Equine Pract 1998; 14:205–219.
80. Ji L, Leichtweis S. Exercise and oxidative stress: sources of free radicals and their impact on anti-oxidant systems. Age 1997; 20:91–106.
81. Mills PC, Smith NC, Casas I, Harris P, Harris RC, Marlin DJ. Effects of exercise intensity and environmental stress on indices of oxidative stress and iron homeostasis during exercise in the horse. Eur J Appl Physiol Occup Physiol 1996; 74:60–66.
82. Chiaradia E, Avellini L, Rueca F, et al. Physical exercise, oxidative stress and muscle damage in racehorses. Comp Biochem Physiol B Biochem Mol Biol 1998; 119:833–836.
83. White A, Estrada M, Walker K, et al. Role of exercise and ascorbate on plasma antioxidant capacity in thoroughbred race horses. Comp Biochem Physiol A Mol Integr Physiol 2001; 128:99–104.
84. Siciliano PD, Parker AL, Lawrence LM. Effect of dietary vitamin E supplementation on the integrity of skeletal muscle in exercised horses. J Anim Sci 1997; 75:1553–1560.
85. Brady PS, Ku PK, Ullrey DE. Lack of effect of selenium supplementation on the response of the equine erythrocyte glutathione system and plasma enzymes to exercise. J Anim Sci 1978; 47:492–496.
86. Roneus B, Hakkarainen J. Vitamin E in serum and skeletal muscle tissue and blood glutathione peroxidase activity from horses with the azoturia-tying-up syndrome. Acta Vet Scand 1985; 26:425–427.
87. Step DL, Divers TJ, Cooper B, Kallfelz FA, Karcher LF, Rebhun WC. Severe masseter myonecrosis in a horse. J Am Vet Med Assoc 1991; 198:117–119.
88. Owen RR, Moore JN, Hopkins JB, Arthur D. Dystrophic myodegeneration in adult horses. J Am Vet Med Assoc 1977; 171:343–349.
89. Lofstedt J. White muscle disease of foals. Vet Clin North Am Equine Pract 1997; 13:169–185.
90. Beech J, Lindborg S, Braund KG. Potassium concentrations in muscle, plasma and erythrocytes and urinary fractional excretion in normal horses and those with chronic intermittent exercise-associated rhabdomyolysis. Res Vet Sci 1993; 55:43–51.
91. Shintani S, Shiigai T, Tsukagoshi H. Marked hypokalemic rhabdomyolysis with myoglobinuria due to diuretic treatment. Eur Neurol 1991; 31:396–398.
92. Bain FT, Merritt AM. Decreased erythrocyte potassium concentration associated with exercise-related myopathy in horses. J Am Vet Med Assoc 1990; 196:1259–1261.
93. Johnson PJ, Goetz TE, Foreman JH, Vogel RS, Hoffmann WE, Baker GJ. Effect of whole-body potassium depletion on plasma, erythrocyte, and middle gluteal muscle potassium concentration of healthy, adult horses. Am J Vet Res 1991; 52:1676–1683.
94. Muylle E, van den Hende C, Nuytten J, Deprez P, Vlaminck K, Oyaert W. Potassium concentration in equine red blood cells: normal values and correlation with potassium levels in plasma. Equine Vet J 1984; 16:447–449.
95. Freestone JF, Gossett K, Carlson GP, Church G. Exercise induced alterations in the serum muscle enzymes, erythrocyte potassium and plasma constituents following feed withdrawal or furosemide and sodium bicarbonate administration in the horse. J Vet Intern Med 1991; 5:40–46.
96. Tiidus PM. Oestrogen and sex influence on muscle damage and inflammation: evidence from animal models. Curr Opin Clin Nutr Metab Care 2001; 4:509–513.
97. Harris PA. The equine rhabdomyolysis syndrome in the United Kingdom: epidemiological and clinical descriptive information. Br Vet J 1991; 147:373–384.
98. Freestone JF, Carlson GR. Muscle disorders in the horse: a retrospective study. Equine Vet J 1991; 23:86–90.
99. Beech J, Lindborg S, Fletcher JE, Lizzo F, Tripolitis L, Braund K. Caffeine contractures, twitch characteristics and the threshold for Ca(2+)-induced Ca2+ release in skeletal muscle from horses with chronic intermittent rhabdomyolysis. Res Vet Sci 1993; 54:110–117.
100. Lindholm A. Relationship between back problems and muscle disorders: options for prevention and therapy. Conference on Equine Sports Medicine and Science, Waseningen, 1998.
101. Collinder E, Lindholm A, Rasmuson M. Genetic markers in standardbred trotters susceptible to the rhabdomyolysis syndrome. Equine Vet J 1997; 29:117–120.
102. McGowan CM, Fordham T, Christley RM. Incidence and risk factors for exertional rhabdomyolysis in thoroughbred racehorses in the United Kingdom. Vet Rec 2002; 151:623–626.
103. Frauenfelder HC, Rossdale PD, Ricketts SW, Allen WR. Changes in serum muscle enzyme levels associated with training schedules and stage of the oestrous cycle in Thoroughbred racehorses. Equine Vet J 1986; 18:371–374.
104. Beyer IW, Karmali R, Demeester-Mirkine N, Cogan E, Fuss MJ. Serum creatine kinase levels in overt and subclinical hypothyroidism. Thyroid 1998; 8:1029–1031.
105. Lochmuller H, Reimers CD, Fischer P, Heuss D, Muller-Hocker J, Pongratz DE. Exercise-induced myalgia in hypothyroidism. Clin Invest 1993; 71:999–1001.
106. Foreman JH. Metabolic causes of equine exercise intolerance. Vet Clin North Am Equine Pract 1996; 12:537–554.
107. Waldron-Mease E. Hypothyroidism and myopathy in racing Thoroughbreds and Standardbreds. J Equine Med Surg 1979; 3:124–128.
108. Harris P, Marlin D, Gray J. Equine thyroid function tests: a preliminary investigation. Br Vet J 1992; 148:71–80.
109. Harris PA, Snow DH, Greet TR, Rossdale PD. Some factors influencing plasma AST/CK activities in thoroughbred racehorses. Equine Vet J 1990; 9:66–71.
110. Stanley O, Hillidge CJ. Alopecia associated with hypothyroidism in a horse. Equine Vet J 1982; 14:165–167.
111. Lowe JE, Baldwin BH, Foote RH, Hillman RB, Kallfelz FA. Equine hypothyroidism: the long term effects of thyroidectomy on metabolism and growth in mares and stallions. Cornell Vet 1974; 64:276–295.
112. Harris PA. An outbreak of the equine rhabdomyolysis syndrome in a racing yard. Vet Rec 1990; 127:468–470.
113. Lentz LR, Valberg SJ, Balog EM, Mickelson JR, Gallant EM. Abnormal regulation of muscle contraction in horses with recurrent exertional rhabdomyolysis. Am J Vet Res 1999; 60:992–999.

114. Mlekoday JA, Mickelson JR, Valberg SJ, Horton JH, Gallant EM, Thompson LV. Calcium sensitivity of force production and myofibrillar ATPase activity in muscles from Thoroughbreds with recurrent exertional rhabdomyolysis. Am J Vet Res 2001; 62:1647–1652.
115. MacLeay JM, Valberg SJ, Sorum SA, et al. Heritability of recurrent exertional rhabdomyolysis in Thoroughbred racehorses. Am J Vet Res 1999; 60:250–256.
116. Hildebrand S, Arpin D, Cardinet G. Exertional rhabdomyolysis related to malignant hyperthermia using the halothane-caffeine contracture test. In: Gillespie J, Robinson N, eds. Equine exercise physiology, vol. 2. Davis, CA: ICEEP; 1987:786.
117. Hildebrand SV, Arpin D, Cardinet G 3rd. Contracture test and histologic and histochemical analyses of muscle biopsy specimens from horses with exertional rhabdomyolysis. J Am Vet Med Assoc 1990; 196:1077–1083.
118. Hodgson DR. Exercise-associated myopathy: is calcium the culprit? Equine Vet J 1993; 25:1–3.
119. Lentz LR, Valberg SJ, Mickelson JR, Gallant EM. In vitro contractile responses and contracture testing of skeletal muscle from Quarter Horses with exertional rhabdomyolysis. Am J Vet Res 1999; 60:684–648.
120. Allen GC, Fletcher JE, Huggins FJ, Conti PA, Rosenberg H. Caffeine and halothane contracture testing in swine using the recommendations of the North American Malignant Hyperthermia Group. Anesthesiology 1990; 72:71–76.
121. Bina S, Karan SM, Lojeski EW, Mongan PD, Muldoon SM. Prolonging viability of swine muscle biopsy specimens in malignant hyperthermia testing. Anesth Analg 2001; 93:781–786.
122. Roberts MC, Mickelson JR, Patterson EE, et al. Autosomal dominant canine malignant hyperthermia is caused by a mutation in the gene encoding the skeletal muscle calcium release channel (RYR1). Anesthesiology 2001; 95:716–725.
123. Kochling A, Wappler F, Winkler G, Schulte am Esch JS. Rhabdomyolysis following severe physical exercise in a patient with predisposition to malignant hyperthermia. Anaesth Intensive Care 1998; 26:315–318.
124. d'Allaire S, DeRoth L. Physiological responses to treadmill exercise and ambient temperature in normal and malignant hyperthermia susceptible pigs. Can J Vet Res 1986; 50:78–83.
125. Waldron-Mease E, Klein LV, Rosenberg H, Leitch M. Malignant hyperthermia in a halothane-anesthetized horse. J Am Vet Med Assoc 1981; 179:896–898.
126. Manley SV, Kelly AB, Hodgson D. Malignant hyperthermia-like reactions in three anesthetized horses. J Am Vet Med Assoc 1983; 183:85–89.
127. Klein L, Ailes N, Fackelman GE, Kellon E, Rosenberg H. Postanesthetic equine myopathy suggestive of malignant hyperthermia. A case report. Vet Surg 1989; 18:479–482.
128. Fujii J, Otsu K, Zorzato F, et al. Identification of a mutation in porcine ryanodine receptor associated with malignant hyperthermia. Science 1991; 253:448–451.
129. Jurkat-Rott K, McCarthy T, Lehmann-Horn F. Genetics and pathogenesis of malignant hyperthermia. Muscle Nerve 2000; 23:4–17.
130. Mickelson JR, Gallant EM, Litterer LA, Johnson KM, Rempel WE, Louis CF. Abnormal sarcoplasmic reticulum ryanodine receptor in malignant hyperthermia. J Biol Chem 1988; 263:9310–9315.
131. Ward TL, Valberg SJ, Gallant EM, Mickelson JR. Calcium regulation by skeletal muscle membranes of horses with recurrent exertional rhabdomyolysis. Am J Vet Res 2000; 61:242–247.
132. Tilgen N, Zorzato F, Halliger-Keller B, et al. Identification of four novel mutations in the C-terminal membrane spanning domain of the ryanodine receptor 1: association with central core disease and alteration of calcium homeostasis. Hum Mol Genet 2001; 10:2879–2887.
133. Monnier N, Procaccio V, Stieglitz P, Lunardi J. Malignant-hyperthermia susceptibility is associated with a mutation of the alpha 1-subunit of the human dihydropyridine-sensitive L-type voltage-dependent calcium-channel receptor in skeletal muscle. Am J Hum Genet 1997; 60:1316–1325.
134. Protasi F. Structural interaction between RYRs and DHPRs in calcium release units of cardiac and skeletal muscle cells. Front Biosci 2002; 7:d650–658.
135. Peluso A, Bianchini A. Malignant hyperthermia susceptibility in patients with Duchenne's muscular dystrophy. Can J Anaesth 1992; 39:1117–1118.
136. Valentine B, de Lahunta A, Divers TJ, Ducharme N, Orcutt R. Clinical and pathologic findings in two draft horses with progressive weakness, and abnormal gait characteristic of shivers syndrome. J Am Vet Med Assoc 1999; 215:1661–1665.
137. Valberg S, Jones J, Smith B, Somerville B. Limitations to performance caused by skeletal muscle enzyme deficiencies. Equine Vet J 1995; 18(suppl):205–208.
138. DiMauro S, Tsujino S, Shanske S, Rowland LP. Biochemistry and molecular genetics of human glycogenoses: an overview. Muscle Nerve 1995; 3:S10–17.
139. Valberg SJ, Macleay JM, Billstrom JA, Hower-Moritz MA, Mickelson JR. Skeletal muscle metabolic response to exercise in horses with 'tying-up' due to polysaccharide storage myopathy. Equine Vet J 1999; 31:43–47.
140. Valberg SJ, Townsend D, Mickelson JR. Skeletal muscle glycolytic capacity and phosphofructokinase regulation in horses with polysaccharide storage myopathy. Am J Vet Res 1998; 59:782–785.
141. Shulman RG, Bloch G, Rothman DL. In vivo regulation of muscle glycogen synthase and the control of glycogen synthesis. Proc Natl Acad Sci USA 1995; 92:8535–8542.
142. Bao Y, Kishnani P, Wu JY, Chen YT. Hepatic and neuromuscular forms of glycogen storage disease type IV caused by mutations in the same glycogen-branching enzyme gene. J Clin Invest 1996; 97:941–948.
143. Valberg SJ, Ward TL, Rush B, et al. Glycogen branching enzyme deficiency in quarter horse foals. J Vet Intern Med 2001; 15:572–580.
144. Valberg SJ. Personal communication, 2002.
145. Pickar JG, Spier SJ, Snyder JR, Carlsen RC. Altered ionic permeability in skeletal muscle from horses with hyperkalemic periodic paralysis. Am J Physiol 1991; 260:C926–933.
146. Powell KA, Campbell LC, Tavare JM, Leader DP, Wakefield JA, Gould GW. Trafficking of Glut4-green fluorescent protein chimaeras in 3T3-L1 adipocytes suggests distinct internalization mechanisms regulating cell surface glut4 levels. Biochem J 1999; 344 Pt 2:535–543.
147. Treadway JL, Hargrove DM, Nardone NA, et al. Enhanced peripheral glucose utilization in transgenic mice expressing the human GLUT4 gene. J Biol Chem 1994; 269:29956–29961.

148. Hayashi T, Wojtaszewski JF, Goodyear LJ. Exercise regulation of glucose transport in skeletal muscle. Am J Physiol 1997; 273:E1039–1051.
149. Cheatham B. GLUT4 and company: SNAREing roles in insulin-regulated glucose uptake. Trends Endocrinol Metab 2000; 11:356–361.
150. Richter EA, Derave W, Wojtaszewski JF. Glucose, exercise and insulin: emerging concepts. J Physiol 2001; 535:313–322.
151. Ivy JL, Kuo CH. Regulation of GLUT4 protein and glycogen synthase during muscle glycogen synthesis after exercise. Acta Physiol Scand 1998; 162:295–304.
152. Carlström B. Uber die atiologie und pathogenese der kreuzlahme des pferdes (Haemaglobinaemia paralytca). Scand Arch 1931; 62:1–69.
153. Valberg S, Haggendal J, Lindholm A. Blood chemistry and skeletal muscle metabolic responses to exercise in horses with recurrent exertional rhabdomyolysis. Equine Vet J 1993; 25:17–22.
154. Bloom BA, Valentine BA, Gleed RD, Cable CS. Postanaesthetic recumbency in a Belgian filly with polysaccharide storage myopathy. Vet Rec 1999; 144:73–75.
155. Guertl B, Noehammer C, Hoefler G. Metabolic cardiomyopathies. Int J Exp Pathol 2000; 81:349–372.
156. McGowan CM, Posner RE, Christley RM. Incidence of exertional rhabdomyolysis in polo horses in the USA and the United Kingdom in the 1999/2000 season. Vet Rec 2002; 150:535–537.
157. Valberg SJ, Geyer C, Sorum SA, Cardinet GH 3rd. Familial basis of exertional rhabdomyolysis in quarter horse-related breeds. Am J Vet Res 1996; 57:286–290.
158. Meyer TS, Fedde MR, Cox JH, Erickson HH. Hyperkalaemic periodic paralysis in horses: a review. Equine Vet J 1999; 31:362–367.
159. Reynolds J, Potter G, Greene L, et al. Genetic-diet interactions in the hyperkalemic periodic paralysis syndrome in Quarter Horses fed varying amounts of potassium. J Equine Vet Sci 1998; 18:591–600.
160. Cox J. An episodic weakness in four horses associated with intermittent serum hyperkalemia and the similarity of the disease to hyperkalemic periodic paralysis in man. Proceedings of the 31st Annual Meeting of the American Association of Equine Practitioners, 1985; vol. 21:383–391.
161. Cox J, DeBowes R. Episodic weakness caused by hyperkalemic periodic paralysis in horses. Comp Cont Educ Pract Vet 1990; 12:83–88.
162. Spier SJ, Carlson GP, Holliday TA, Cardinet GH 3rd, Pickar JG. Hyperkalemic periodic paralysis in horses. J Am Vet Med Assoc 1990; 197:1009–1017.
163. Naylor JM. Hyperkalemic periodic paralysis. Vet Clin North Am Equine Pract 1997; 13:129–144.
164. Guglick MA, MacAllister CG, Breazile JE. Laryngospasm, dysphagia, and emaciation associated with hyperkalemic periodic paralysis in a horse. J Am Vet Med Assoc 1996; 209:115–117.
165. Carr EA, Spier SJ, Kortz GD, Hoffman EP. Laryngeal and pharyngeal dysfunction in horses homozygous for hyperkalemic periodic paralysis. J Am Vet Med Assoc 1996; 209:798–803.
166. Beech J, Fletcher JE, Tripolitis L, Lindborgh S. Effects of phenytoin in two myotonic horses with hyperkalemic periodic paralysis. Muscle Nerve 1992; 15:932–936.
167. Glazier DB, Littledike ET, Evans RD. Electrocardiographic changes in induced hyperkalemia in ponies. Am J Vet Res 1982; 43:1934–1937.
168. Cornick JL, Seahorn TL, Hartsfield SM. Hyperthermia during isoflurane anaesthesia in a horse with suspected hyperkalaemic periodic paralysis. Equine Vet J 1994; 26:511–514.
169. Robertson SA, Green SL, Carter SW, Bolon BN, Brown MP, Shields RP. Postanesthetic recumbency associated with hyperkalemic periodic paralysis in a quarter horse. J Am Vet Med Assoc 1992; 201:1209–1212.
170. Castex AM, Bertone JJ. ECG of the month. Sinus tachycardia and hyperkalemia in a horse. J Am Vet Med Assoc 1989; 194:654–655.
171. Church S. Hyperkalaemic periodic paralysis in Australian quarter horses. Aust Vet J 1995; 72:314–316.
172. Beech J, Lindborg S. Prophylactic efficacy of phenytoin, acetazolamide and hydrochlorothiazide in horses with hyperkalaemic periodic paralysis. Res Vet Sci 1995; 59:95–101.
173. Bailey JE, Pablo L, Hubbell JA. Hyperkalemic periodic paralysis episode during halothane anesthesia in a horse. J Am Vet Med Assoc 1996; 208:1859–1865.
174. Naylor JM, Robinson JA, Crichlow EC, Steiss JE. Inheritance of myotonic discharges in American quarter horses and the relationship to hyperkalemic periodic paralysis. Can J Vet Res 1992; 56:62–66.
175. Stewart RH, Bertone JJ, Yvorchuk-St Jean K, Reed SM, Neil WH Jr. Possible normokalemic variant of hyperkalemic periodic paralysis in two horses. J Am Vet Med Assoc 1993; 203:421–424.
176. Naylor JM. Equine hyperkalemic periodic paralysis: review and implications. Can Vet J 1994; 35:279–285.
177. Spier SJ, Carlson GP, Harrold D, Bowling A, Byrns G, Bernoco D. Genetic study of hyperkalemic periodic paralysis in horses. J Am Vet Med Assoc 1993; 202:933–937.
178. Traub-Dargatz JL, Ingram JT, Stashak TS, et al. Respiratory stridor associated with polymyopathy suspected to be hyperkalemic periodic paralysis in four quarter horse foals. J Am Vet Med Assoc 1992; 201:85–89.
179. Reed SM, Hegreberg GA, Bayly WM, Brown CM, Paradis MR, Clemmons RM. Progressive myotonia in foals resembling human dystrophia myotonica. Muscle Nerve 1988; 11:291–296.
180. Montagna P, Liguori R, Monari L, et al. Equine muscular dystrophy with myotonia. Clin Neurophysiol 2001; 112:294–299.
181. Steinberg S, Botelho S. Myotonia in a horse. Science 1962; 137:979–980.
182. Naylor JM, Jones V, Berry SL. Clinical syndrome and diagnosis of hyperkalaemic periodic paralysis in quarter horses. Equine Vet J 1993; 25:227–232.
183. Robinson JA, Naylor JM, Crichlow EC. Use of electromyography for the diagnosis of equine hyperkalemic periodic paresis. Can J Vet Res 1990; 54:495–500.
184. Naylor JM. Selection of quarter horses affected with hyperkalemic periodic paralysis by show judges. J Am Vet Med Assoc 1994; 204:926–928.
185. Bowling AT, Byrns G, Spier S. Evidence for a single pedigree source of the hyperkalemic periodic paralysis susceptibility gene in quarter horses. Anim Genet 1996; 27:279–281.
186. Rose B, Post T, Narins R. Clinical physiology of acid–base and electrolyte disorders. New York: McGraw-Hill; 2000.
187. Bendheim PE, Reale EO, Berg BO. beta-Adrenergic treatment of hyperkalemic periodic paralysis. Neurology 1985; 35:746–749.

188. Fletcher JE, Erwin K, Beech J. Phenytoin increases specific triacylglycerol fatty esters in skeletal muscle from horses with hyperkalemic periodic paralysis. Biochim Biophys Acta 1993; 1168:292–298.
189. Yudkowsky ML, Beech J, Fletcher JE. Phenytoin alters transcript levels of hormone-sensitive lipase in muscle from horses with hyperkalemic periodic paralysis. Arch Biochem Biophys 1998; 358:264–270.
190. Duren S. Feeding management of horses with hyperkalemic periodic paralysis. World Equine Vet Res 1998; 3:5–8.
191. Cox J, DeBowes RM, Bayer J. Response of normal and acetazolamide treated horses to oral potassium chloride challenge. Proceedings of the 6th Annual Veterinary Medical Forum, 1988.
192. Hoskins B. Studies on the mechanism of action of acetazolamide in the prophylaxis of hyperkalemic periodic paralysis. Life Sci 1977; 20:343–349.
193. Alberts MK, Clarke CR, MacAllister CG, Homer LM. Pharmacokinetics of acetazolimide after intravenous and oral administration in horses. Am J Vet Res 2000; 61:965–968.
194. Smith CA. Hyperkalemic periodic paralysis presents medical and ethical challenge. J Am Vet Med Assoc 1993; 202:1203–1209.
195. Steiss J, Naylor JR. Episodic muscle tremors in a quarter horse: Resemblance to hyperkalemic periodic paralysis. Can Vet J 1986; 27:332.
196. Cannon SC. Ion-channel defects and aberrant excitability in myotonia and periodic paralysis. Trends Neurosci 1996; 19:3–10.
197. Hoffman EP. Voltage-gated ion channelopathies: inherited disorders caused by abnormal sodium, chloride, and calcium regulation in skeletal muscle. Annu Rev Med 1995; 46:431–441.
198. Rudolph JA, Spier SJ, Byrns G, Hoffman EP. Linkage of hyperkalaemic periodic paralysis in quarter horses to the horse adult skeletal muscle sodium channel gene. Anim Genet 1992; 23:241–250.
199. Rudolph JA, Spier SJ, Byrns G, Rojas CV, Bernoco D, Hoffman EP. Periodic paralysis in quarter horses: a sodium channel mutation disseminated by selective breeding. Nat Genet 1992; 2:144–147.
200. Naylor JM, Robinson JA, Bertone J. Familial incidence of hyperkalemic periodic paralysis in quarter horses. J Am Vet Med Assoc 1992; 200:340–343.
201. Zhou J, Spier SJ, Beech J, Hoffman EP. Pathophysiology of sodium channelopathies: correlation of normal/mutant mRNA ratios with clinical phenotype in dominantly inherited periodic paralysis. Hum Mol Genet 1994; 3:1599–1603.
202. Hanna WJ, Tsushima RG, Sah R, McCutcheon LJ, Marban E, Backx PH. The equine periodic paralysis Na+ channel mutation alters molecular transitions between the open and inactivated states. J Physiol 1996; 497 (Pt 2):349–364.
203. Cannon SC, Hayward LJ, Beech J, Brown RH Jr. Sodium channel inactivation is impaired in equine hyperkalemic periodic paralysis. J Neurophysiol 1995; 73:1892–1899.
204. Lehmann-Horn F, Iaizzo PA, Hatt H, Franke C. Altered gating and conductance of Na+ channels in hyperkalemic periodic paralysis. Pflugers Arch 1991; 418:297–299.
205. Cannon SC, Brown RH Jr, Corey DP. A sodium channel defect in hyperkalemic periodic paralysis: potassium-induced failure of inactivation. Neuron 1991; 6:619–626.
206. Ricker K, Camacho LM, Grafe P, Lehmann-Horn F, Rudel R. Adynamia episodica hereditaria: what causes the weakness? Muscle Nerve 1989; 12:883–891.
207. Steele D, Naylor JM. Hyperkalemic periodic paralysis, plasma lactate and exercise tolerance. J Equine Vet Sci 1996; 202:933–937.
208. Maxson-Sage A, Parente EJ, Beech J, Lindborg S, May LL, Teleis DC. Effect of high-intensity exercise on arterial blood gas tensions and upper airway and cardiac function in clinically normal quarter horses and horses heterozygous and homozygous for hyperkalemic periodic paralysis. Am J Vet Res 1998; 59:615–618.
209. McKerrell RE. Myotonia in man and animals: confusing comparisons. Equine Vet J 1987; 19:266–267.
210. Jamison JM, Baird JD, Smith-Maxie LL, Hulland TJ. A congenital form of myotonia with dystrophic changes in a quarterhorse. Equine Vet J 1987; 19:353–358.
211. Hegreberg GA, Reed SM. Skeletal muscle changes associated with equine myotonic dystrophy. Acta Neuropathol 1990; 80:426–431.
212. Lindholm A. Diagnosis of muscular problems. In: Lindner A, ed. Laboratory diagnosis for sports horses. Wageningen: Wageningen Pers; 1998:55–61.
213. Andrews FM, Spurgeon TL, Reed SM. Histochemical changes in skeletal muscles of four male horses with neuromuscular disease. Am J Vet Res 1986; 47:2078–2083.
214. Roneus B, Lindholm A, Jonsson L. Myotoni hos hast. Svensk Veterinartidning 1983; 35:217–220.
215. Brook JD, McCurrach ME, Harley HG, et al. Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3′ end of a transcript encoding a protein kinase family member. Cell 1992; 69:385.
216. Larkin K, Fardaei M. Myotonic dystrophy – a multigene disorder. Brain Res Bull 2001; 56:389–395.
217. Meola G. Clinical and genetic heterogeneity in myotonic dystrophies. Muscle Nerve 2000; 23:1789–1799.
218. Johansson A, Carlstrom K, Ahren B, et al. Abnormal cytokine and adrenocortical hormone regulation in myotonic dystrophy. J Clin Endocrinol Metab 2000; 85:3169–3176.
219. Mastrogiacomo I, Pagani E, Novelli G, et al. Male hypogonadism in myotonic dystrophy is related to (CTG)n triplet mutation. J Endocrinol Invest 1994; 17:381–383.
220. DiMauro S, Bonilla E, Davidson M, Hirano M, Schon EA. Mitochondria in neuromuscular disorders. Biochim Biophys Acta 1998; 1366:199–210.
221. Valberg SJ, Carlson GP, Cardinet GH 3rd, et al. Skeletal muscle mitochondrial myopathy as a cause of exercise intolerance in a horse. Muscle Nerve 1994; 17:305–312.
222. Larsson NG, Oldfors A. Mitochondrial myopathies. Acta Physiol Scand 2001; 171:385–393.
223. Xu X, Arnason U. The complete mitochondrial DNA sequence of the horse, *Equus caballus*: extensive heteroplasmy of the control region. Gene 1994; 148:357–362.
224. Turner AS, Trotter GW. Fibrotic myopathy in the horse. J Am Vet Med Assoc 1984; 184:335–338.
225. Bishop R. Fibrotic myopathy in the gracilis muscle of a horse. Vet Med Small Anim Clin 1972; 67:270.
226. Irwin DH, Howell DW. Fibrotic myopathy, haematomas and scar tissue in the gaskin area of the thoroughbred. J S Afr Vet Assoc 1981; 52:65–66.
227. Reef VB. Equine diagnostic ultrasound. Philadelphia: Saunders; 1998:145–147.

228. Valentine BA, Rousselle SD, Sams AE, Edwards RB. Denervation atrophy in three horses with fibrotic myopathy. J Am Vet Med Assoc 1994; 205:332–336.
229. Gomez-Villamandos R, Santisteban J, Ruiz I, Avila I. Tenotomy of the tibial insertion of the semitendinosus muscle of two horses with fibrotic myopathy. Vet Rec 1995; 136:67–68.
230. McIlwraith W, Robertson J. McIlwraith & Turner's equine surgery: advanced techniques. Baltimore, MD: Williams and Wilkins; 1998:213–215.
231. Beauchamp JR, Heslop L, Yu DS, et al. Expression of CD34 and Myf5 defines the majority of quiescent adult skeletal muscle satellite cells. J Cell Biol 2000; 151:1221–1234.

CHAPTER 7

Skeletal physiology: responses to exercise and training

Allen E. Goodship and Roger K.W. Smith

Introduction

Role of the skeleton

The mammalian skeleton provides protection for vital organs, a reservoir of minerals and a structural support for the body. Its major role, however, is provision of structural support and a means of locomotion using jointed bones together with muscles, tendons and ligaments. These components have evolved to optimize posture and locomotion for the lifestyle of individual species. The type of joints and position of muscle and tendon attachment relative to lever arms and fulcra provide an optimal mechanical advantage. As a structure the skeleton has evolved to provide maximum strength with minimal mass. The skeleton comprises a series of morphologically distinct elements – bones. The shape and size of these individual bones are determined by genetic and functional factors to prove an appropriate structure for functional demands with low risk of failure and without incurring excess energy expenditure. The demands for energetic efficiency are greater in animals evolved for high-speed locomotion, such as horses.

The horse has not only evolved to become a high-speed animal, but has also been the subject of selective breeding as an elite animal athlete. The Thoroughbred race horse is a prime example of selection for speed. However, it has been suggested that this selection process has reached its limit on the basis of classic race times remaining similar for many years. The Thoroughbred has arisen from a somewhat limited gene pool and this may have resulted in a plateau of performance.[1] This is in contrast to the performance of human athletes in which records are broken almost year on year. However, an alternative explanation is that training methods to condition race horses have not developed to optimize the capacity of the adaptive responses of the musculoskeletal system. In human athletics the application of sports science has undoubtedly contributed to the enhancement of performances over recent years. Equine sports science is not yet developed or applied to the same extent. In addition, many training systems continue to be based on empirical and traditional methods.

The skeleton has a unique capacity to respond to changes in mechanical loading in the short term and can, therefore, optimize for energetic efficiency in relation to changes in mechanical demands. There is a need not only to understand these mechanisms in general but to apply the information to specific training regimens for equine athletes.

Skeletal requirements for the horse

The requirements for the skeleton in the horse are, in common with other animals, related to functional demands, imposed by both evolutionary process and short-term conditioning. Domestication and the varied requirements for man's interaction with this species have resulted in a wide range of breeds and types of horse, with great variation in conformation. Selective breeding has resulted in adaptation of this species for the different specific purposes. Some breeds are massive and the bones are relatively high in mass to accommodate needs for strength and endurance but they are not able to sustain high speeds. Others have been selected for speed, the Thoroughbred race horse perhaps being the best example of skeletal development for speed. As such, the requirements for the skeleton in these horses are those of low mass and high strength.

The 'design' of the equine skeleton is a refinement of the basic mammalian pattern. The horse is an unguligrade

animal, a member of the order Perissodactyla, the odd-toed ungulates standing on the hoof of the third digit. The major muscle masses of the limbs are positioned proximally to reduce the energy required to move the limb as it swings backward and forward in cursorial locomotion. Muscle forces are transferred to distal bones across joints by means of long tendons. The tendons and ligaments have also evolved to play a major role in the energetic efficiency of locomotion, many acting as energy-storing springs.

Bone mass is also minimized at the distal extremities and safety margins decrease toward the distal extremity of the limbs. This has been related by Currey[2] to the incidence of fractures in race horses[3] being higher in the distal bones than those located proximally.

Selection for high-speed gait is also reflected in the morphology of the equine skeleton. The lever arms at the elbow and hock result in small muscle contractions producing fast extensive movement of the lower limb segments.

Skeletal refinements in the elite equine athlete are basically fine tuning of this general pattern. New methods of analysis of skeletal conformation are being used to assess the level of performance in several different types of horse.[4] However, these systems have not yet been perfected any more than many other methods for identifying potential winners at an early age. With advances in understanding of the factors that optimize efficiency and the development of complex computer modeling systems, it may eventually be possible to identify athletic performance of individual horses at an early age.

The ability to select and train elite equine athletes must result from a sound understanding of many aspects of the pathobiology of the horse, from the cell and molecular level to that of the whole animal. One of the most important systems in relation to locomotor performance is the musculoskeletal system. The major structural support tissue is bone.

Bone as a tissue

Bone as a tissue is a member of the family of connective tissues. These are characterized by being a composite of cells and extracellular matrix. The matrix in the case of bone is a composite of an organic, predominantly collagenous component and an inorganic hydroxyapatite component.

Bone cells and interactions

Adult bone tissue comprises three major populations of cells, each with a specific functional role but with both cell-to-cell interactions and also cell–matrix interactions. It is the coordinated interaction of the activities of these cell populations that optimizes the morphology of bones in relation to changing mechanical demands. Understanding these mechanisms and applying the principles to training regimens has the potential to improve performance and minimize injury in conditioning of equine athletes.

Osteoblasts

These cells are derived from local lining cells. The flattened mononuclear cells become plump when activated and synthesize bone matrix in the form of osteoid (Fig. 7.1). The osteoid then becomes mineralized over a period of weeks to form bone matrix. In rapidly forming surfaces some osteoblasts are entrapped in their own matrix and these then become osteocytes (Fig. 7.2). The osteoblasts communicate with osteoclasts and enable activation of osteoclasts to allow bone resorption. Osteoblasts also produce colony-stimulating factor that increases numbers of pre-osteoclasts from mononuclear precursors in the bone marrow and also osteoclast activation factor that activates the pre-osteoclasts and initiates resorption of bone matrix (Fig. 7.3). The coupling of bone resorption and subsequent bone formation has recently been shown to involve a receptor on the osteoblast cell membrane known as RANK ligand (RANKL) which binds to RANK present on the surface of pre-osteoclasts and induces activation of the intracellular cascades to activate the osteoclasts. The RANKL can also bind to a protein called 'osteoprotegerin,' OPG, which prevents binding with and activation of osteoclasts. Thus a regulation of coupling of these cells

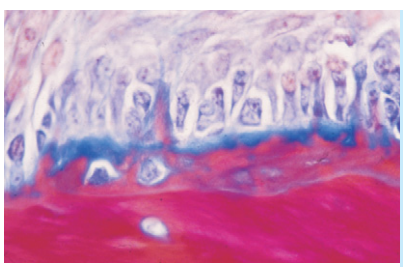


Fig. 7.1
A photomicrograph of bone showing the bone-forming cells called 'osteoblasts'. The blue staining matrix is the precalcified osteoid. Cells can be seen becoming entrapped in matrix to become osteocytes.

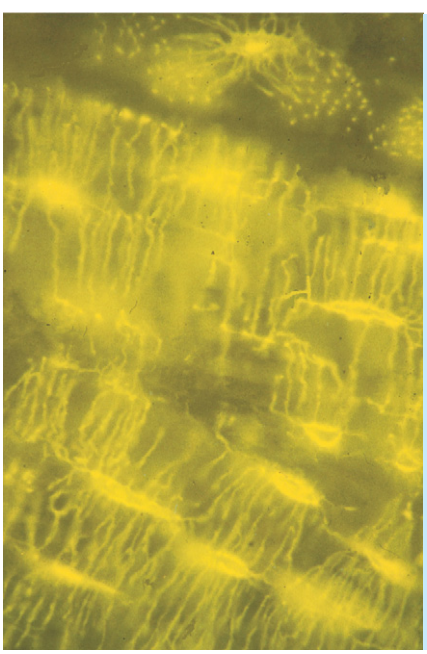


Fig. 7.2
Bone cells – osteocytes entrapped within bone matrix showing communication via cytoplasmic processes within canaliculi.

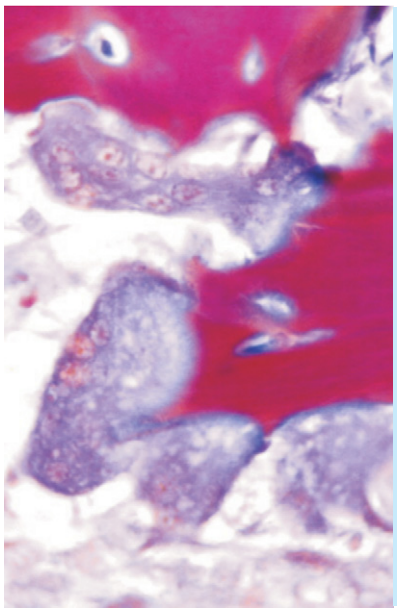


Fig. 7.3
A photomicrograph showing bone resorption by osteoclasts.

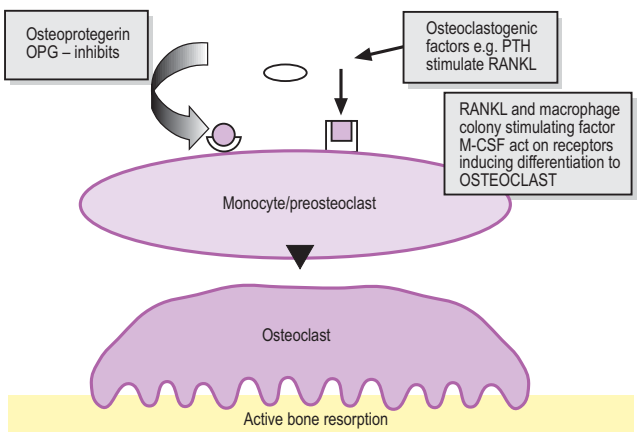


Fig. 7.4
Coupling of the bone remodeling cycle.

and associated amounts of bone resorption and formation is effected by this system (Fig. 7.4).[5,6] Other systemic factors can also influence this system; for example, parathyroid hormone (PTH) can 'blunt' OPG influence. The osteoblasts can also secrete collagenase, an enzyme that removes the surface layer of osteoid, unmineralized bone matrix, on bone surfaces and allows osteoclasts access to the bone matrix. Boyde et al used in vitro systems to measure bone resorption activity of osteoclasts and also to show the interactions between osteoblasts and osteoclasts.[7] Hormonal influences on calcium metabolism and bone resorption act indirectly on receptors on the osteoblast which in turn regulates osteoclast recruitment and activity. Thus the osteoblast is central to the control of the bone modeling and remodeling process.

Osteoclasts

These cells are derived from circulating monocytes. They are multinucleate cells (Fig. 7.3) which, when activated, reside on a bone surface with a ruffled border to isolate the local environment between the cell and the bone surface. The perimeter of the cell membrane forms a seal against the underlying bone involving adhesion molecules, the integrins to isolate the local environment beneath the cell which is then lowered in pH by an active proton pump generating hydrogen ions.[8] The pH falls to around 2–3 and the bone matrix and embedded osteocytes are resorbed, forming a resorption pit, and the resorption products are trafficked through the cell.[9] As indicated above, this process is regulated by the osteoblasts, which in turn communicate with the third population of cells – the osteocytes. The bone-resorbing osteoclasts are also influenced directly by some specific hormones such as calcitonin.

Osteocytes

These cells arise from osteoblasts that become trapped in the bone matrix within lacunae. They are cells with many long cytoplasmic processes within small tunnels in the matrix called canaliculi (Fig. 7.2). Processes from adjacent cells connect by means of gap junctions allowing cell-to-cell communication. A recent finding by Skerry and co-workers has been the identification of glutamate transport systems involved in osteocyte cell signaling.[10] This transmitter also operates in the central nervous system, where complex interneuronal signaling occurs. The presence of such a signaling mechanism among osteocyte bone cells provides supporting evidence that this population of cells plays a role in the overall perception of mechanical environment on a bone and co-ordinates an appropriate response to ensure optimal bone size and architecture.

The osteocytes and their cell processes are surrounded by extracellular fluid. The mechanical loading of a bone results in deformation and movement of this extracellular fluid within the matrix around the cells. Extracellular fluid contains ions and the movement of this ionic fluid with respect to the charged surfaces of the matrix induces electrical potentials. These electrical charges are referred to as 'streaming potentials' which are also thought to influence the cell activity and provide a putative mechanotransduction pathway.[11,12] The gap junctions linking cell communication are also modulated in number by mechanical loading of bone and thus may play a role in regulation of bone form in response to functional demands.[13]

The networks of osteocytes also communicate with the surface lining cells and osteoblasts. Thus the integration of the cell populations by the osteoblasts provides a complex but extremely sensitive mechanism to enable bone mass and architecture to be optimized for the changing mechanical demands throughout life.

Lining cells

Quiescent bone surfaces are covered by lining cells which have the capacity to respond to both mechanical and biological signals and are activated to change shape into plump, metabolically active osteoblasts. These cells are found in the osteogenic layer of the periosteum or endosteum; these membranes comprise a deep cellular layer and a more superficial fibrous layer (Fig. 7.5). Some pluripotent cells have been demon-

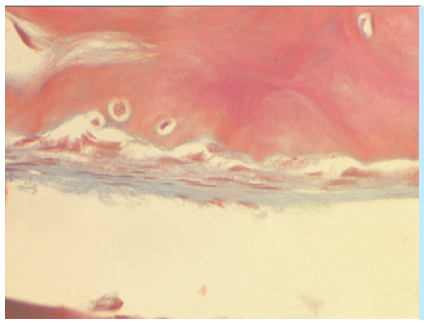


Fig. 7.5
Lining cells on a bone surface – periosteum, comprising a fibrous outer layer and an osteogenic or cambium inner layer of cells.

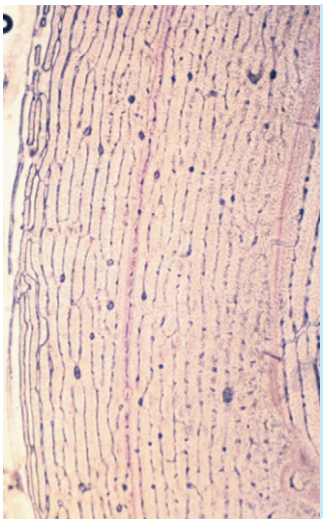


Fig. 7.6
Photomicrograph of a transverse section of laminar bone.

strated in the osteogenic cellular layer and these have been shown to have the capacity to differentiate into other connective tissues such as cartilage. There is currently considerable interest in the various types of pluripotent cells in the adult as a source of 'stem' cells that play a role in tissue regeneration. These quiescent lining cells are activated by mechanical or hormonal stimuli to generate a bone-forming front of metabolically functional osteoblasts involved in a modeling or remodeling process to maintain or restructure the matrix.

Bone matrix

The extracellular matrix of bone is composed of two major components: first, the collagenous organic component of predominantly type I collagen, imparting high tensile strength, and second, the inorganic salt hydroxyapatite, imparting high compressive strength. The apatite crystals are deposited onto the collagen and gradually become orientated in a preferred direction with age.[14]

As a composite material, bone matrix is anisotropic and the architecture of the matrix in relation to the osteocytes forms the basic unit of structure, termed the lamella. The architecture of the lamellae can be observed under polarized light microscopy as the collagen is a birefringent material. The architecture of these bone lamellae in different geometrical arrangements forms the basis of the different histological types of bone. Concentric circumferential lamellae form osteons and when these are formed in the original development of the bone they are termed 'primary osteons'. A similar architecture is also seen in the secondary osteons that are formed to repair damage such as micro-cracks or infill porosities within the cortex. Lamellae formed around vascular networks or plexi result in laminar or the less regular plexiform bone often seen in ungulates like the horse (Fig. 7.6). This type of bone allows very rapid increases in cross-sectional area with later consolidation.[2] Lamellar bone can also form circumferential lamella on the entire periosteal and endosteal surfaces of individual bones (Fig. 7.7).

In embryological development and in the early stages of fracture repair a rapidly forming bone with irregular lamellae, coarse collagen fibers and large osteocyte lacunae is seen. This is called 'woven' bone and is rapidly remodeled to the various types of organized lamellar bone, such as primary and secondary osteonal bone, previously termed 'Haversian' bone (Fig. 7.8).

Bone morphology has been related to the mechanical loading requirements of different specific bones. For example,

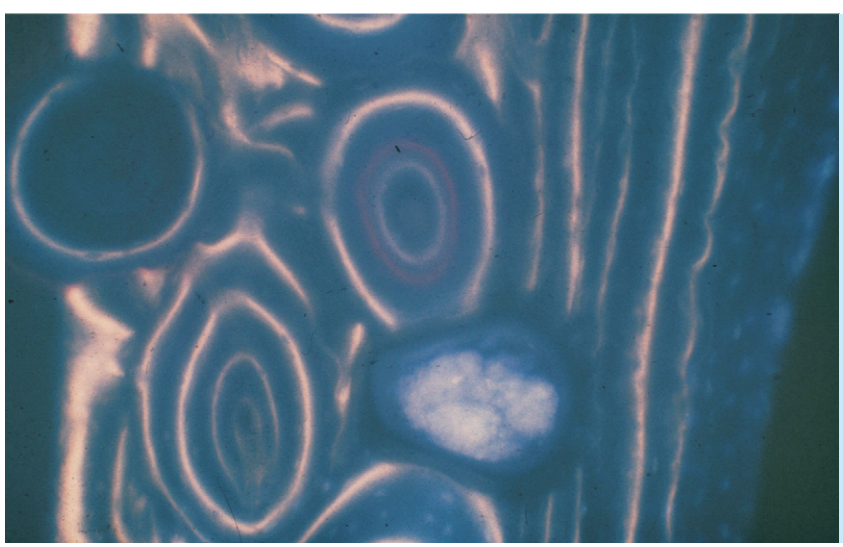


Fig. 7.7
Photomicrograph of a transverse section of cortical bone to show secondary osteons at different stages of formation in the process of remodeling and endosteal circumferential lamellar bone.

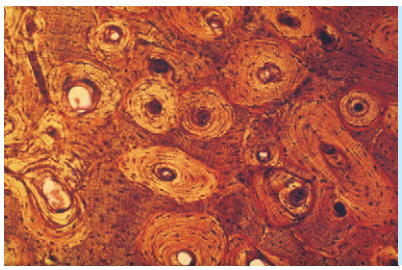


Fig. 7.8
Photomicrograph of a transverse section of highly remodeled secondary osteonal cortical bone.

the orientation of collagen fibers in the cranial and caudal cortices of the radius reflects the mechanical requirements of this bone. Strain gauge studies have shown that this bone is loaded in both compression and bending with principal tensile strains aligned with the long axis of the bone in the cranial cortex and principal compressive strains aligned to the long axis in the caudal cortex.[15] The arrangement of collagen fibers in relation to this pattern of loading has been demonstrated by Riggs et al.[16] This has been supported by a comprehensive analysis of matrix morphology in the equine radius by Mason et al, in which the analysis of primary bone and bone within secondary osteones of the cranial and caudal cortices of the radius were arranged appropriately to optimize for the pattern of functional loading.[17] Mason et al also confirmed a predominant longitudinal arrangement of collagen fibers in the cranial cortex of this bone, to resist the functional tensile strains at this location.[17] Any consistent changes in the magnitude and pattern of loading induce a modeling response in which the bone cell activity will modify the matrix to maintain the optimization of the overall bone architecture in relation to the new prevailing loading conditions. Matrix, and embedded osteocytes, can be removed by osteoclasts and new matrix formed by osteoblasts. This coupled cellular activity allows bone as both a material and structure to be changed in terms of mass and distribution throughout life.

Matrix molecular composition

Bone matrix comprises approximately 65% inorganic mineral, largely hydroxyapatite, and 35% organic material and water.

As with all connective tissue matrices, there is a high proportion of water in the order of 25%, dependent upon type of bone. The remaining matrix is predominantly type I collagen together with a small proportion of minor collagens and non-collagenous proteins, including proteoglycans and glycoproteins. Some growth factors such as TGF-β and bone morphogenetic proteins are also present in abundance within bone matrix; these peptides act as biological signaling molecules for mitogenesis and differentiation of bone-forming cells. They are released with osteoclastic resorption of the matrix and can act in autocrine and paracrine manner on the osteoblasts.

Bone matrix components include osteonectin, bone sialoprotein, osteopontin and osteocalcin, a protein that can be used in blood assays together with collagen propeptides that have been investigated as a non-invasive method to monitor bone cell activity during growth, development and training of horses.[18,19]

Material properties

The material properties of bone matrix vary and are largely related to the degree of mineralization, particularly with respect to modulus of elasticity. Bone such as the tympanic bulla, with a very high mineral volume fraction and density, has a high modulus eminently suitable for conduction of sound, whereas deer antler is low in mineral content and has a low modulus, again appropriate to avoid fracture in its role in fighting. Bone matrix is an anisotropic brittle elastic material and the elastic modulus is related to the level of mineralization. The influence of mineralization on material properties has also been evaluated during growth and maturation. In immature horses the level of mineralization is low and increases to a higher level with maturation to adult equine bone. With development and increased mineralization there is a significant correlation with changes in mechanical properties; it is suggested that such changes may be measured non-invasively using ultrasound transmission systems. This would provide the potential to monitor material properties of bone during growth and possibly during training.[20]

The material properties and morphology of specific bones determine the structural properties of the individual skeletal elements. Thus changes in the mechanical competence of bones as structures may be a consequence of either changes in the material properties of the constituent tissue or an alteration in the structural distribution of the material in relation to the magnitude and distribution of the loads applied at a particular time. The dynamic nature of bone tissue provides the ability to optimize structure in response to changes in matrix material properties.

Mechanical characteristics

Bone tissue as a material contributes to the mechanical characteristics of the individual skeletal elements. The architectural arrangement of the material is predominantly related to the general functional requirements of the particular skeletal elements. In the long bones the diaphysis is tubular to resist the functional loading patterns of bending and torsion. In engineering terms these loading patterns can be sustained with maximum strength and minimal material by tubular structures with the material distributed at a distance from the neutral axis. For example, if a solid beam is subjected to bending, one surface will experience tensile stresses and the opposite surface compression stresses. At some plane between

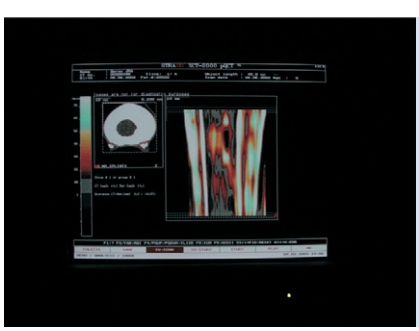


Fig. 7.9
Data from a pqCT scan of an equine MC3 bone to show the variation in cortical thickness and the presence of the medullary cavity as the region of the 'neutral axis'.

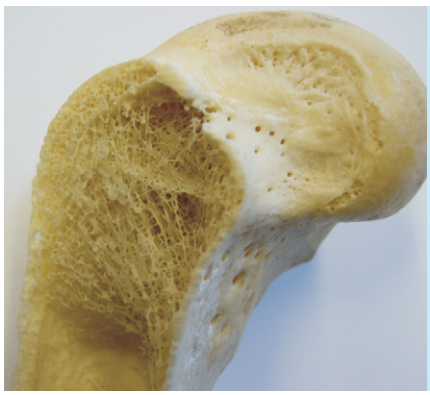


Fig. 7.10
Photograph of the metaphysis and epiphysis of a long bone sectioned longitudinally to show the cortical shell supported by internal cancellous spongy bone.

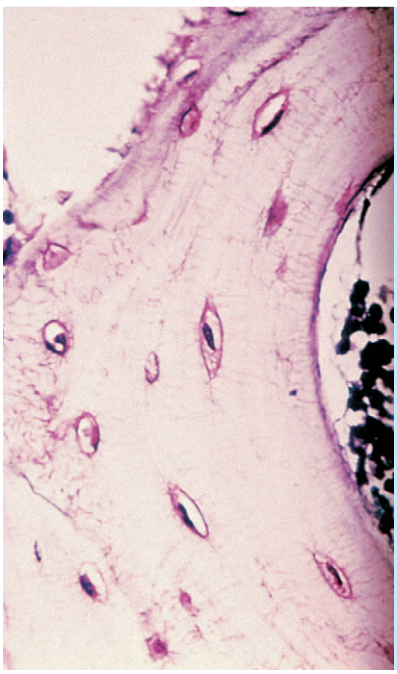


Fig. 7.11
Photomicrograph of histological section of a bone trabeculum to show lamellar bone structure.

these two surfaces there will be neither tensile nor compressive stresses (the neutral axis), thus no material is required in this region. When bone tissue organizes into the components of the skeleton, its structure is based on optimization of energetic efficiency. Thus to minimize the mass of material, bone is not present in the medullary cavity (Fig. 7.9). The relative thickness of the cortices also reflects the loading patterns of a particular bone. These changes may be measured using radiographic and ultrasound transmission techniques.[21]

At the extremities of the long bones and in short bones the functional loads are predominantly those of axial compression. This is reflected in a different architecture with a thin cortical shell supported by internal cancellous bone (Fig. 7.10). The plates and rods of bone are termed trabecula and formed of aligned bone lamellae (Fig. 7.11). These rods and plates are not randomly arranged but strategically placed in relation to the trajectories of principal compressive and tensile stresses. In the cancellous bone of the epiphyses, underlying the articular surfaces of the synovial joints, the trabecula are orthogonal (perpendicular) to the articular surface. This architecture of the plates and rods again allows the use of minimal material to provide maximum strength and minimize energy requirements for locomotion. In short bones that are loaded predominantly in compression, the internal structure is of strategically arranged bony trabecula. Some short bones, such as the calcaneus, are subjected to bending moments. The internal cancellous architecture reflects this with arcades of trabecular bone arranged orthogonally to resist the principal compressive and tensile stresses. Nature reflects the calculated stress-related bracing seen in some engineering structures such as the Fairbairn crane in which the loading and principal stresses resemble those of the femur (Fig. 7.12).

The increased diameter of the bones in the regions of the epiphyses and the presence of subchondral trabecular bone act both to reduce stresses on the articular cartilage and provide a compliant structure to absorb impact loads. Thus any changes in the compliance of the trabecular bone will influence the loading of the overlying cartilage and can indirectly induce changes in the articular cartilage.

Bone as a structure/organ

Adult bone form is determined by a combination of genetic and environmental influences. Fell demonstrated that certain anatomic features of the developing skeleton are formed as a consequence of inherent genetic control whereas others require a functional loading to form.[22] An elegant study by Chalmers investigated the development of a mouse femur implanted into the spleen when at the cartilage anlage (precursor) stage of development.[23] This cartilaginous bone precursor developed into a bone with the basic form of the femur but lacked the architectural refinements seen in the normal adult mouse femur. The refinements, such as a waisted femoral neck, cortical thickness and trabecular architecture, are induced as a consequence of functional loading and are determined by the prevailing loading conditions (Fig. 7.13).

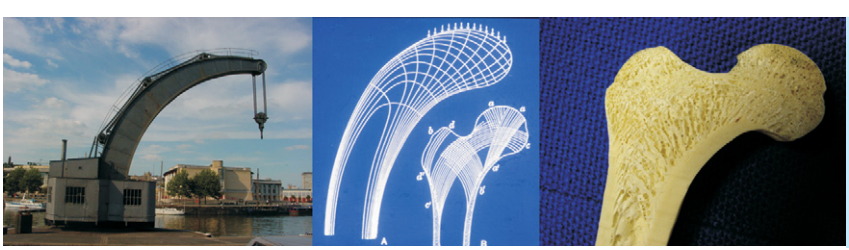


Fig. 7.12
Comparison of the structure and stress distribution of the Fairbairn crane and proximal femur.

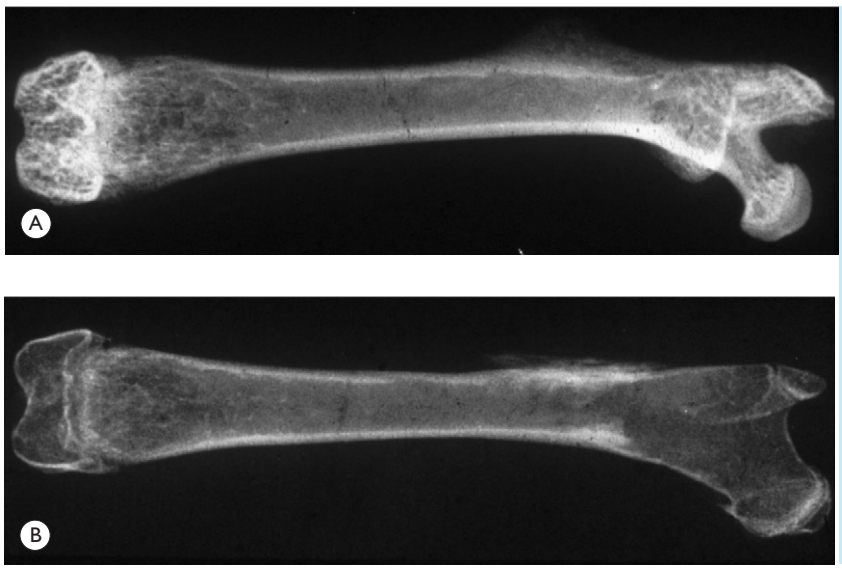


Fig. 7.13
Radiographs of mouse femora, showing the adaptations to functional environment (A) from the basic genetic template (B). Adapted from Chalmers et al 1962.

There is a dynamic interaction between the loads imposed on the skeleton and the morphology of the bones at any point in time throughout life. It is therefore important to appreciate these interactions in order to condition the skeleton for the demands of athletic performance and to understand the modes and mechanisms of failure.

Skeletal development

Growth

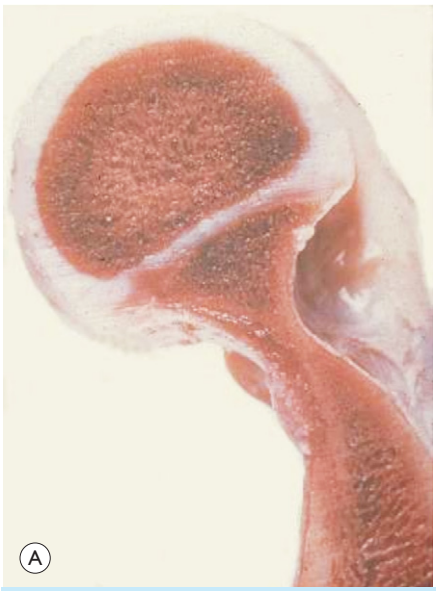
Ossification

The skeleton is developed both pre- and postnatally. The majority of the bones of the skeleton, particularly the appendicular skeleton, are preformed as miniature replicas in hyaline cartilage. This has the advantage of enabling rapid three-dimensional growth. The material and structural properties of hyaline cartilage are adequate to support the low level of loading prevailing in utero. In preparation for the postnatal changes in loading with gravitational and muscular forces, a more appropriate material must replace the hyaline cartilage. This is accomplished by vascular invasion, calcification and removal of cartilage and replacement with lamellar bone. This process is endochondral ossification. In a few sites of the skeleton, for instance the bones of the vault of the skull, bone is formed by direct ossification of a fibrous type I collagen scaffold. This process is intramembranous ossification.

The bones associated with locomotion are formed by both endochondral and intramembranous ossification. This allows simultaneous longitudinal and circumferential growth of the bones.

Endochondral ossification The initial vascular invasion of the cartilage replica occurs in the midshaft. In this region the chondrocytes within the lacunae undergo hypertrophy and the extracellular matrix becomes calcified. It is now thought that the endothelial cell invasion occurs in the non-calcified territorial and pericellular matrices following cell death[24] and that cell death in the growth plate occurs through an apoptotic pathway.[25] The calcified cartilaginous matrix is then removed by chondroclasts derived from vascular cells and replaced by woven and then lamellar bone. These spicules of bone become strategically organized and form the cancellous bone structure of the metaphysis, termed the primary spongiosa. In human growth this has been suggested by Byers et al as a critical component of the growth process and the development of the mineralization of the primary spongiosa may be of importance in relation to bone-altering disease in later life.[26] These authors also suggest that the secondary spongiosa retains a constant bone mineral volume throughout development. Thus in the developing horse the mechanical loading from exercise during growth and maturation could affect the level of mineralization of the primary spongiosa.

Simultaneously with the longitudinal growth, the fibrous layer covering the replica bone, the perichondrium, initiates ossification of the fibrous tissue and forms a cuff of bone which develops to form cortices of the tubular diaphysis. This process forms the 'primary' ossification center and is followed by further vascular invasion at one or both ends of the developing bone to form secondary ossification centers. The secondary ossification centers are separated from the primary center by plates of hyaline cartilage known as the growth plate or physis. This process allows for both circumferential and longitudinal growth and enlargement of the bone. The longitudinal growth occurs by utilizing the interstitial growth potential of hyaline cartilage in the proliferative zone of the growth plate. The physis has a distinct structural pattern relating to specific functional activities. The epiphyseal side of the plate is characterized by a resting zone of randomly arranged cells within an extracellular matrix. These cells give rise to the zone of proliferation in which the chondrocyte population is actively dividing. These cells then align into palisades extending toward the metaphysis, with the cells closest to the metaphysis showing hypertrophy of the lacunae. In this zone of hypertrophy the matrix becomes



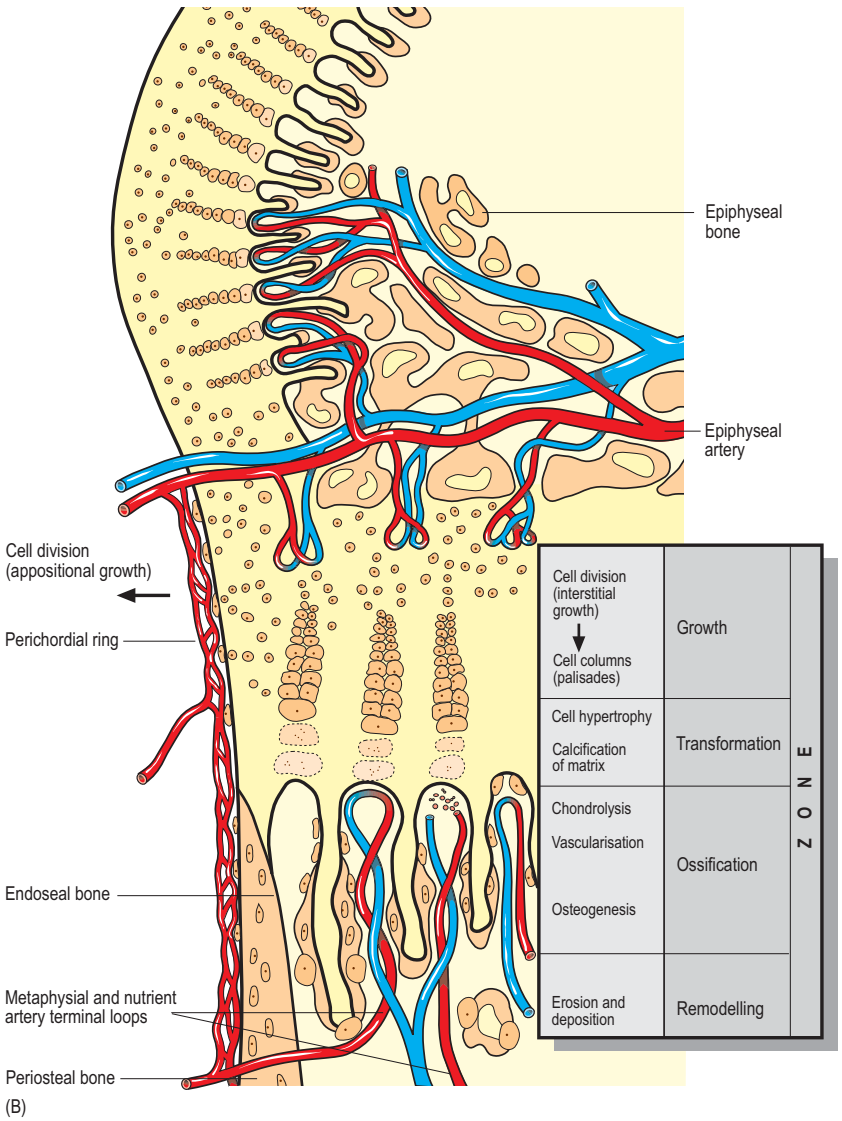


Fig. 7.14
(A) The growing spheroid and discoid physes in an immature growing long bone sectioned longitudinally. (B) Diagram to show the arrangement of palisades in the two physes.

calcified and is removed by chondroclasts. Osteoblasts then deposit woven bone on the calcified cartilage scaffold. This tissue is rapidly remodeled to lamellar bone and forms the trabecular rods and plates of the spongiosa that support the metaphyseal cortex. The width of the physis is increased by appositional growth from the overlying perichondrium. The physis can be described as a discoid physis contributing to the increase in longitudinal growth and width of the metaphysis. The epiphysis also acts as a spheroid physis to increase the size of the epiphysis by radial growth. The early articular cartilage is thick and arranged in a similar pattern to the physeal plate with the proliferating chondrocytes close to the articular surface and a radial arrangement of palisades toward the center of the epiphysis (Fig. 7.14). The secondary ossification centers and spheroid physes form the cancellous bone that supports the articular cartilage. Abnormalities in the process of ossification can lead to specific orthopedic conditions such as angular deviations of the limbs and osteochondral dysplasias.

The limited thickness of the physis in normal animals allows growth without excessive deformation of the cartilage which would result in angular deformations of the growing bone. In some conditions where ossification is inhibited and the cartilaginous component of the physis increases in thickness, limb deformities occur during growth. A classic example is dietary rickets. Rapid growth can also result in angular deformities of the long bones.

Intramembranous ossification As the bones increase in length there is also an increase in overall width of the metaphysis and diaphysis of the bone, accomplished by appositional bone growth on the periosteal surface. In the developing bone a cuff of periosteal bone is formed. The periosteum comprises an outer fibrous layer and an inner osteogenic 'cambium' layer. In this osteogenic layer cells differentiate into osteoblasts which deposit osteoid directly onto collagen type I fibers. This process ultimately forms lamellar bone. In ungulates the type of lamellar bone formed is laminar or plexiform bone. This primary vascular bone is capable of a rapid increase in cross-sectional area. In this type of bone a rapid appositional growth occurs with subsequent infilling of lamellae within the laminae of the vascular network.[27] Thus bone growth occurs to the age of skeletal maturity by means of these two processes.

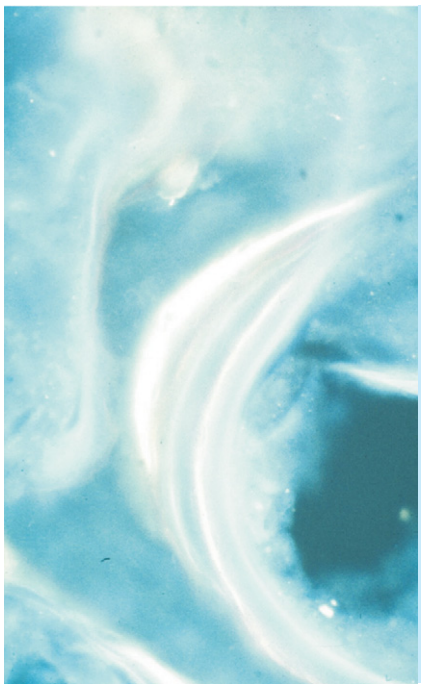


Fig. 7.15
Photomicrograph of a fluorochrome-labeled section of trabecular bone, showing apposition on one surface indicating a modeling change in architecture.

Modeling and remodeling

During the processes of both bone growth and adaptation to changes in loading, the shape or architecture of the bone is changed by cellular activity to remove and form bone. Unlike cartilage, bone cannot increase in size by interstitial growth; only by these processes of removal and formation of bone surfaces can the relative proportions of curvatures and the positions of tuberosities be maintained. Changes in shape result from removal and formation of bone at the same time but at different locations; this process is termed modeling and allows changes in three-dimensional tissue space (Fig. 7.15).

Modeling is determined both by growth and by mechanical loading. As a long bone increases in length the flared metaphysis is narrowed into the diaphysis by bone resorption on the periosteal surface and bone formation on the endosteal surface. In the diaphyseal region increase in bone width during growth occurs by periosteal appositional growth and endosteal bone resorption (Fig. 7.16).

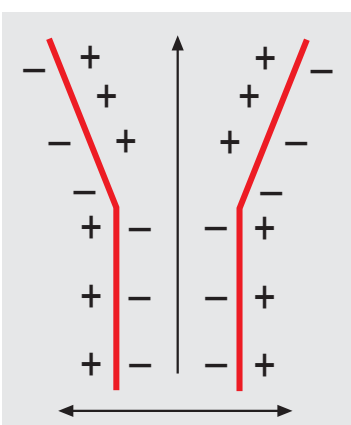


Fig. 7.16
Diagram of modeling changes at metaphysis and diaphysis during growth.

Within the bone matrix microdamage can occur as a consequence of repeated loading cycles. Repetitive loading in many inert materials results in accumulation of microdamage and ultimately, the gross fracture of the structure. Although bone is a structural material it is living and there are cell-to-cell and cell-to-matrix interactions. Thus changes in matrix can initiate cellular responses to maintain and adjust the matrix. Microdamage is a stimulus to induce osteoclastic resorption of the damaged matrix followed by deposition of lamellar bone by osteoblasts. This dynamic repair process occurs throughout life and during normal functional loading of the skeleton. It is termed remodeling and involves the resorption and removal of bone at the same site but at different points in time (Fig. 7.7). Bone that is formed in remodeling is called secondary bone. These secondary osteons continue to increase in level of mineralization for several weeks after formation of the osteon has been completed. The secondary bone is not as strong as primary bone but is stronger than the damaged matrix. The remodeling process results in the formation of 'secondary osteons'. The initial resorption is effected by a cutting cone of osteoclasts traveling longitudinally within the cortical bone, followed by lining osteoblasts that secrete the new circumferential lamellar bone with entrapment of osteoblasts within the matrix to become the osteocytes within the circumferential lamellae (Fig. 7.17). A glycoprotein layer is formed between the newly formed secondary osteon and the adjacent bone tissue which forms the cement line.

Bones as structures

Individual bones have specific morphologic features related to their functional contribution to the skeleton as a whole. The types of bones can be divided broadly into long bones, such as the femur, humerus, radius, tibia and the metacarpal/tarsal bones, short bones, such as the carpal, tarsal and distal phalangeal bones, and flat bones, such as the scapula, and some bones of the skull and pelvis. In addition, some bones are not directly involved in the structural support of the body but contribute to the mechanical arrangements of tendons in facilitating the change in direction of tensile forces. These bones, often associated with tendons, are the sesamoid bones, of which the patella, proximal and distal (navicular) sesamoids are examples.

The long bones can be divided into regions: the epiphyses, metaphyses and diaphysis. These regions show different morphologic arrangements of the bone tissue. The epiphyseal and metaphyseal regions comprise a thin cortical shell of compact bone supported by internal cancellous bone, sometimes termed spongy or trabecular bone. This internal arrangement of bone tissue comprises plates and rods of bone with spaces or cancelli filled with marrow or fat. The bone tissue in these areas often shows a definite pattern of trabecular arcades. This arrangement of internal spongy bone is also seen in the short bones. The geometric pattern is particularly noticeable on radiographs and especially those of the proximal femur and calcaneus (Fig. 7.18).

The internal structure of spongy bone has been of interest to scientists, engineers and surgeons since the time of Galileo. In the 1890s comparisons were made between the pattern of

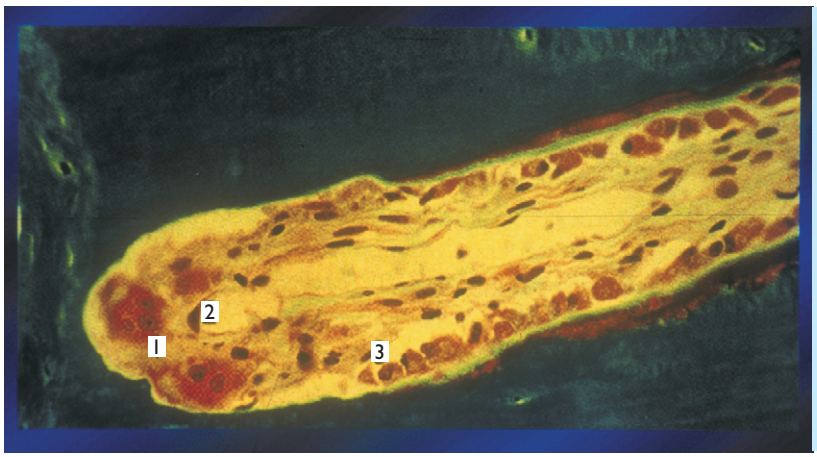


Fig. 7.17
A 'cutting cone' of osteoclasts (1) followed by a blood capillary (2) and osteoblasts (3) infilling with circumferential lamellae to form a secondary osteon.

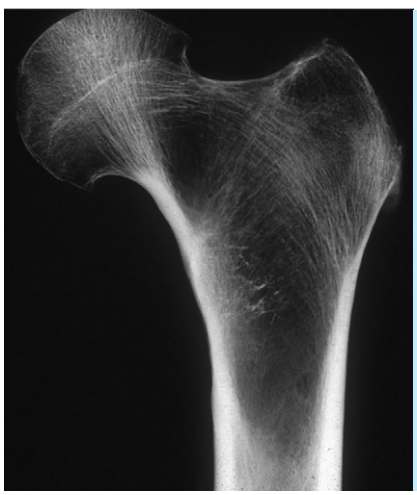


Fig. 7.18
Radiograph of the proximal human femur to show trabecular arcades.

cancellous bone and analysis of stress trajectories in engineering structures. The proximal region of the femur with the femoral neck and head is loaded in a manner very similar to that in engineering structures like the Fairbairn crane and the trabecular architecture reflects the lines of principal tensile and compressive stresses calculated for these structures (see Fig. 7.12).

Recent developments in technology have allowed the distribution of principal strains to be measured in the living skeleton and the data from such studies have provided supporting evidence that these bone trabeculae are strategically placed to optimize the strength of the structure with minimal mass of tissue. In animals this is important to reduce the energetic cost of locomotion. The thickness and structural density of trabecular bone also reflect the magnitude of the loads taken in that region of the bone. This has been shown in training studies; for example, the trabeculae in the dorsal region of the third and radial carpal bones are thicker than those in the more palmar regions in horses that have been trained for peak athletic performance. These observations can be used in diagnosis of bony changes related to mechanical loading of the skeleton. The site-specific changes, such as those in the carpal bones, are often found to be related to predilection sites of skeletal injury and pathology so knowledge of these interactions can enhance diagnostic and prognostic clinical skills.

The arrangement of bone tissue in the diaphyseal region of long bones is markedly different. This region is similar to a tube, hence the term tubular bone. The wall of the tube comprises compact cortical bone, of differing thickness, and a medullary cavity containing blood vessels, marrow and fat. This arrangement of bone reflects a different mechanical loading pattern; whereas in the short bones the loads are predominantly compressive loads, in the long bones spanned by tendons and ligaments there are large bending and torsional moments in addition to compressive loading.

Again, the biologic drive is to reduce the energetic costs of locomotion, whilst ensuring adequate structural strength to avoid failure during physiologic loading levels. In engineering design these requirements to provide maximum strength in bending and torsion using a minimal mass of material are met by a wide-diameter, thin-walled tube. This essentially places the material at the greatest distance from the neutral axis, where there are neither tensile nor compressive stresses. In long bones the medullary cavity represents the average neutral axis relative to the loading pattern of the bone. Thus strength is maximized and mass minimized to reduce the energy costs associated with moving the limb. In animals evolved for high-speed locomotion there is a high biologic drive to reduce energy costs. In engineering structures the material type, mass and distribution all contribute to the ability of the structure to resist functional loads. However, to allow for occasional overload a safety margin is normally incorporated into the design, such that the structure will not fail as a consequence of occasional overload. Studies have shown that the skeleton also incorporates a safety margin although this is not uniform in relation to skeletal location. The neck of the femur in humans is known to be able to withstand about five times bodyweight. The disadvantage of a safety margin is the additional mass of material. This becomes significant in the more distal regions of the limb since additional mass increases the momentum of the swinging limb and this in turn would result in a significantly increased energy requirement in decelerating and accelerating the limb, particularly in high-speed equine athletes.

Currey, analyzing data from Vaughan & Mason, showed that a higher incidence of fractures during racing occurred in the more distal bones of the limb and hypothesized that this could be explained by a lower safety margin in the more distal limb bones.[3]

Although the diaphysis of long bones is essentially tubular, the distribution of bone in terms of cortical thickness may be non-uniform around the circumference of the bone. This reflects different levels of resistance to bending in different planes and the associated distribution of bone mass.

Factors controlling shape and size

Genetic influences

Both between species and within species, the variation in the specific geometry of individual bones is a consequence of two main factors. First, a genetic component that will control a basic bone mass. Second, a response to prevailing mechanical conditions which will modify the basic genetic pattern in relation to both the magnitude and the distribution of loads applied to the particular bone.

Disuse will result in a tendency toward the genetic basic bone mass. Abnormal loading will induce a concomitant abnormality in the size and shape of the bone. Chalmers in 1962 demonstrated these controling factors by transplantation of the cartilage precursor of the mouse femur to the spleen, where it developed with adequate blood supply but devoid of mechanical input.[23] Although the basic shape of a femur could be recognized, this bone lacked the refinements in both mass and architecture exhibited by the normal functionally located bone in littermates (see Fig. 7.13). Further evidence that certain anatomic features of specific bones were genetically predetermined and others were formed as a consequence of local stimuli was provided by Fell using isolated limb buds from developing embryos in organ culture.[22] Genetic modification of a basic anatomic skeletal pattern is often seen in relation to attaining specific conformation for either visual or functional requirements. Even within specific breeds of horse certain genetic strains are evident and linked to differences in bone mass and architecture. Other factors influenced by selective breeding, which could be described as genetic modification, such as muscle mass, may have an indirect influence on bone mass as a consequence of increased levels of mechanical loading of the bones. As both a tissue and a structure, bone has the property of functional adaptation.

Environmental influences

Other factors such as nutrition and hormonal environment may also influence the ability of a bone to attain the full genetic potential. However, one of the most potent environmental influences on bone mass and architecture is the prevailing mechanical environment.

Functional loading of bone refines the inherent genetic form. The levels of mechanical input can vary throughout life with an associated response in terms of skeletal adaptation.

Both during growth and maturation and in the skeletally mature adult, bone responds to mechanical loading. The relationship of the pathophysiology of functional adaptation to training and conditioning regimens in general and in the horse in particular is important in maximizing performance and minimizing skeletal injury. In determining the aspects of functional loading that influence the bone cell populations and consequently are important in controling the architecture of the skeleton, it was essential to be able to quantify the functional environment of the skeleton.

Although techniques were available to measure strains on cadaveric bone, using photoelastic coatings, stress coat and electronic strain gauges, it had not been possible to quantify the effects of loads on the living skeleton until the cyanoacrylate tissue adhesives became available. In the early 1970s Lanyon & Smith[28] and van Cochran[29] made the first measurements of strain in the living skeleton. The ability to bond foil rosette strain gauges to living bone allowed both the magnitude and distribution of the principal strains on the surfaces of a number of bones to be measured during activities such as locomotion. From these measurements it was possible to determine the loading patterns of different specific bones. For example, the radius in quadrupeds is loaded in bending with principal tensile strain aligned to the long axis of the bone on the cranial cortex and principal compressive strain aligned to the long axis of the bone on the caudal cortex,[16] whereas the tibia showed a significant component of torsional loading.[30] The physiologic loading pattern of these long bones can be used in determining the appropriate fixation methods to treat fractures in these bones.

Strain distributions on the surface of bones with defined internal trabecular arcades again provide confirmatory data to show the strategic alignment of the trabeculae of spongy bone with the directions of principal tensile and compressive strains.[31] This technique increased the understanding of the response of bone to changes in mechanical demands, a mechanism called functional adaptation.

Functional adaptation of bone

General principles

The bony skeleton provides structural support for the body throughout life and also enables locomotion by virtue of the linked skeletal elements forming a system of rigid levers upon which forces can be exerted by muscles through tendons and ligaments. Articulations between the individual bones allow energetically efficient movement. The basic genetically determined bone mass is optimized for energetic efficiency and to accommodate the loads imposed. Thus throughout life as the activities change, the process of functional adaptation enables the appropriate adjustments to be made to the mass and architecture of the skeleton. The biologic signals that induce bone cell activity and control the adaptive process are

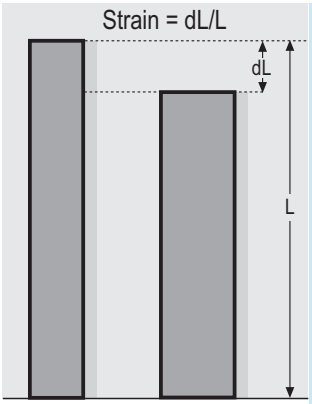


Fig. 7.19
Diagram to show deformation or 'strain'.

related to the deformation of the tissue as a consequence of the loads applied by muscles and gravity. Deformation is termed 'strain' and is the change in length in relation to the original length (Fig. 7.19). Although the response of bone to mechanical loading has been known for some time, the ability to quantify imposed changes in mechanical environment of the skeleton and relate these to the consequent biologic response of the bone has only been possible using the technique of in vivo strain measurement.

Dynamic strain similarity

By applying strain gauges to the living skeleton of a variety of species, from fish through reptiles, birds and mammals, including the horse and human, the level of bone deformation during peak physiologic activity has been shown to be remarkably similar.[32] Thus it was hypothesized that bone had evolved in this wide range of species to optimize to a threshold level of deformation, irrespective of histological structure. A simple strain-controlled feedback loop was proposed. If an increase in loading resulted in an elevated strain above the threshold value, this triggered the bone cell populations to synthesize bone matrix to increase the mass of bone and thus for the new loading conditions to reduce the increased levels of deformation back to the threshold values. In the event of a decrease in loading and consequent level of deformation, the bone cells would respond by activating a net bone resorption and decrease bone mass.

Optimization of mass and architecture (Wolff's Concepts)

In the event of a persistent change in the normal pattern of loading, the bone strain patterns would be altered and this persistent change in strain distribution would initiate a redistribution of bone through a modeling response to alter the architecture of the bone as a structure. Such changes may involve structural optimization by changes in both the distribution and mass of bone.

Early studies in which the strain on the skeleton was increased and an adaptive response was evoked supported the theory of a strain control feedback mechanism. The characteristics of the mechanical osteogenic stimulus were elucidated by a series of studies in which bones were subjected to known strain characteristics and the consequent osteogenic response was measured. These studies were of two basic types: those in which a defined mechanical regimen was imposed on a bone following surgical intervention and those in which an exercise regimen was applied to the intact skeleton. Increased loading of parts of the skeleton induced by removal of adjacent bone or by attachment of loading devices to isolated bones allowed the imposition of a specific strain environment. The early studies inducing increased loading by removal of an adjacent bone and consequent overloading of the remaining ones by normal locomotion demonstrated an adaptive response to increase the overall cross-sectional area and thus restore the strain levels to the functional optimal values, thus supporting one of Wolff's hypotheses.[33,34]

Osteogenic mechanical stimuli

The nature of the mechanical stimulus that elicited an osteogenic response was investigated by a more controlled study of specific mechanical variables and their influence on adjustment of bone mass and architecture.

Such studies involved the use of implants attached to the bone and used to impose controlled mechanical stimulation. These experiments elucidated some of the osteogenic aspects of the strain environment. During normal strain distributions, such as those occurring during walking, the level of osteogenic response, in terms of increased cross-sectional area of bone, to imposed strains was found to show a high correlation with the rate of bone deformation.[35] This suggests that training using a normal type of exercise requires a high loading rate to elicit an osteogenic response. A more refined method of studying the exact nature of mechanical signals that stimulate bone formations was developed by using isolated segments of bone. Ideally an organ culture might be used for such studies but culture of bone is difficult in terms of culturing a significant mass of true ossified tissue and the absence of the hormonal regulation and its interaction with mechanical cues precludes such models.

Using isolated bone models in vivo, it was possible to define in a more specific manner the strain characteristics that induced bone formation.[36] The effect of numbers of cycles of loading applied on a daily basis was investigated, together with the effect of magnitude of the imposed strain. It was shown that there was a 'dose–response' effect with strains below the normal physiologic threshold inducing bone resorption and a consequent decrease in cross-sectional area and those above the physiologic threshold showing an increase related to strain magnitude. From these experimental studies a number of mathematical models were derived in which it appeared that there was a window of strain magnitude that retained bone mass with neither resorption nor formation. This was termed the 'lazy zone'.[37] Strain magnitudes outside this zone induced either bone resorption or bone for-

mation. Interestingly, Rubin & Lanyon investigated the relationship between the number of loading cycles imposed on a daily basis and the resultant effect on bone mass in terms of bone mineral content and cross-sectional area.[36] This work showed that a maximal effect on bone mass could be attained with only 36 cycles of loading at 0.5 Hz each day. Any additional cyclical loading did not attain a greater effect on bone mineral density or cross-sectional area. Bone mass was shown to be maintained with as few as four loading cycles per day, whereas complete cessation of loading resulted in a decrease in bone, predominantly by endosteal resorption leading to a reduced cortical thickness, together with some increase in cortical porosity. This study suggests that short periods of osteogenic cyclical deformation can induce a maximal adaptive response. In terms of conditioning bone in equine athletes this might be interpreted as a short period of daily trotting. The stimulus appears to require cyclical deformation as the application of constant load did not induce bone adaptation.[38]

Hillam & Skerry developed a non-invasive method of loading the rat forearm and used this model to demonstrate that mechanical loading could modify the normal modeling patterns seen during growth.[39] A short period of cyclical loading changed a bone resorption surface to a bone-forming surface. The applied loading induced an aberrant strain distribution. This model was also used by Mason et al in determining the gene activation patterns associated with mechanical loading and putative signaling molecules in the transduction and integration of mechanically induced bone remodeling.[40] Forwood & Turner used a similar approach by applying a bending moment to the rat tibia and confirmed the response to high strain rate cyclical deformation in a mammalian model. This suggests the principles can be extrapolated to other species, including the horse.[41]

Thus the principles of these findings have implications for the training of young horses using a diverse exercise regimen. Perhaps on the basis of this evidence, horses that are used for competitive events that involve movements outside the natural range on a frequent basis should be introduced to such exercises at an early age when the architecture of the skeleton could be influenced to adapt to these loading demands and thus resist damage and failure in adulthood. Events such as jumping, dressage, trotting, racing and pacing may be candidates for such practice. However, any training regimens must be introduced over an adequate time period with a graded increase to accommodate adaptation and avoid damage.

Rate of adaptation

Adaptation to loading in bone can be initiated by short periods of cyclical loading. Therefore, to prolong this type of exercise or to introduce long periods of such exercise too rapidly, particularly on a hard surface, may lead to induction of microcracks and ultimately the gross fracture of the bone. Damage even to the delicate internal architecture of the trabecular bone with subsequent stiffening, particularly of subchondral regions, may reduce the absorption of high impact loads and inflict damage upon the overlying articular cartilage (Fig. 7.20).[42] Mechanical factors may thus initiate a cascade of events leading to degenerative joint disease. The joint must be considered as an organ and changes to one component tissue or structure will impact on the whole joint.[43] Interestingly, Chen et al observed differences in heel strike transients between races with different incidence of degenerative joint disease so it is possible that conformation may influence the transmission of impact transients in equine limbs and predispose to degenerative joint disease. This localized adaptive hypertrophy of trabecular bone can be seen following imposed exercise regimens, for instance the dorsal regions of the third and radial carpal bones.[45] Furthermore, with an osteogenic exercise regimen given for only a short period each day, these localized bone changes occur extremely rapidly.[46] This localized change in loading can induce a change in both bone and cartilage, the osteochondral unit. Increased exercise in the adult horse results in a thickening of the trabecula of the subchondral bone, a thickening of the subchondral plate and a thickening of both the calcified and hyaline layers of the overlying articular cartilage.[47] Experimental studies have also shown the sensitivity of cancellous bone to changes in mechanical loading and these data can be indirectly related to training methods in the horse.[48]

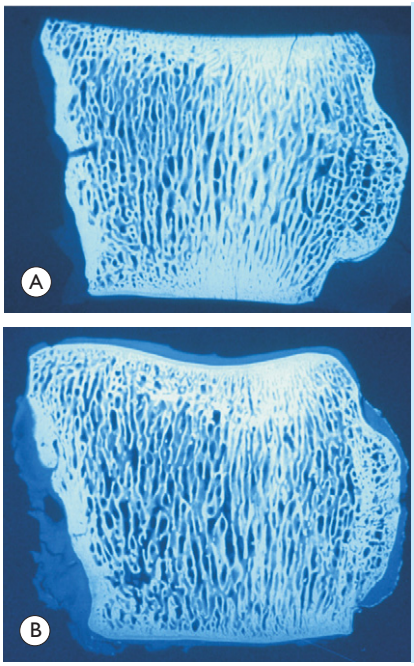


Fig. 7.20 Photomicroradiograph to show localized adaptive hypertrophy of trabecular and subchondral bone to imposed exercise (A) compared to control (B).

These morphological changes result in a change to the mechanical properties of the microstructure which can be measured by indentation techniques[49] and micromechanical testing of single trabeculae.[50] The adaptation within a bone in relation to a very specific pathway of load transmission through the bones of the skeleton is seen particularly well in the carpal bones where significant differences are found between the dorsal and palmar regions of these bones. Long-term loading with associated stiffening of the bone in the dorsal region may relate to the common occurrence of cartilage fibrillation and breakdown in this region.

Microdamage

Horses that are given this type of training regimen, especially if the training is imposed over a short period of time, show the clinical signs of 'bucked shins'. If the training is based upon a structured increase in duration of short periods of exercise that induces high bone strain, the bone will adapt and the physiologic adaptation will condition the bone for athletic exercise rather than a pathophysiologic response leading to 'bucked shins'. This response is also seen in racing greyhounds and can lead to overt fractures.

Microcracks

Accumulation of microcracking within the bone matrix results in a remodeling response in which the secondary bone has inferior properties to primary bone. Crack formation is seen as a fractal pattern of matrix damage (Fig. 7.21). Microcracks have been demonstrated in several species of athletic individuals such as the horse[51,52] and the racing greyhound.[53] Cracks can be observed by bulk staining the bone prior to histological sectioning in order to confirm that the cracks are not processing artefacts. The cracks can be seen as stained defects within the matrix (Fig. 7.21). When the level of magnification is increased these defects in the bone matrix can be seen to continue at an ultrastructural level (Fig. 7.22). This damage to bone matrix through which the delicate processes of the osteocytes pass can potentially alter the interaction between cell and matrix and cell-to-cell communication. Processes such as generation of streaming potentials by movement of ionic fluid through the macro-, micro- and nanoporosities of bone will be altered. These changes may be the cause of the known response to microdamage such as apoptosis and osteonal remodeling. Experimental studies using the non-invasively loaded rat

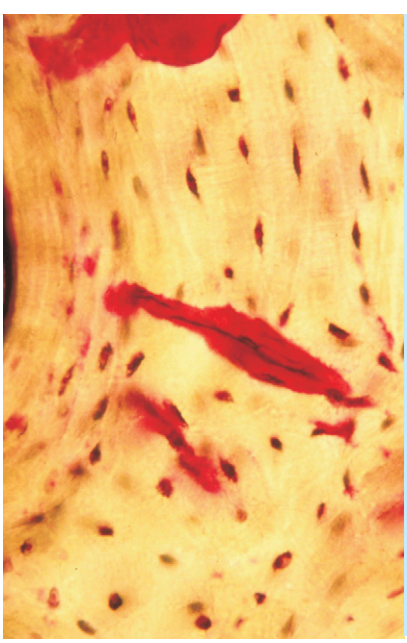


Fig. 7.21 Photomicrograph of a section of cortical bone stained to show a microcrack within the matrix.

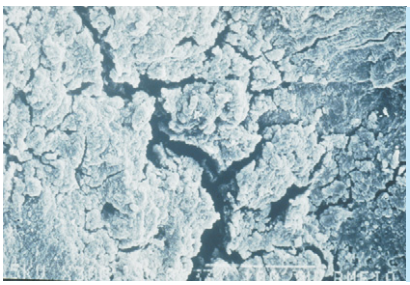


Fig. 7.22 Scanning electron micrograph of a microcrack in bone matrix, showing the fractal pattern of damage.

antebrachium have demonstrated that a rapid application of osteogenic cyclical loading will lead to a change in structural stiffness, indicating a plastic postyield deformation of the bone. The bone will fracture if such loading is continued. However, if bones treated in this way are examined histologically a short time after loading has stopped, an increased porosity is seen as osteoclastic cutting cones target the intracortical damage. A predominance of secondary osteons is found on examination after a longer period of time.

Once primary bone has been remodeled the bone type has been permanently changed. These changes, seen in the experimental model used by Bentolila et al, are closely related to those seen in studies on the induction of sore/bucked shins using a high volume of high strain rate exercise.[54] The effect on subsequent adaptation and failure of highly remodeled bones compared to those in which a gradual adaptation of primary bone has been induced is not really known. Epidemiological studies on race track fractures and relation to training methods are few. One such study by Wood et al (personal communication) has shown that certain types of training regimens are associated with a higher odds risk of fatal failure related to commencement of training at an earlier age. Short bursts of high-speed training in the months before racing reduces the fracture risk (Parkin personal communication). This appears to agree with marker data showing increased bone formation with short periods of fast work.[55] Also Boston & Nunamaker[56] report the advantages of short-distance breezing rather than long-distance gallops in reducing 'bucked shins'.

Osteocyte apoptosis

In addition to the overt fracture of the matrix at the ultrastructural to gross level, there is an effect of this type of loading-induced damage on the cellular component of the bone tissue. Osteocytic apoptosis rates are modified and some effects are also seen on gene expression.[57] Interestingly, estrogen treatment also modulates osteocyte apoptosis.[58] Recent observations by Ehrlich et al that mechanical cues to bone cells are mediated through the estrogen receptor may explain this commonly observed response.[59]

Remodeling

The consequence of exercise-mediated microdamage through a rapid imposition of cyclical mechanical loading is seen either as

overt fracture or, more often, as an increase in formation of secondary osteons to limit crack propagation and replace damaged matrix. However, secondary bone has been shown to be inferior in terms of material properties and may compromise mechanical properties of the bone as a structure.

Thus the avoidance of undue secondary osteon formation may prevent the reduction of the mechanical properties of the overall bone structure. Controlled osteogenic exercise during training would induce a more gradual adaptive response and increase the bone mass with minimal damage of the matrix, thus preserving the mechanical properties of the skeletal structure and reducing the risk of catastrophic failure. Training regimens that appear to optimize bone adaptation without matrix damage comprise short periods of high-intensity exercise.

In physiologic loading exercise at a high rate of deformation was found to be a potent osteogenic stimulus.[46,56] However, strain distributions that differed from those experienced during normal physiologic activities may elicit osteogenic responses at subphysiologic strain magnitudes. It has been suggested that these represent an 'error' signal which, if only imposed occasionally, does not lead to modeling changes; however, a repeated imposition of these unusual strain distributions can induce structural changes in bone architecture. An example is seen in the serving arms of professional tennis players where bone mass can be approximately 30% higher than the non-serving arm.[60] Thus an abnormal gait, particularly if inducing high strain rates, will induce an osteogenic response.

In the horse the level of bone deformation increases as a function of locomotor speed. Thus, as the speed of the walk increases so too does the level of bone deformation. This is also seen in the trot, with an extended trot leading to abnormally high rates of bone strain. In the horse, as speed increases there is normally a change in gait which is controlled by energy efficiency drives; the levels of oxygen increase with speed but there is an optimal speed at each gait for oxygen utilization. At speeds beyond the optimal, the utilization of oxygen becomes less efficient and this leads to a gait transition and further optimal levels of oxygen utilization for the new gait.[61] In addition, at the gait transition the level of bone deformation is reduced.[62] This may represent a means of controling bone mass and also reducing damage due to fatigue loading of bone.

Safety factors

As with most structures, the skeleton can withstand occasional overloads. In designing a structure such as a bridge there is a built-in safety factor to accommodate unforeseen overload. The level of overdesign is related to a balance between risk of overload and cost of materials. The architecture of the skeleton has been shown to follow very similar principles to those seen in engineering of structures. An excess of material would minimize risk of structural failure but carry a high cost in terms of energy requirements. These factors may explain the findings that bones toward the proximal region of the limbs have a higher safety factor than those at the distal extremity. For instance, the human femur is able to withstand loads of five times normal bodyweight.

Site-specific fracture incidence

In the horse, an animal evolved for high-speed locomotion, the energy costs of additional mass at the extremity of a long limb, acting like a swinging pendulum, would be high. Currey analyzed the incidence of fractures in race horses reported by Vaughan and showed a higher incidence in the more distal bone of the limb where safety factors would be reduced to decrease energy costs.

Exercise studies in horses have shown a reduced level of functional adaptation in the more distal bones together with an increase in fracture toughness. This may represent a different mechanism to limit crack propagation and consequent fracture.[63]

Gross fractures

As with any structure, a single overload can result in a monotonic failure. Since bone exhibits functional adaptation the mass and architecture are adapted to meet the prevailing magnitude and distribution of load. However, a single excessive load that is greater than the given safety factor will result in failure. The type of failure in terms of damage of the structure at a gross and microscopic level will depend upon the energy and velocity of crack propagation.

When the bones are subjected to load distributions different from those to which the bone has adapted, failure can occur at much lower levels. This type of failure may be seen when limb movements are unco-ordinated such as during recovery from anesthesia or at the end of periods of strenuous activity when muscles are fatigued and limbs loaded asymmetrically (Dow, personal communication).

The risk of fracture may also be increased if a new type of exercise is introduced suddenly without an appropriate period of training for both muscle and bone adaptation.

Training influences on bone adaptation

In general there has been a significant lag between scientific advance and change in the training methods used in the equine world in general and in the horse-racing industry in particular. No doubt some of the biologic mechanisms controlling adaptation of bone to its functional environment could and should be applied to the conditioning of equine athletes. It is also probable that the empirical traditional methods of training do incorporate some scientific principles as a consequence of many years of experience. However, given the highly competitive nature of the equine industry, it is difficult to identify training methods that relate to high and low incidences of injury. Recently a number of epidemiological studies have been performed to identify both the relationships between specific types of training and incidence of bone fractures. The response of the bony skeleton to different quantified training regimens has also been monitored using the minimally invasive techniques of blood markers for assessing bone formation and bone resorption.

Monitoring of skeletal responses to training

The ability to make an objective study on the monitoring of adaptive changes in the skeleton to training requires two components. First, the ability to define and quantify the training input and second, to measure the effect on the bones of the skeleton directly or indirectly. Even in the laboratory these are difficult to achieve; in field studies direct measurements such as radiography, scintigraphy and DEXA/CT scanning are not practical. Therefore, indirect assessments of bone modeling and remodeling are being developed. Blood markers have been used both in controlled studies and in commercial training facilities. In studies using controlled exercise regimens it is possible to relate these to changes in marker levels and to evaluate factors such as seasonal, age and gender-related effects.

Markers of bone adaptation

In a controlled exercise study over 1 year in 2-year-old Thoroughbreds, the effects of the exercise on two biochemical markers of bone formation were determined. These markers were the carboxy-terminal propeptide of type I collagen and the bone-specific alkaline phosphatase. In addition, one potential marker of bone resorption, the pyridinoline cross-linked telopeptide domain of type I collagen, was also monitored. In both the low and high intensity exercised groups there was a significant reduction in marker levels over the year. This is expected as a normal age-related change. However, it was encouraging that the pattern of reduction differed between groups in a way that indicated an increase in bone turnover in the high intensity trained group.[18] These results are encouraging, as they indicate the potential to develop a non-invasive method of monitoring the effects of training on bone.

Direct monitoring of skeletal adaptation

Radiographic techniques

Radiography can be used to visualize some direct responses of the skeleton to increased or decreased mechanical demands. Changes in the architecture and radiographic density of bones can be used to monitor the competence of the skeleton. Standardized positioning and the use of a calibration step wedge allows standardization of exposure by optical digitization, which may then allow a determination of relative bone density in relation to responses to applied training or conditioning regimens. Radiologic methods have been used to assess functional adaptation to exercise in the equine skeleton and a radiographic index has been used to assess the changes in shape of the third metacarpal bone in response to training. Studies have been performed to define the limitations and level of accuracy of this technique that indicated acceptable accuracy providing alignment of the limb, cassette and X-ray machine is accurate. These findings suggest that the radiographic index can be used to measure MC3 bone shape using relatively simple and widely available technology.[64]

Peripheral quantitative computed tomography (pqCT)

Improvements to radiographic methods can be obtained by the use of pqCT. A two-dimensional image showing bone mineral density distributions may be generated and quantitative information on cortical cross-sectional area and second moment of area can be provided (see Fig. 7.9). Thus the effects of training could be monitored in relation to specific regimens. The disadvantage of this technique at present is that, as in MRI, the machine is fragile and the horse has to be anesthetized. Also the aperture of the machine is limited and thus only small peripheral limb segments can be assessed. For experimental studies and in young horses, this technique can provide considerable useful data on the response of specific distal limb bones to imposed exercise.

Dual energy X-ray absorptiometry (DEXA)

This system can be used to determine bone mineral content of the skeleton and regions of the skeleton. These scanners are normally used in assessment of bone density in relation to metabolic bone disease, particularly postmenopausal osteoporosis. The disadvantage in relation to monitoring of equine skeletal responses to training is the need to anesthetize the horse together with the limited area that can be scanned. In humans it is possible to relate individual scan data to population values and provide a fracture risk score. This may be an interesting concept in relation to monitoring of the equine skeleton but is not yet possible.

Nuclear scintigraphy

By attaching an isotope to a bone-seeking bisphosphonate, areas of active bone modeling or remodeling can be labeled. By imaging with a gamma camera these active sites can be located in the living skeleton at specific points in time. Although used predominantly for diagnostic purposes, this technique could identify site-specific skeletal responses to exercise or mechanical loading.

There is a need for an effective non-invasive method to monitor both bone quality and skeletal integrity during development and in both athletic training and competition. Some handheld methods have been tried. Potentially the use of ultrasound in terms of measuring speed of sound through bone and broad-band attenuation can give information on both modulus and structural integrity. The systems are available commercially for human use and also recently for use in the horse. A combination of this type of monitoring and associated adjustment of training schedules could prevent the overt occurrence of conditions such as ‘bucked shins’.

Training strategies to condition the skeleton of the equine athlete

Age-related changes in the skeleton

In a study on fatigue strength, Nunamaker et al measured surface bone strains on the third metacarpal bone of young and old North American Thoroughbred horses to determine the mechanisms involved in fatigue failure of bone leading to fracture.[65] They found greater levels of strain (deformation) at the gallop in the young horses with almost a 40% reduction in strain in the older horses. The significance of this is that the fatigue failure point of a bone depends upon both the magnitude of the deformation and the number of loading cycles to the failure point. Thus if the strain magnitude is reduced there can be a greater number of cycles of deformation prior to failure. In addition, since bone is a dynamic tissue that responds to mechanical deformation, the bone architecture as a structure can be modeled to reduce the bone strain at high loads.

These authors suggest that changes in shape of the third metacarpal bone during growth and maturity may represent a mechanism to reduce strain and mitigate fatigue failure. The high incidence of fatigue failure as seen in 'bucked shins' in young horses subjected to exercise that induces high strains over short periods of time would support this hypothesis. Interestingly, Nunamaker et al also investigated breed differences in the incidence of 'bucked shins', hypothesizing that there might be a breed difference in the material properties of the bone matrix leading to a difference in the fatigue failure patterns.[66] They determined fatigue properties in the bone material of the third metacarpal bone in Thoroughbred and Standardbred horses. No significant differences were found in the mechanical properties of the bone. This may suggest that other factors such as the training methods and type of loading affect the incidence between these two breeds. Perhaps this is indicative that imposed mechanical events, even within a breed of horse, can influence the incidence of such conditions. An understanding of the pathobiology and material properties of bone could be used to determine the appropriate age and exercise regimen to minimize such injuries.

Exercise during development

Most of the training and conditioning of equine athletes occurs after skeletal maturity. In some cases, such as training of race horses, the period of training is relatively short and the ongoing training is also limited to short periods. The training methods are largely empirical based on a traditional approach rather than advances in the science underlying training.

Recently a number of studies have been investigating the concept of introducing conditioning for athletic performance during the period of postnatal growth and development. This approach imposed the distribution of mechanical loads associated with the athletic activity at a time when modeling processes are active in forming the functionally related aspects of skeletal structure. Thus optimization of primary bone development can be attained in relation to the loading patterns that will be experienced during athletic activity. There is some evidence that bone strain can be reduced with gait transition, decreasing by 42% at the trot/canter transition.[62] Thus in activities where gait changes are suppressed as a component of the particular athletic activity, for example in dressage and in racing trotters and pacers, the high strains at high speeds may predispose to microdamage when introduced in the adult. Whereas if these patterns of gait are introduced gradually during the growth and modeling phase of skeletal development, then appropriate skeletal architecture can be attained with lower risk of damage. This, combined with the incremental increases in training load during development, will also increase skeletal mass and may reduce the strain magnitudes that would occur if training is introduced after skeletal development, and thus minimize injuries.

Changes in foot balance in foals have also been shown to induce strain changes of up to 40% reduction in medial metacarpal compressive strains and 100% increase in lateral compressive strains. However, these were found to return to normal distributions after a period of time.[67] As discussed previously, bone adapts to increased strain and changed strain distribution, so a return to normal strain at a local site may reflect an adaptation resulting from changes in mass and distribution of bone. In this study changes in bone mass or architecture as a consequence of the changed loading were not reported. This adaptation to abnormal loading during growth may result in an abnormal architecture of the bone with possible implications for other skeletal components such as joints in later life. Therefore, attention to exercise type, intensity and foot balance during growth and development should optimize the skeleton for athletic activity in the adult. The concept may also apply to other skeletal tissues in which the process of growth can be modified by early conditioning.

Human athletes are frequently identified as children and both train and compete during growth and maturation. In addition, human athletes tend to undertake high volumes of training. The equine athlete, particularly the race horse, is given relatively low volumes of training and spends considerable time in the stable.

Conclusion

Horses as equine athletes must be conditioned and trained to optimize the whole animal for the particular type of athletic activity. An extremely high proportion of all injuries in the equine athlete in general and in the race horse in particular are associated with the musculoskeletal system. Within musculoskeletal injuries, fractures and bone-related pathology

account for a great proportion. Bone both as a tissue and structure is acutely responsive to mechanical loading and thus can be conditioned to withstand the applied loads. In order to maximize performance and minimize injury it is important to appreciate the pathobiology of functional adaptation of bone. This together with appropriate monitoring can enable owners, trainers and veterinarians to apply the science underlying functional adaptation to the training of specific equine athletes, thus improving equine welfare.

References

1. Hill WG. Why aren't horses faster? Nature 1988; 332(6166):678.
2. Currey JD. Ontogenetic changes in compact bone material properties. In: Cowin SC, ed. Bone biomechanics handbook. London, UK: CRC Press; 2001.
3. Vaughan LC, Mason BJE. A clinico-pathological study of racing accidents in horses: a report of a study on equine fatal accidents on racecourses financed by the Horserace Betting Levy Board. Dorking, UK: Bartholomew Press; 1975.
4. Holmstrom M, Magnusson LE, Philipsson J. Variation in conformation of Swedish warmblood horses and conformational characteristics of elite sport horses. Equine Vet J 1990; 22(3):186–193.
5. Teitelbaum SL. Bone resorption by osteoclasts. Science 2000; 289: 1504–1508.
6. Chambers TJ. Regulation of the differentiation and function of osteoclasts. J Pathol 2000; 192(1):4–13.
7. Boyde A, Dillon CE, Jones SJ. Measurement of osteoclastic resorption pits with a tandem scanning microscope. J Microsc 1990; 158(Pt 2):261–265.
8. Vaananen HK, Horton M. The osteoclast clear zone is a specialized cell-extracellular matrix adhesion structure. J Cell Sci 1995; 108(Pt 8):2729–2732.
9. Nesbitt SA, Horton MA. Trafficking of matrix collagens through bone-resorbing osteoclasts. Science 1997; 276(5310):266–269.
10. Mason DJ, Suva LJ, Genever PG, et al. Mechanically regulated expression of a neural glutamate transporter in bone: a role for excitatory amino acids as osteotropic agents? Bone 1997; 20(3):199–205.
11. Cochran GV, Wu DD, Lee BY, et al. Streaming potentials in gap osteotomy callus and adjacent cortex. A pilot study. Clin Orthop 1997; 337:291–301.
12. Cowin SC, Weinbaum S, Zeng Y. A case for bone canaliculi as the anatomical site of strain generated potentials. J Biomech 1995; 28(11):1281–1297.
13. Donahue HJ. Gap junctions and biophysical regulation of bone cell differentiation. Bone 2000; 26(5):417–422.
14. Bacon GE, Goodship AE. The orientation of the mineral crystals in the radius and tibia of the sheep and its variation with age. J Anat 1991; 179:15–22.
15. Biewener AA, Thomason J, Goodship A, Lanyon LE. Bone stress in the horse forelimb during locomotion at different gaits: a comparison of two experimental methods. J Biomech 1983; 16(8):565–576.
16. Riggs CM, Vaughan LC, Evans GP, et al. Mechanical implications of collagen fibre orientation in cortical bone of the equine radius. Anat Embryol (Berl) 1993; 187(3):239–248.
17. Mason MW, Skedros JG, Bloebaum RD. Evidence of strain-mode-related cortical adaptation in the diaphysis of the horse radius. Bone 1995; 17(3): 229–237.
18. Price JS, Jackson B, Eastell R, et al. The response of the skeleton to physical training: a biochemical study in horses. Bone 1995; 17(3):221–227.
19. Price JS, Jackson BF, Gray JA, et al. Biochemical markers of bone metabolism in growing thoroughbreds: a longitudinal study. Res Vet Sci 2001; 71(1):37–44.
20. Bigot G, Bouzidi A, Rumelhart C, Martin-Rosset W. Evolution during growth of the mechanical properties of the cortical bone in equine cannon-bones. Med Eng Phys 1996; 18(1):79–87.
21. Davies HM. Dorsal metacarpal cortex ultrasound speed and bone size and shape. Equine Vet J 2002; 34(suppl): 337–339.
22. Fell HB. Skeletal development in tissue culture. In: Bourne GW, ed. The biochemistry and physiology of bone. London, UK: Academic Press; 1956.
23. Chalmers J, Ray RD. The growth of transplanted foetal bones in different immunological environments. J Bone Joint Surg 1962; 44B:149–164.
24. Farnum CE, Wilsman NJ. Cellular turnover at the chondro-osseous junction of growth plate cartilage: analysis by serial sections at the light microscopical level. J Orthop Res 1989; 7(5):654–666.
25. Adams CS, Shapiro IM. The fate of the terminally differentiated chondrocyte: evidence for microenvironmental regulation of chondrocyte apoptosis. Crit Rev Oral Biol Med 2002; 13(6):465–473.
26. Byers S, Moore AJ, Byard RW, Fazzalari NL. Quantitative histomorphometric analysis of the human growth plate from birth to adolescence. Bone 2000; 27(4):495–501.
27. Currey JD. Differences in the blood supply of bone of different histological types. Q J Microsc Sci 1960; 101: 351.
28. Lanyon LE, Smith RN. Bone strain in the tibia during normal quadrupedal locomotion. Acta Orthop Scand 1970; 41(3):238–248.
29. Van Cochran GB. A method for direct recording of electromechanical data from skeletal bone in living animals. J Biomech 1974; 7(6):563–565.
30. Hartman W, Schamhardt HC, Lammertink JL, Badoux DM. Bone strain in the equine tibia: an in vivo strain gauge analysis. Am J Vet Res 1984; 45(5):880–884.
31. Lanyon LE. Experimental support for the trajectorial theory of bone structure. J Bone Joint Surg (Br) 1974; 56(1):160–166.
32. Rubin CT, Lanyon LE. Dynamic strain similarity in vertebrates; an alternative to allometric limb bone scaling. J Theor Biol 1984; 107(2):321–327.
33. Goodship AE, Lanyon LE, McFie H. Functional adaptation of bone to increased stress. An experimental study. J Bone Joint Surg (Am) 1979; 61(4):539–546.
34. Lanyon LE, Goodship AE, Pye CJ, MacFie JH. Mechanically adaptive bone remodelling. J Biomech 1982; 15(3):141–154.
35. O'Connor JA, Lanyon LE, MacFie H. The influence of strain rate on adaptive bone remodelling. J Biomech 1982; 15(10):767–781.
36. Rubin CT, Lanyon LE. Regulation of bone formation by applied dynamic loads. J Bone Joint Surg (Am) 1984; 66(3):397–402.
37. Prendergast PJ, Taylor D. Prediction of bone adaptation using damage accumulation. J Biomech 1994; 27(8):1067–1076.
38. Lanyon LE, Rubin CT. Static vs dynamic loads as an influence on bone remodelling. J Biomech 1984; 17(12): 897–905.

39. Hillam RA, Skerry TM. Inhibition of bone resorption and stimulation of formation by mechanical loading of the modeling rat ulna in vivo. J Bone Miner Res 1995; 10(5):683–689.
40. Mason DJ, Hillam RA, Skerry TM. Constitutive in vivo mRNA expression by osteocytes of beta-actin, osteocalcin, connexin-43, IGF-I, c-fos and c-jun, but not TNF-alpha nor tartrate-resistant acid phosphatase. J Bone Miner Res 1996; 11(3):350–357.
41. Forwood MR, Turner CH. Skeletal adaptations to mechanical usage: results from tibial loading studies in rats. Bone 1995; 17(4 suppl):197S–205S.
42. Boyde A, Jones SJ, Radcliffe R, et al. Nonexplosive fracture in a cannon bone: a case report. J Scanning Microsc 1997; 19(3):209–211.
43. Radin EL, Burr DB, Caterson B, et al. Mechanical determinants of osteoarthrosis. Semin Arthritis Rheum 1991; 21(3 suppl 2):12–21.
44. Chen WL, O'Connor JJ, Radin EL. A comparison of the gaits of Chinese and Caucasian women with particular reference to their heelstrike transients. Clin Biomech 2003; 18(3):207–213.
45. Firth EC, Delahunt J, Wichtel JW, et al. Galloping exercise induces regional changes in bone density within the third and radial carpal bones of Thoroughbred horses. Equine Vet J 1999; 31(2):111–115.
46. Firth EC, Goodship AE, Delahunt J, Smith T. Osteoinductive response in the dorsal aspect of the carpus of young thoroughbreds in training occurs within months. Equine Vet J 1999; 30(suppl):552–554.
47. Murray RC, Whitton RC, Vedi S, et al. The effect of training on the calcified zone of equine middle carpal articular cartilage. Equine Vet J 1999; 30(suppl):274–278.
48. Iwamoto J, Yeh JK, Aloia JF. Differential effect of treadmill exercise on three cancellous bone sites in the young growing rat. Bone 1999; 24(3):163–169.
49. Murray RC, Vedi S, Birch HL, et al. Subchondral bone thickness, hardness and remodelling are influenced by short-term exercise in a site-specific manner. J Orthop Res 2001; 19(6):1035–1042.
50. Bini F, Marinozzi A, Marinozzi F, Patane F. Microtensile measurements of single trabeculae stiffness in human femur. J Biomech 2002; 35(11):1515–1519.
51. Reilly GC, Currey JD. The development of microcracking and failure in bone depends on the loading mode to which it is adapted. J Exp Biol 1999; 202(Pt 5): 543–552.
52. Fleck C, Eifler D. Deformation behaviour and damage accumulation of cortical bone specimens from the equine tibia under cyclic loading. J Biomech 2003; 36(2):179–189.
53. Tomlin JL, Lawes TJ, Blunn GW, et al. Fractographic examination of racing greyhound central (navicular) tarsal bone failure surfaces using scanning electron microscopy. Calcif Tissue Int 2000; 67(3):260–266.
54. Bentolila V, Boyce TM, Fyhrie DP, et al. Intracortical remodeling in adult rat long bones after fatigue loading. Bone 1998; 23(3):275–281.
55. Jackson BF, Lonnell C, Verheyen K, et al. Biochemical markers of bone turnover in racehorses are influenced by training and gender. J Bone Miner Res 2002; 17(7):1334.
56. Boston RC, Nunamaker DM. Gait and speed as exercise components of risk factors associated with onset of fatigue injury of the third metacarpal bone in 2-year-old Thoroughbred racehorses. Am J Vet Res 2000; 61(6):602–608.
57. Noble BS, Peet N, Stevens HY, et al. Mechanical loading: biphasic osteocyte survival and targeting of osteoclasts for bone destruction in rat cortical bone. Am J Physiol Cell Physiol 2003; 284(4):C934–C943.
58. Tomkinson A, Gevers EF, Wit JM, et al. The role of estrogen in the control of rat osteocyte apoptosis. J Bone Miner Res 1998; 13(8):1243–1250.
59. Ehrlich PJ, Noble BS, Jessop HL, et al. The effect of in vivo mechanical loading on estrogen receptor alpha expression in rat ulnar osteocytes. J Bone Miner Res 2002; 17(9):1646–1655.
60. Jones HH, Priest JD, Hayes WC, et al. Humeral hypertrophy in response to exercise. J Bone Joint Surg (Am) 1977; 59(2):204–208.
61. Hoyt DF, Taylor CR. Gait and energetics of locomotion in horses. Nature 1981; 292:239–240.
62. Rubin CT, Lanyon LE. Limb mechanics as a function of speed and gait: a study of functional strains in the radius and tibia of horse and dog. J Exp Biol 1982; 101:187–211.
63. Reilly GC, Currey JD, Goodship AE. Exercise of young thoroughbred horses increases impact strength of the third metacarpal bone. J Orthop Res 1997; 15(6):862–868.
64. Walter LJ, Davies HM. Analysis of a radiographic technique for measurement of equine metacarpal bone shape. Equine Vet J 2001; 33(suppl):141–144.
65. Nunamaker DM, Butterweck DM, Provost MT. Fatigue fractures in thoroughbred racehorses: relationships with age, peak bone strain, and training. J Orthop Res 1990; 8(4):604–611.
66. Nunamaker DM, Butterweck DM, Black J. In vitro comparison of Thoroughbred and Standardbred racehorses with regard to local fatigue failure of the third metacarpal bone. Am J Vet Res 1991; 52(1):97–100.
67. Firth EC, Schamhardt HC, Hartman W. Measurements of bone strain in foals with altered foot balance. Am J Vet Res 1988; 49(2):261–265.

CHAPTER 8

Tendon and ligament physiology

Roger K.W. Smith and Allen E. Goodship

Introduction

Role and definition of tendons and ligaments

The distinction between tendons and ligaments has been largely an anatomic one – tendons join muscle to bone whereas ligaments join bone to bone. Although this division is generally true, topographic, biomechanic, ultrastructural and matrix compositional investigations have revealed a merging of these two structures in a continuum from 'pure' tendon to 'pure' ligament.

In connecting muscle to bone, tendons have been considered rather inert structures that are involved in the movement of joints. However, while this 'positional' function is still an important one, certain tendons in cursorial animals have developed another role in acting as springs to store energy for efficient locomotion. This is particularly true in the horse, where the tendinous structures on the palmar aspect of the metacarpal region – the superficial digital flexor tendon (SDFT) and the musculus interosseous medius tendon (suspensory ligament; SL), in particular, and the deep digital flexor tendon (DDFT) – act to support the hyperextended metacarpophalangeal joint during weight bearing (Fig. 8.1), releasing energy when the limb is protracted (Fig. 8.2). Hence, at fast gaits, the horse effectively bounces up and down on springs, similar to a child's pogo stick. As further modifications to this role, the digital flexor tendons have accessory 'ligaments', which attach the tendon directly to bone to provide a direct bone-to-bone tendinous connection when under full weight bearing.

It would be expected, and indeed found, that these tendons would have mechanical characteristics for this function as a spring, while tendons with a more 'traditional' positional role (e.g. human digital flexor tendons and the common digital extensor tendon (CDET) of the horse) would require stiffer characteristics. Up to a two-fold difference in structural stiffness has been found between equine digital flexor and extensor tendons.[1]

Periarticular ligaments, while having similar composition to tendons, are anatomically more complex, with multiple bundles of fascicles that frequently spiral and are taut and relaxed at different joint positions, depending on the fascicle bundle. In addition to their role in providing support for the joint, they also provide proprioceptive information. The

Fig. 8.1
Galloping horse, showing the hyperextended metacarpophalangeal joint under weight bearing.

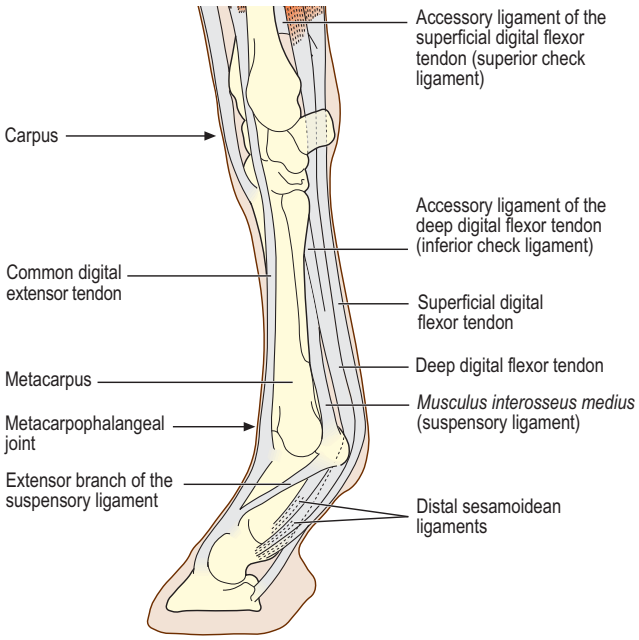


Fig. 8.2
Topographical anatomy of the distal limb of the horse (adapted from Adam's *Lameness in horses*, 3rd edn, reproduced with permission).

fibrous joint capsule is usually closely associated with these periarticular ligaments and functions in a similar way. Consequently, fibrous joint capsule is also an 'honorary' ligament.

Incidence of injury

Strain-induced injury of the tendons and ligaments is the most common orthopedic injury in athletic animals, be they equine or human. Recent epidemiologic surveys of race horse injuries sustained at UK race tracks between 1996 and 1998 showed that of all limb injuries (82% of all incidents), almost one-half (46%) were due to flexor tendon and/or SL injuries.[2] As observed clinically, this study confirmed that these injuries were much more common in older horses racing over jumps (steeplechasers or hurdlers) than in younger race horses racing on the flat. Furthermore, the data from these flat races correlated well with previous data published from studies in the USA (0.760 per 1000 starts in 1992).[3] However, this epidemiologic data, being obtained from only those injuries occurring during racing, represents only the tip of the iceberg. More recent studies investigating the incidence of superficial digital flexor tendinitis in horses during training showed that almost one-half (43%) of horses had evidence of tendon pathology, and that this incidence increased with age.[4] These data correlate well with similar ultrasonographic studies evaluating Achilles tendon damage in professional human athletes.[5] Other data recorded for training and racing injuries in flat race horses in Japan showed not only a rising incidence from 6.39% for 2-year-olds to 17.43% in 5-year-olds, but also, more worryingly, a rising overall incidence from 1990 to 2000 (Oikawa & Kasashima, personal communication). The reason for this is unclear but, interestingly, the incidence of Achilles tendinopathy in man has doubled in incidence in Europe in the last 10 years, believed to be associated with greater levels of exercise and increased longevity.[6–8]

The incidence in non-race-horses and for other strain-induced injuries of other tendons and ligaments have not been reported, although all horses involved in athleticism appear to be highly susceptible to tendon and ligament injuries. An interesting exception is ponies, which rarely suffer from superficial digital flexor tendinopathy, although they do have a relatively high incidence of desmitis of the accessory ligament of the DDFT.

Pathogenesis of tendon injury

Tendons and ligaments can be injured in one of two ways – overstrain or percutaneous penetration/laceration. The latter will not be considered further in this chapter. Overstrain injuries are believed to occur by one of two mechanisms. They can result from a sudden overloading of the structure, which overwhelms its resistive strength. This type of injury is probably the mechanism for most ligament and some DDFT injuries in the horse. However, for the most common strain-induced injuries in the horse, involving the palmar soft tissue structures of the metacarpal region, the clinical injury is believed to be preceded by a phase of degeneration. The evidence for this preceding degeneration is based on four observations:

1. The identification of 'asymptomatic' lesions, both grossly and microscopically, in post-mortem studies of normal horses.[9,10] Care, however, should be made in distinguishing gross central discolorations in otherwise normal tendons, which are more likely to represent early clinical injury than the preceding degeneration as compositional analyses reveal some opposite changes to that seen induced by exercise (see below) and many of these lesions can be identified ultrasonographically (Fig. 8.3).
2. Many, if not all, clinical strain-induced tendinopathies are bilateral with one limb more severely affected than the other. Careful ultrasonographic examination will reveal changes in the contralateral limb in many cases. In those seemingly unilateral cases, blood-flow studies have demonstrated increases in the 'normal' contralateral tendon, which would suggest that it is not totally unaffected.[11]
3. Epidemiologic studies have demonstrated close associations between age and exercise, and tendon injury.[2,4]
4. Following on from these epidemiologic observations, experimental investigations have demonstrated evidence of degeneration associated with a synergistic action of both age and exercise (see below).[12,13]

Thus, degeneration is usually the first phase of tendinopathy. This can be likened to 'molecular inflammation',[14] which does not provoke a repair process, as after clinical injury, but

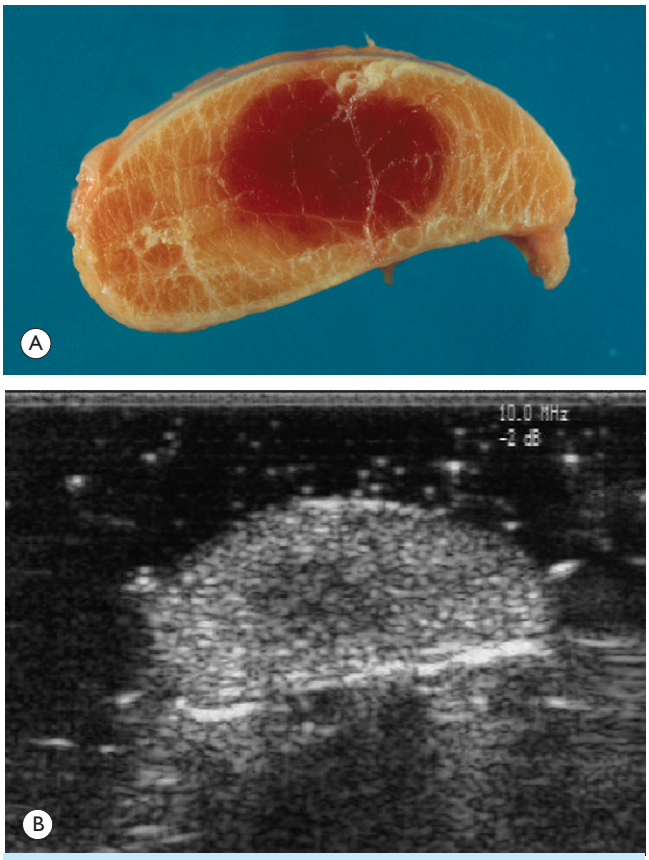


Fig. 8.3
(A) Central discolored region of 'asymptomatic' superficial digital flexor tendon (SDFT) – these 'lesions' are probably more representative of subtle clinical injury than the degenerative stage of tendinitis because they can be visualized ultrasonographically in a water bath as core lesions characteristic of clinical injury (B).

rather progressively weakens the tendon. Any change in the structural properties of the tendon does not have to be great as the tendon is already operating close to its tolerance limit. Clinical injury occurs when the highest stresses encountered by the tendon overwhelm its structural integrity, resulting in irreversible damage. Once this occurs, the damage created induces a repair process characterized by inflammation followed by fibroplasia (scar tissue formation).

This process allows the incorporation of risk factors that have been identified for tendinitis. These risk factors act to increase the peak loads on the SDFT, thereby increasing the risk of structural disruption. One of the most important factors is the speed of the horse. The faster the horse is going, the greater the risk of tendinitis.[2] Thus, hard going is associated with tendinitis as it increases the speed of the horse and also increases the peak impact loading.[2] Slower surfaces (including soft going) tend to be protective. Other factors, such as the weight the horse is carrying, fatigue, and the shoeing, can all influence peak tendon loads in this way. Low heels was thought to be protective of tendinitis as this conformation tends to increase the load in the DDFT, a secondary supporter of the metacarpophalangeal joint, thereby reducing the support necessary from the SDFT and SL. However, as the highest loading in the DDFT is towards the end of the weight-bearing phase, this may not have an influence on the initial high level loading of the SDFT at the onset of weight bearing.

Once the peak load on the tendon overcomes its structural strength, there is physical disruption to the tendon matrix. This varies in degree from fibrillar slippage, with breakage of cross-linking elements, to fibrillar rupture and, in some cases, complete separation of tendon tissue. This damage initiates a reparative sequence of events not dissimilar to that in other soft tissues, such as skin, which is characterized by phases of inflammation, followed by fibroplasia (see Tendon injury and repair, p. 143), which results in the replacement of normal tendon tissue with scar. With the formation of abundant scar tissue, the healed tendon becomes strong but it is functionally inferior to normal tendon. As a structure, healed tendon is stiffer than normal tendon, which compromises the tendon function and predisposes to reinjury, often at sites adjacent to the original injury.[15]

Structure of tendon

Biology of the muscle/tendon/bone unit

The musculature in the limb of the horse is proximally positioned to minimize the weight of the distal limb. This enables the horse to achieve efficient high speed locomotion through increased stride length and reduced energetics of limb protraction. This means that the tendons associated with these muscles have to be long to traverse the joints on which they act and, consequently, the digital flexor tendons, for example, are some 45 cm in length.

The horse's distal limb has reduced the number of phalanges to a single digit (with vestigial digits, the splint bones, either side of the third metacarpus) which has simplified the tendon and ligament anatomy (see Fig. 8.2). The distal fore and hindlimb therefore has an arrangement of three palmarly positioned structures – SDFT and DDFT with their associated accessory ligaments, and the SL – which serve to support the hyperextended metacarpo/metatarsophalangeal joint, and two or three dorsally positioned digital extensor tendons, which function only to extend the distal limb during protraction. Hence the loads experienced by these tendon groups are very different – the extensor tendons experience only low loads while the palmar tissues are subjected to high loads of weight bearing (7–10 kN on the SDFT).[16]

The horse has further adapted the basic muscle–tendon–bone unit in order to withstand the high weight-bearing loads and for its palmar soft tissue structures to act as an elastic unit for energy storage and efficient locomotion. Thus, the superficial digital flexor muscle has a much larger amount of connective tissue within it and has an accessory ligament (accessory ligament of the SDFT; proximal, or superior, check ligament) that 'bypasses' the muscle belly to insert on the distal radius. These two adaptations allow the musculo-

tendinous unit to withstand greater loads than would be possible by the muscle itself. The SL has taken this adaptation even further. It was originally derived from a muscle and still contains a variable amount of muscle within its mid and proximal regions. It could therefore be classified as a structure in which the tendon component has replaced the muscular tissue. However, its cellular morphology more closely resembles a ligament and, in the absence of a significant muscle belly, is usually classified as a ligament.

The muscle belly of the SDFT is not redundant, however, although its proposed role is different from the classical function of flexing the limb. Recent data have suggested that this muscle serves to fix the origin of the tendon. In vitro maximal contraction of the muscle has demonstrated a maximum of only 2 mm of muscle shortening.[17] It is hypothesized that the muscle acts to dampen the high-frequency damaging peak loads when the foot is placed on the ground at high speeds. Thus, loading of the SDFT can be considered an essentially passive process where energy is stored by the elastic properties of the tendon and returned when the limb flexes.

As a further adaptation to the long tendon length and the hyperextended metacarpo-/metatarso/phalangeal joint, the digital flexor tendons are contained within synovial sheaths in regions where they pass over high motion joints (the carpal sheath proximally and the digital sheath distally). While these structures protect the tendons from shear damage, they limit the ability of the tendons to heal, both because they are bathed in a synovial environment but also because the thick surrounding layer (paratenon) of extrasynovial tendon is absent within the confines of a tendon sheath. The paratenon is believed to be important in supplying fibroblasts capable of repairing tendon after injury.

Tendon receives its nutrients from three potential sources – intratendinous blood supply emanating from the musculotendinous junction and its osseous insertion, from blood vessels entering the tendon via mesotenon attachments within tendon sheaths or the paratenon, and from the synovial fluid within the tendon sheath. The relevant importance of these components depends on the tendon and tendon site. For the metacarpal region of the SDFT, studies have suggested that the intratendinous supply is the most important,[18] as necrosis was only achieved by ligation of the blood vessels within the tendon whereas stripping the paratenon had no effect.

The blood flow in the SDFT has been recorded between 1 and 2 mL/min/100 g,[10,11,19] which is of similar magnitude to that within resting skeletal muscle. Blood flow has been shown to increase two-fold with exercise,[11] although this can be delayed in horses that have not been trained. Injury caused an even greater increase in blood flow (> 300%), which has been recorded in both limbs of a horse with clinically unilateral tendinitis, further confirming the bilateral nature of the disease.

Tendon as a connective tissue

Although seemingly homogeneous on initial gross inspection, tendon is, in fact, composed of a complex arrangement of extracellular proteins in which are embedded cells, blood vessels, lymphatics, and nerves.

Tendon cells

Little is known about the cells that populate equine tendon. Although they are collectively known as tenocytes, they are unlikely to be a uniform population of cells because they differ considerably in nuclear morphology on light microscopy and when grown in culture. Previous descriptions have described three types[10] although a fourth type is evident within the endotenon tissue (Fig. 8.4; Table 8.1), and in other species, the synovial cells lining the outside of the tendon are differentiated from those within the tendon.[20]

The function of these cell types is not known but their location, morphology and presence in young or adult tendon propose functions which are reflected in the type classification (Table 8.1). The actual synthetic activity of these different types is unknown because there are currently no markers for identifying each type, nor methods for selectively recovering them from tendon tissue. Tenocytes have been often likened to fibroblasts and, while they have many

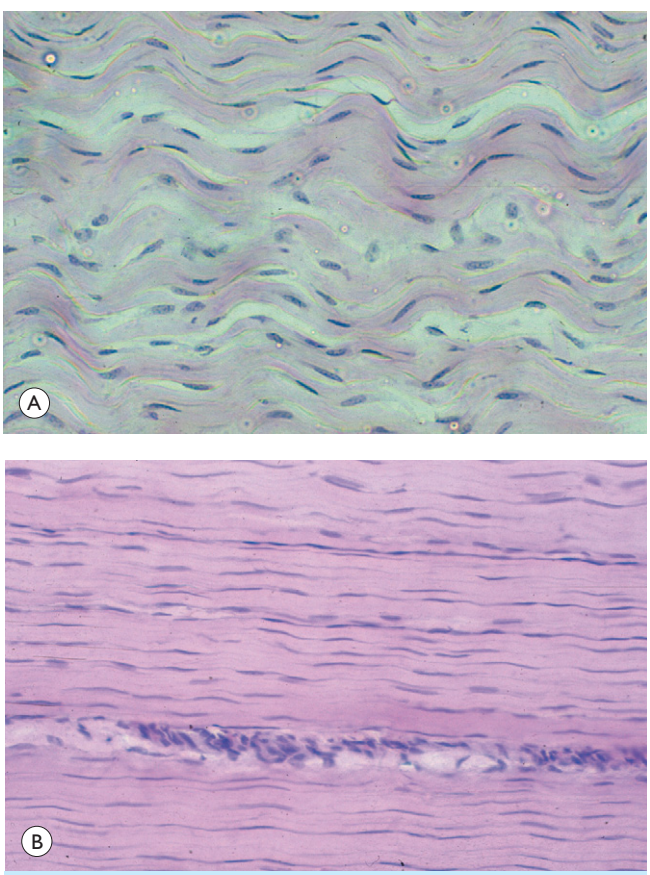


Fig. 8.4
H&E histologic sections showing the different morphologies of tenocyte nuclei in young (A) and mature (B) equine tendon. Note the large numbers of cell nuclei within the endotendon in the mature tendon.

Table 8.1 Types of cells within tendon and ligament based on nuclear morphology and location.

Cell classification	Type	Nuclear morphology	Location
I	'Resting'	Spindle-shaped nuclei lying between collagen fibers	Within the tensional region of all adult tendons
II	'Active'	Cigar-shaped nuclei lying between collagen fibers	Within young tendon and both young and adult ligaments
III	'Chondrocytic'	Round nuclei	In compressed regions of tendons and areas of chondroid metaplasia
IV	'Precursor'	Round nuclei with prominent nucleoli	Endotendon

similarities, it is unlikely that all these tenocyte types are identical to the fibroblasts seen in the skin or scar tissue. Recent studies have shown that fibroblasts recovered from different tissues behave differently in terms of the amount of certain proteins they synthesize (Smith & Heingard, unpublished data).

Work performed on laboratory animal[21] and equine (Ralphs, personal communication) tendons has shown that tenocytes have a large number of cytoplasmic extensions, which connect to neighboring cells via gap junctions. This provides a synctium that could provide an efficient system for mechanotransduction, similar to that occurring between osteocytes in bone.

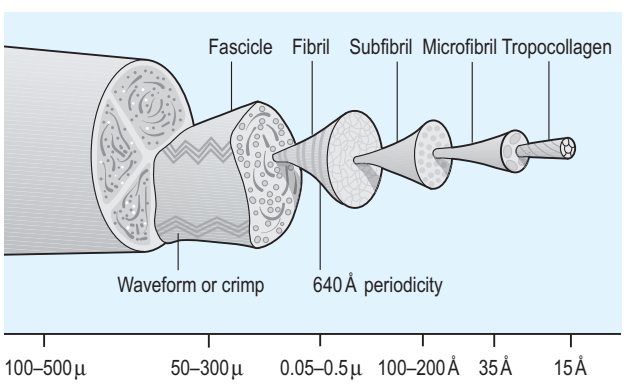


Fig. 8.5
Hierarchic arrangement of collagen in tendon (courtesy of the Veterinary Clinics of North America: Equine Practice, reproduced with permission).

Tendon matrix

As the cellular component of tendon is small, the functional properties of tendon rely on the extracellular matrix. This is determined, in turn, by both the composition and, equally importantly, the arrangement of these proteins within the matrix. It is constructed from a series of increasingly sized subunits into a hierarchic arrangement (Fig. 8.5).

Morphology

Crimp

'Crimp' refers to the characteristic waveform seen in longitudinal tendon histologic sections (Fig. 8.6). Originally suspected to be a preparation artifact, it is now known to be a real feature of tendon fascicles that is responsible for the 'toe' region of the stress–strain curve for tendon where tendon elongates with only a low level of applied stress

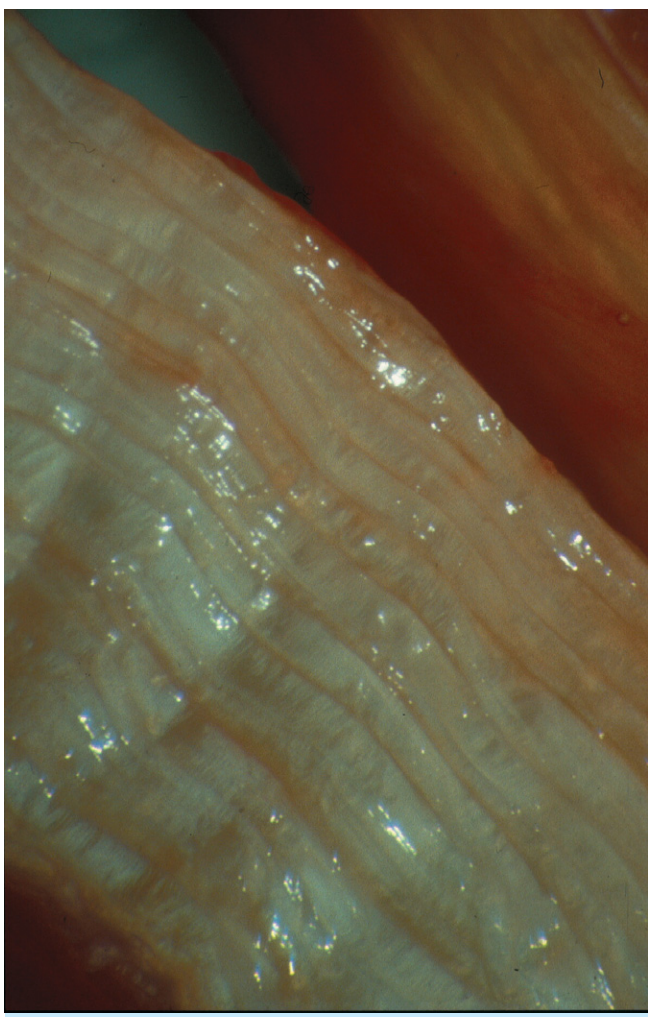


Fig. 8.6
'Crimp' pattern seen in the fascicles of the accessory ligament of the deep digital flexor tendon.

(Fig. 8.7). It is thus eliminated within the first 2% of tendon elongation and hence is unlikely to be present when the tendon receives normal weight-bearing load when standing. However, the 'toe' region has important implications for the overall strain capabilities of the tendon. Crimp can be described by its angle and length and these change as the animal ages (see p. 140).

Ultrastructural morphology

Collagen fibrils, the basic 'building block' of tendon, appear as banded filament on transmission electron microscopy of longitudinal sections of tendon. Transverse sections show the collagen fibrils as electron dense circular structures of varying sizes. The distribution of collagen fibril diameters can be determined from these sections, as well as assessment of the mass average diameter, which takes into account the relative proportion of the area taken up by different-sized fibrils.

Investigations on the development of tendon in laboratory animals have shown that collagen fibrils aggregate, resulting in thicker collagen fibrils. Recent work has proposed a regulatory mechanism for this process where only unipolar (N–C terminals) collagen fibrils can fuse resulting in a bipolar fiber (C–C terminals).[22,23] Thus, as the tissue matures, the proportion of unipolar fibrils becomes depleted, limiting the final size of the collagen fibril.

Whereas this process might also occur in the early development of equine tendon, the picture is much more complicated after birth. The adult SDFT has a bimodal distribution of fibrils with large numbers of small fibrils and lower numbers of large-diameter fibrils[24] (Fig. 8.8). Furthermore, there are differences between tendons, with the DDFT having fewer small-diameter and greater numbers of large-diameter fibrils.[25]

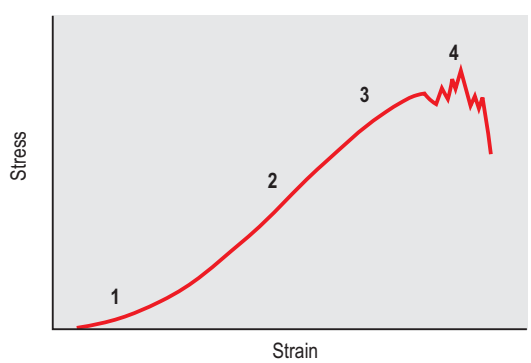


Fig. 8.7
Stress–strain curve for tendon. Zone 1 refers to the toe region, thought to be associated with the elimination of crimp; zone 2 to the linear phase from which the elastic modulus is calculated; zone 3 to the yield point after which irreversible damage occurs; and zone 4 to where individual tendon fibers rupture leading to complete failure (courtesy of the Veterinary Clinics of North America: Equine Practice, reproduced with permission).

Molecular composition

Tendon is predominantly composed of water, which makes-up approximately two-thirds of the weight of the tissue. The presence of this water is fundamental to maintaining the elasticity of the tissue because dehydration results in an increase in stiffness and tendons containing less water tend to be stiffer (Birch, personal communication). Although unsubstantiated at present, movement of water through compartments within the tendon might result in 'streaming potentials', which could provide a mechanism for mechanotransduction, whereby mechanical forces on the tendon influence the metabolic activity of the tenocytes.

The remaining third of the content of tendon (the dry weight) is predominantly composed of type I collagen. This protein is a major component of all connective tissues. Each type I collagen molecule is constructed within the endoplasmic reticulum of the cell from two α1 (I) chains and one α2 (I) chain, which forms a triple helix with non-helical N and C terminal extensions (propeptides) and is known as a procollagen molecule. These individual collagen molecules are assembled by cleavage of their propeptides at the N and C terminal ends by specific N- and C- proteinases, either after secretion into the immediate pericellular environment or intracellularly (Kadlar, personal communication). This results in a tropocollagen molecule that is 285 nm long and 1.4 nm wide. These molecules are then assembled into collagen fibrils in a highly organized fashion, each collagen molecule overlapping its neighbor by a quarter length (the 'quarter stagger' arrangement that is responsible for giving the banded pattern seen in electron microscopy), so that five collagen molecules make up a subunit of the collagen fibril. Although collagen molecules will spontaneously self-assemble, other proteins are likely to play a role in orchestrating this assembly (see below).

The fibrils are stabilized by the formation of covalent cross-links between lysine/hydroxylysine residues in adjacent fibrils, catalyzed by the enzyme lysyl oxidase. The collagen fibrils are in turn assembled in a longitudinally oriented pattern into increasingly larger subunits, which ultimately form the collagen fibers seen under light microscopy. These collagen fibers are further associated into tendon fascicles, which can be identified on the cut surface of a tendon (Fig. 8.9).

Non-collagenous components

While 80% of the dry weight of tendon is composed of collagen, the remaining 20% (5–6% of the wet weight of the tendon) is comprised of a wide variety of non-collagenous proteins. Although these are only a small component of the tissue, recent work has suggested they are vital for the organization and function of the tissue.[26]

During growth of the digital flexor tendons, one of the most abundant proteins is cartilage oligomeric matrix protein (COMP). This protein consists of five 'arms', joined at their N termini and with globular C termini (Fig. 8.10). There are only low levels of this protein in tendon at birth but it accumulates during growth within the digital flexor tendons with

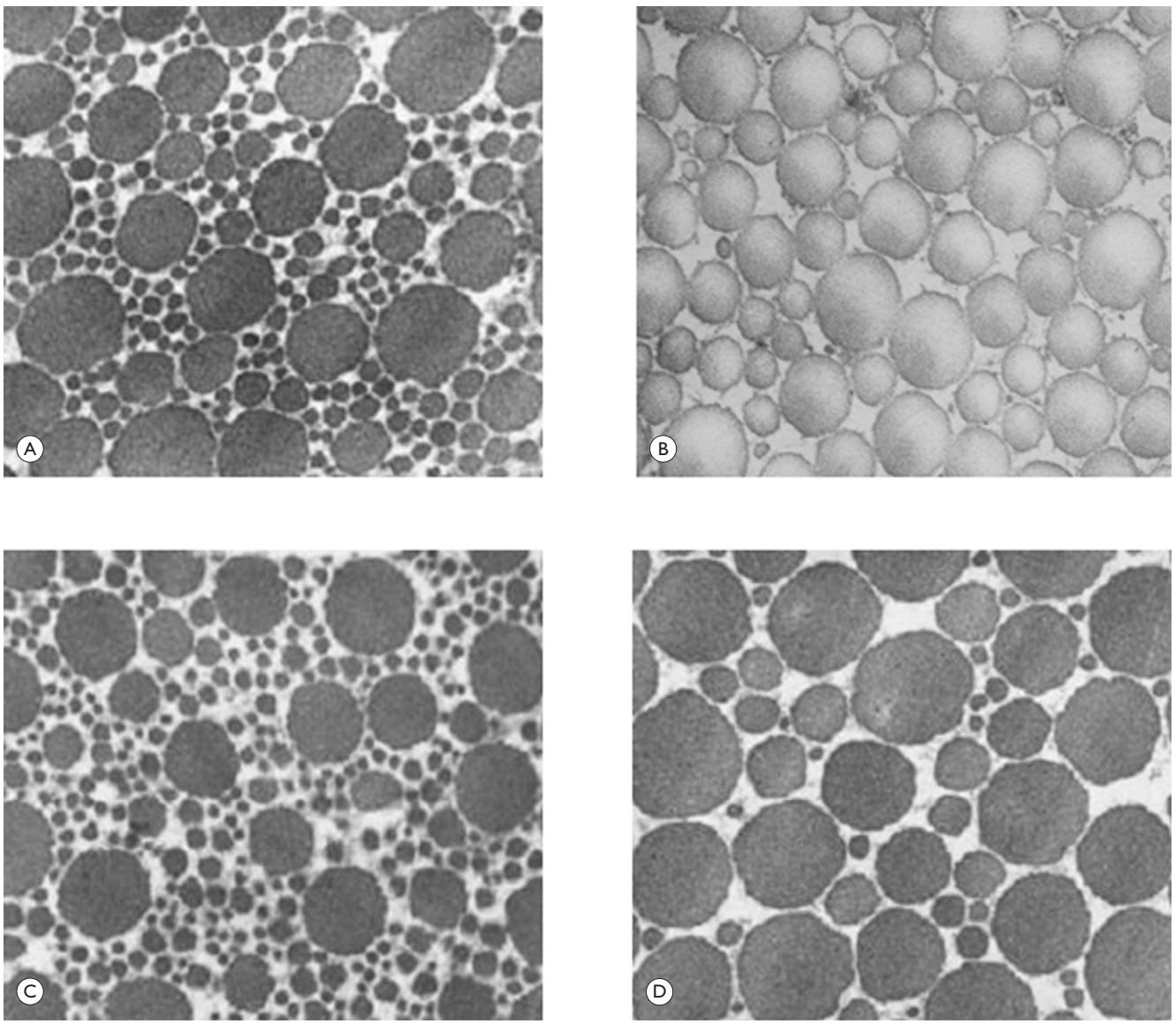


Fig. 8.8
Collagen fibril morphology in (A) the superficial digital flexor tendon, (B) the deep digital flexor tendon, (C) the suspensory ligament, and (D) the common digital extensor tendon. Note the similarities of the primary supporters of the metacarpophalangeal joint (superficial digital flexor tendon), and the positional tendon (common digital extensor tendon) with the deep digital flexor tendon.

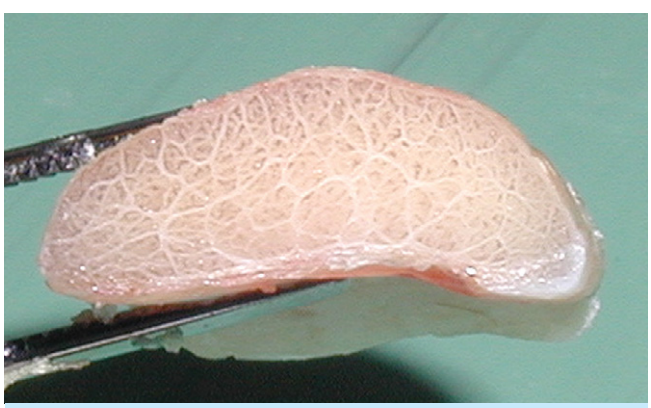


Fig. 8.9
The cut surface of the superficial digital flexor tendon (SDFT), showing the fascicular arrangement.

the highest levels achieved in the tensional region of the SDFT at skeletal maturity in the horse (at approximately 2 years of age) of approximately 10 mg/g wet weight.[27] This equates to approximately 30 mg/g dry weight or approximately 1% of the wet weight. After the period of growth, however, levels of COMP in the tensional, but not the compressed, region of the SDFT fall (see p. 145).

The function of COMP has not been completely determined but it is known to bind fibrillar collagens (including type I) via a zinc-dependent mechanism.[28] This interaction with collagen occurs via the globular C terminal domains at four equally spaced sites along the collagen molecule.[29] The size of the arms is such that it cannot interact with more than one site on one collagen molecule but instead can order five collagen molecules for assembly into a collagen fibril during

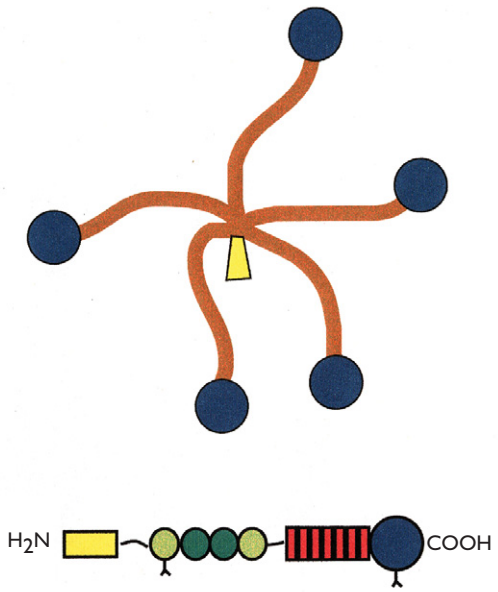


Fig. 8.10
A cartilage oligomeric matrix protein (COMP) molecule (courtesy of Dr K Rosenberg and *Comparative Biochemistry and Physiology*, reproduced with permission).

the earliest stages of collagen fibril formation. As it does not bind to formed collagen fibrils, COMP is displaced from the fibril. This makes its role as a structural protein within the formed tendon matrix a difficult one to rationalize. However, recent studies have shown that COMP can accelerate collagen fibrillogenesis in vitro and it is possible that this protein acts more as an 'organizational' molecule rather than in a structural role (Heinegård, personal communication). This would be supported by observations that the highest levels are present during the growth of the tendon when matrix is being synthesized and that levels fall after skeletal maturity when there is little change in the structural properties of the tendon. While possibly not important for the structural integrity of the matrix once it has formed, it is potentially critically important in the formation of soft tissue collagenous matrices that are designed to withstand loads, as it is present only in tendon, ligament, cartilage, intervertebral disk, and meniscus. Indeed, initial data relating mechanical properties of SDFT at skeletal maturity to COMP levels demonstrate a significant positive relationship.[26] Thus, the hypothesis is advanced that the more COMP synthesized during growth, the stronger the resulting tendon. In further support of this function, a functional 'knock-out' of the protein caused by a naturally occurring mutation in the COMP gene shows a tendon phenotype.[30]

Proteoglycans

Proteoglycans consist of a central protein core with O-linked glycosaminoglycan side-chains. They can be divided into two classes – the large proteoglycans (such as aggrecan, the large proteoglycan of cartilage, and the soft tissue equivalent, versican) and the small proteoglycans (such as decorin, biglycan, fibromodulin, lumican, and mimican) all of which are present in equine tendon. The large proteoglycans have numerous highly sulfated glycosaminoglycan side-chains, which hold water and therefore are present where the tendon has to resist compression. The small proteoglycans are closely associated with the collagen fibrils and are believed to regulate collagen fibril diameters. 'Knock-out' of the decorin gene in mice resulted in large, irregular-sized collagen fibrils believed to be caused by unregulated lateral fusion and this was associated with weak and fragile skin.[31] Fibromodulin knock-out mice showed paradoxically smaller collagen fibrils but also a compensatory increase in another small proteoglycan, lumican, which binds to the collagen molecule at the same site to fibromodulin,[32] demonstrating that many of these small proteoglycans can 'cross-function'. However, tensile testing of the mice's tail tendons showed a significant reduction in tensile strength in the adult fibromodulin null mice,[33] consistent with the hypothesis that although another small proteoglycan can do the same job, it does so less well.

Other proteins

There is a wide variety of other proteins in tendon whose functions are only partially elucidated. There is a variety of minor collagens, including type III, predominantly surrounding the fascicles within the endotendon tissue, and type VI, especially in the digital flexor tendons, which also appears to be regulated by mechanical load. Thrombospondin 4, tenescin-C, fibronectin, hyaluronic acid, and small amounts of elastin are also present but their contribution to the function of equine tendon is unclear.

Tendon-specific differences in structure and composition

Considerable debate still surrounds the simple question as to whether all tendons are constructed from the same material and/or have the same basic material properties. Our data would suggest that neither the composition nor the material properties are the same for all tendons, with differences reflecting the functional requirements. Thus, along the length of the digital flexor tendons in all animals weight bearing on a hyperextended metacarpophalangeal joint, where compressive forces are applied to the tendons as they change direction around the palmar aspect of the metacarpophalangeal joint, there is an accumulation of those matrix proteins most suited to resisting that compression. Thus, the tendon has a fibrocartilage-like composition in this region.[34,35]

Between tendons, there are differences in hydration, collagen content and some of the non-collagenous proteins. Thus, when comparing the digital flexor tendons, which are weight-bearing tendons, with the digital extensor tendons, which are positional tendons, the flexor tendons have higher hydration and lower collagen content, which is reflected in differences in

stiffness. Probably the most dramatic difference is seen in the COMP content during growth.[36] Both tendons have similarly low levels at birth but there is a dramatic rise in COMP levels in the superficial digital flexor tendon to 10 times levels at birth, while levels in the common digital extensor tendon do not alter. This probably reflects the different functional requirements between these weight-bearing and positional tendons. Interestingly, similar differences in COMP levels and other minor matrix components, such as type VI collagen, are observed between weight-bearing (e.g. Achilles tendon) and positional (e.g. anterior tibial tendon) tendons in man (Smith & Heinegård, personal communication).

Functional characteristics of tendon

Tendon and ligaments transmit forces to move the equine skeleton, or for support of the distal limb in the case of the digital flexor tendons, or, as ligaments, to maintain joint integrity. At heel strike, the loads rise the quickest in the soft tissue structures primarily supporting the metacarpophalangeal joint – the SDFT and the SL. High-frequency transients are also a feature of the early phase of weight bearing in these tendons. The load in the deep digital flexor tendon is slower to rise, which may help to explain why the SDFT and SL are the most prone to injury.

Load/deformation characteristics

The biomechanical properties of a tendon can be defined in vitro by its structural (as an organ) or material (as a tissue) properties. To establish these data, tendons can be recovered from cadavers and pulled to failure in a material testing machine. Anchoring of the tendon ends is problematical as final rupture often occurs at the tendon–clamp interface, which can result in artificially low values. Furthermore, data varies depending on a number of factors including rate of loading. Thus, comparisons between data sets performed in different ways should be made with caution.

In vitro loading experiments generate a load–deformation curve from which the structural properties of ultimate tensile strength (kN) and stiffness (N/mm) can be derived (see Fig. 8.7). There are four regions to the curve:

1. The 'toe' region, where there is non-linear stretch to the tendon. This is associated with the elimination of the crimp pattern of the collagen fibrils.
2. Linear deformation – it is this area of the curve from which the stiffness is determined (load divided by deformation for the linear portion of the curve). The mechanism for this elongation is not known but arises from elongation of the collagen fibrils and/or sliding of fibrils relative to one another. Recent work has suggested that interfibrillar (and even interfascicular) deformation is much greater than intrafibrillar/intrafascicular deformation, suggesting that tenocytes survive in a 'strain-protected' environment where they experience considerably lower deformation than that recorded for the whole structure.[37]
3. Yield region – irreversible lengthening of the tendon occurs at these deformations, possibly arising from covalent cross-link rupture and slippage of collagen fibrils.
4. Rupture, where the stress–strain curve falls quickly to zero as the collagen fibrils sequentially rupture.

Knowing the cross-sectional area of the tendon and its length, the stress (force per unit area) can be plotted against strain (change in length over original length), from which the material properties of ultimate tensile stress (N/mm^2) and Young's modulus of elasticity (E; MPa) can be calculated. As both the cross-sectional area and original length are assumed to be constant, the stress–strain curve has a similar shape to the load–deformation.

Ultimate tensile strength and stress

The ultimate tensile strength for the equine SDFT (rupturing at the midmetacarpal region) in the horse is approximately 12 kN or 1.2 tonnes. The approximate ultimate tensile stress is 100 MPa for the equine SDFT, which agrees well with previously documented figures for other species (45–125 MPa).[38,39]

Ultimate tensile strain

Equine flexor tendons can extend 10–12% of their length, and values of up to 20% have been reported[10] before the tendon ruptures. However, the ultimate tensile strain reflects only the final strain before rupture and includes that yield portion of the stress–strain curve that represents irreversible damage to the tendon tissue. In addition, the ultimate tensile strain may not be constant along the length of the SDFT in vitro.[40] Recent work has demonstrated that the normal strains in the digital flexor tendons in vivo (in ponies) are in the region of 2–4% at the walk and 4–6% at the trot.[41] Riemersma and colleagues[41] also noted that different results were obtained in vivo to in vitro, thereby indicating caution in the interpretation of in vitro measurements. Other studies have shown that, in the galloping Thoroughbred, strain changes between heel-strike and maximum weight bearing can reach 16% in the SDFT.[42] Such strains – far greater than usually expected in tendons from most other species – may reflect the importance of the digital flexor tendon as an elastic energy store where maximum deformation stores the most energy.

Cyclical loading and preconditioning effects

The biomechanical parameters mentioned above can only act as guides to the mechanical properties of tendons as tendon is a viscoelastic tissue.[39] Its time-dependent and history-dependent properties indicate a more complex structure than a simple elastic substance.

Hysteresis

The property known as hysteresis is demonstrated by the difference in the stress–strain relationship when the tendon is loaded compared to when it is unloaded (Fig. 8.11). The area between these two curves represents the energy lost during the loading cycle. This is usually about 5% in equine tendons. Much of this energy is lost as heat and is responsible for the rise in temperature within the tendon core associated with repeated loading (as in an exercising horse).[43] These temperatures can rise to as high as 46°C, which is potentially damaging to either tendon matrix or tenocytes. However, tenocytes recovered from the center of equine SDFT remain viable when subjected to rises in temperature of this magnitude, whereas those recovered from the periphery of the tendon do not.[44] This property is also present in fetal tenocytes, which suggests that the tendon has an inherent genetic adaptation to this physical process.

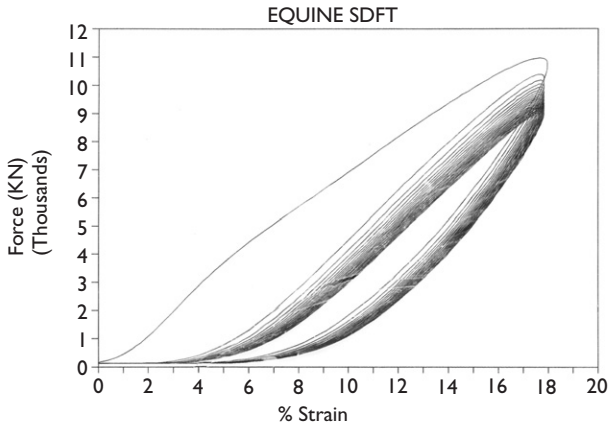


Fig. 8.11
The effect of repeated loading and unloading of tendon. The loading and unloading curves are different resulting in a loss of energy (hysteresis). Repeated loading shifts the curve to the right (conditioning).

Conditioning

The viscoelastic properties of tendon are demonstrated by movement of the stress–strain curve to the left or right (Fig. 8.11). Loading rate has only a minimal effect on tendon biomechanics; a rapid loading rate will move the curve slightly to the left, indicating a stiffer tendon.[45] Repeated loading, in contrast, results in shifting of the curve to the right (i.e. the tendon becomes less stiff), a process known as conditioning. This change is recoverable but significant resting time is necessary.[45] This property, however, has been demonstrated in vitro and may not reflect the normal behavior in vivo.

Contribution of tendon mechanics to the energetics of locomotion

With tendon loading under weight bearing being essentially a passive process, energy is stored in the extension of the tendon. As the energy stored in the tendon is represented by the area under the stress–strain curve, for this system to operate with maximum efficiency, the tendon must stretch as much as possible. As this tendon will rupture with in vitro testing at between 12 and 20%, the SDFT in vivo strain levels of up to 16% at the gallop[42] demonstrate that the high efficiency comes at a cost – there is little tolerance in the system and the tendon is prone to overstrain injury. Consequently, any small deterioration in the mechanical properties would have a significant effect on the risk of tendon injury.

The tendon returns energy with an efficiency of approximately 93%,[46] which provides considerable energy-saving for the horse. Predicted efficiencies of locomotion in the horse at different gaits calculated from the energy expenditure required for limb and trunk movement and the movement of the horse, and the energy production by the muscles (which have an efficiency of approximately 30%) shows an efficiency of greater than 100% at the gallop. This discrepancy is due to the energy-storage capacities of the locomotor soft tissues, in particular the SDFT and SL. Thus, these structures are critical to the optimum efficiency of equine locomotion.

Age and exercise effects on tendon pathophysiology

With preceding tendon degeneration proposed as an important factor in the initiation of equine superficial digital flexor tendinopathy, investigations have concentrated on changes occurring with the tendon matrix associated with aging and exercise. The importance of these factors on tendon physiology has been supported by epidemiologic studies in both horses (superficial digital flexor tendinopathy)[2,4] and man (Achilles tendinopathy).[6–8]

A combination of in vivo and post-mortem studies on 'normal' horses, both domesticated (trained) and ferral (untrained), and analyses of tendons from a number of experimental exercise studies has shone new light into the influence of both exercise and aging on equine tendon. These studies have investigated mechanical, morphological (ultrasonographic and histologic), ultrastructural, compositional, and metabolic changes in association with aging and exercise in equine tendon. The effects of these two factors have been found to be different between immature (growing) and mature (adult) tendon. The age at which equine digital flexor tendon matures is estimated at approximately 2 years of age from these studies.

Mature (adult) tendon

Mechanical changes

There is a large variation in mechanical properties between individuals – more than two-fold for ultimate tensile strength[10] so that alterations in both structural and material

properties are difficult to determine. In vitro testing from a large number of horses has demonstrated a decrease in ultimate tensile stress with age although this was not significant.[47] In further support of this hypothesis, human studies in vivo have demonstrated a decrease in stiffness in the Achilles tendon with age.[48] As this was an in vivo study, no ultimate tensile strength measurements are possible, although reduced stiffness is often associated with reduced strength in collagenous soft tissues.

The effect of exercise on the mechanical properties of tendon and ligament are variable, although much of this variation may be due to different ages and species used.

Morphological changes

The crimp pattern of equine SDFT was found to reduce in both angle and length with age.[49,50] Furthermore, the imposition of exercise resulted in an accelerated loss of this crimp in a heterogeneous manner – the central region of the tendon was disproportionately affected.[51] This may help to explain the occurrence of central 'core' lesions seen clinically as the central fascicles, having less crimp, straighten first and are therefore loaded preferentially, becoming the first ones to rupture.[49]

Other studies have assessed the change in fascicle pattern with aging and training.[52] Here, a significant reduction in the number of fascicles with a thickening of the interfascicular (endotenon) tissue was found associated with aging. This correlates well with the location of TGF-β in maturity (see 'Metabolic changes' below) and is consistent with this part of the tendon being the most labile portion of the tendon.

The effect of exercise on the cross-sectional area of tendon has shown inconsistent results. Ultrasonographic and gross cross-sectional measurements during experimental treadmill exercise in young adult horses failed to show any significant change with exercise over and above that caused by growth in digital flexor tendons.[53] In contrast, the common digital extensor tendon did show a significant increase with exercise, confirming similar findings in exercise studies on mini-pigs.[54] Another study, following cross-sectional area changes with the onset of training showed a significant increase.[55] However, two of the seven horses followed developed evidence of clinical tendon injury and so it is difficult to relate such increases in cross-sectional area to either adaptation or injury.

Ultrastructural changes

Collagen fibril diameters, calculated using transmission electron microscopy, in the adult SDFT in horses show a biphasic distribution, with a large number of small (40 nm) fibrils and a low number, but broader range, of large fibrils, while very old tendons have a more unimodal distribution characteristic of fetal and newborn tendon.[24] The bimodal distribution was unaffected by a short-term (4.5 months) experimental treadmill exercise program in ~2-year-old horses but there was a shift to smaller diameter collagen fibrils in the longer term study (18 months) where the horses were over 3 years of age[56] (Fig. 8.12). This effect was believed to be due to the disruption of large fibrils rather than the formation of new ones as the collagen content and 'age' (as determined by non-enzymatic glycation) were unaltered.

Compositional changes

Collagen content varies little with age and exercise but the non-collagenous component of tendon is much more labile.

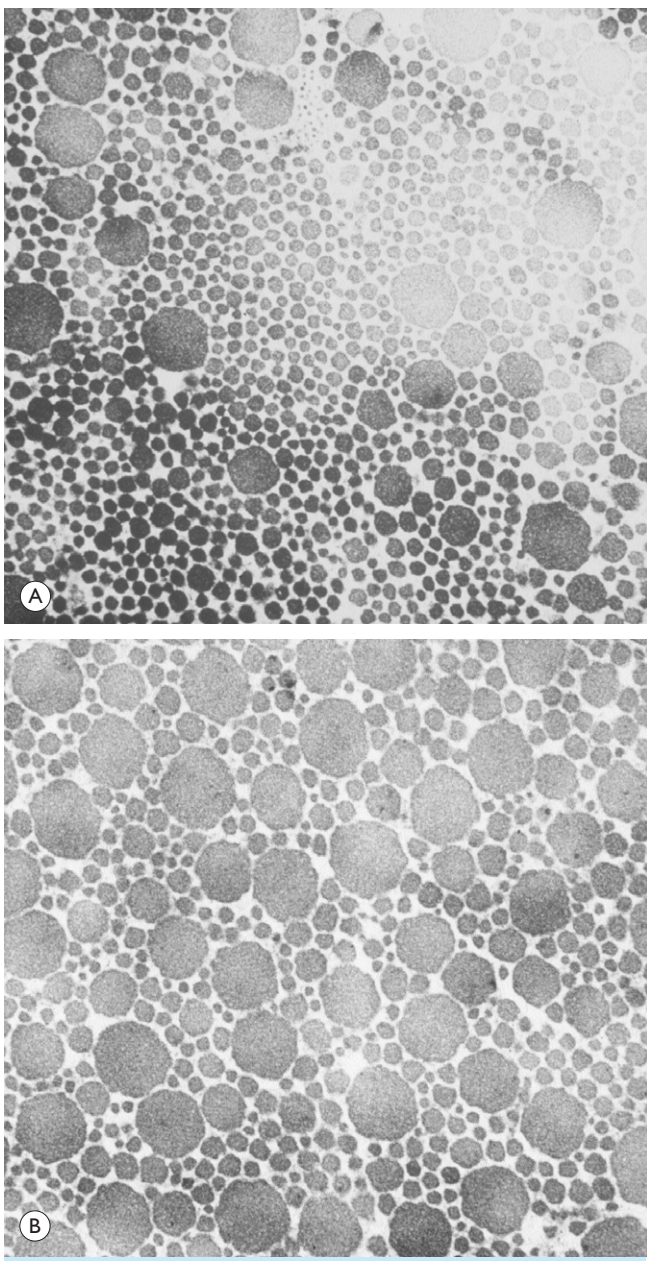


Fig. 8.12
Transmission electron microscopy of superficial digital flexor tendon in 3-year-old Thoroughbreds after 18 months of treadmill exercise (A), compared with controls that received only walking exercise (B). Exercise has induced a greater number of small-diameter fibrils (courtesy of the *Equine Veterinary Journal*, reproduced with permission).

Analysis of tendons from a wide range of ages, together with those from experimental exercise studies has shown a decrease in glycosaminoglycan (GAG) levels with age and exercise, where both act synergistically.[57] This is in contrast to the central discolored regions seen as an occasional coincidental finding at post-mortem, which contain increased GAG levels suggestive of scar tissue formation[58] (see Fig. 8.3). GAGs are part of proteoglycan molecules but vary in amount between different proteoglycan species. Thus, the small proteoglycans of tensile tendon contain only one or two side-chains of GAGs while the large proteoglycans, more characteristic of areas of tendon under compression (e.g. where the digital flexor tendons change direction at the level of the metacarpophalangeal joints contain large numbers of GAG side-chains. Thus, changes in GAG levels within tendon probably reflect more changes in the large, rather than small, proteoglycan species.

Another non-collagenous protein, COMP, which is abundant within the digital flexor tendons of horses, shows marked changes with age and exercise. Levels are low at birth but rapidly increase with tendon growth during the first 2 years of life. Once maturity is reached, which is at approximately 2 years in tendon, levels rapidly decline but only within the tensile (metacarpal) regions of the digital flexor tendons.[27] The superimposition of exercise at this time results in a significant increase in the loss of COMP from this area of the tendon.[12] In contrast, levels of COMP within the low loaded tendons, such as the common digital extensor tendon are also low at birth but do not alter significantly with growth and aging[36] although exercise did alter levels in immature tendon (see below).

Metabolic changes

Recent studies investigating the distribution of the growth factor, TGF-β, a potent anabolic growth factor and stimulus for COMP synthesis *in vitro* has demonstrated reduction in the presence of the three isoforms of TGF-β after skeletal maturity, although TGF-β1, believed to be most associated with scar tissue formation in wound healing, remains prominent within the interfascicular (endotenon) tissue where age-associated thickening occurs.[59]

These findings have resulted in the hypothesis that the tensile region of the digital flexor tendons of the horse lose their ability to adapt to exercise after skeletal maturity and both age and exercise provoke degeneration in the tendon matrix, characterized by a loss in non-collagenous proteins. In support of this hypothesis, analysis of matrix gene expression in bovine digital flexor tendons has shown prominent matrix gene expression at birth and during growth but a complete absence of gene expression in the tensile (but not compressed) regions.[60] Interestingly, COMP levels are also maintained in the compressed regions of equine digital flexor tendons and this area is frequently spared clinical injury. The mechanism for this failure of tenocytes to produce tendon matrix in the adult is unclear, but might involve either an absence of appropriate growth factor stimulus or cellular senescence. Certainly, investigations into the synthetic response by equine tenocytes to mechanical load (biaxial stretch) and growth factors (TGF-β) in vitro have demonstrated little response to mechanical load alone.[13] TGF-β has a major effect on protein synthesis and, when combined with mechanical load, is synergistic. However, tenocytes recovered from aged flexor tendons do demonstrate a small, but significant, reduced response to load and TGF-β suggesting that the failure of an adaptive response in adult tendon is potentially due to a combination of the absence of growth factors and, to a small degree, cellular 'senescence'. Interestingly, this age effect is not apparent in tenocytes recovered from digital extensor tendons.

Mechanisms of strain-induced degeneration

The close association between age and exercise suggests that number of loading cycles is important. It is logical to presume that the highest loading rates are likely to be the most damaging, so the amount of time spent at the fastest gaits (canter and gallop) where strains can reach 16% with an initial strain rate of up to 200%/s are likely to be the most contributory for degeneration. To combat these deleterious effects of exercise, it has been proposed that the muscle of the SDFT primarily acts to fix the origin of the tendon and dampen the potentially harmful high frequency vibrations.[17]

The actual mechanism for the degeneration of the tendon is currently unknown although there are several possibilities. These mechanisms can be either physical or metabolic processes. The physical energy imparted to the tendon under weight-bearing load can produce direct damage to the matrix by disrupting cross-links or actual matrix proteins. An indirect physical effect of weight bearing is via the energy lost through hysteresis. This results in a temperature rise within the center of the tendon.[61] While the tenocytes in the superficial digital flexor tendon have been shown to be resistant to these temperature rises,[44] this temperature could still be damaging to matrix proteins. Loading cycles can induce cellular activity with potentially the release of proteolytic enzymes.[62] Furthermore, cleaved matrix proteins, generated either from direct physical forces or from enzymatic cleavage, can also provoke further matrix degradation.[63] Further work is necessary to elucidate the mechanisms of soft tissue degeneration so that preventative strategies can be developed.

Immature (growing) tendon

Although there appeared to be a failure in adaptive response to exercise in mature digital flexor tendon in the studies outlined above, is this also the case in immature tendon? Two recent studies have addressed this question – the first involving three different exercise regimes (box rest, box rest with enforced exercise (training), and pasture exercise) in Warmblood foals from 6 weeks to 5 months of age[64] and an increasing amount of treadmill exercise in Thoroughbred foals from 6 weeks to 15 months of age.[65]

Mechanical changes

In the Warmblood study, foals kept at pasture had significantly stronger tendons structurally at 5 months of age than the other two groups largely due to the development of a larger cross-sectional area (see below) as the ultimate tensile stress at rupture (material property) was not different between groups. By 11 months of age, after all three groups had received a 6-month period of low-level exercise, the differences between groups were largely no longer present.

Morphological changes

The recent study by Kasashima and colleagues[64] has documented a significant increase in the rate of increase in cross-sectional area of the superficial digital flexor tendon with treadmill exercise administered for only a small period each day in addition to pasture exercise. Interestingly, the variation in tendon cross-sectional area between limbs increased in both exercise and control groups towards the end of the study. In the study on Warmblood foals, the cross-sectional area was significantly larger at 5 months of age in the foals kept on pasture in comparison to those maintained on box rest or box rest with small bouts of enforced intense exercise. These differences were no longer significant at 11 months after all three groups had received a similar level of low-level exercise for 6 months.

Ultrastructural changes

Fetal and newborn equine SDFT has a uniform fibril size of moderate diameter (i.e. not universally small).[24,66] During growth, a bimodal distribution of fibril sizes, with the largest number of small (~40 nm) diameter fibrils and lower numbers of large fibrils (> 200 nm in diameter) becomes apparent within the first year of life.[66] These small fibrils may represent either new collagen fibrils waiting to be incorporated into larger fibrils, different collagen (type III has universally smaller fibril diameters than type I) or the disruption of larger diameter fibrils. This change in fibril diameter distribution appears to be influenced by loading and exercise, as different exercise regimes given to foals altered the time at which the small fibrils appeared.[66] Pasture exercise resulted in the most rapid appearance, with a predominance of small fibrils present by 5 months of age. Foals maintained in a box had a delayed onset of this 'adult' phenotype.

In comparison, treadmill exercise given to foals from 6 weeks to 15 months of age failed to alter the fibril diameter distribution between controls and exercised foals (Kasashima, personal communication) although these foals also had access to pasture exercise, which may have been sufficient to induce the bimodal distribution of fibrils.

Compositional changes

COMP levels have been found to be exquisitely sensitive to loading in vivo early in life. COMP failed to accumulate in the digital flexor tendons of an 11-week-old foal that had been non-weight-bearing on one limb for 6 weeks. This effect was not marked if the period of non-weight-bearing occurred after COMP had accumulated within the digital flexor tendons.[27]

In 5-month-old foals given pasture exercise, box rest, or box rest with enforced exercise (training) from 7 days of age demonstrated changes in molecular composition with respect to exercise.[66] Both COMP and PSGAG levels were lowest in the training group, suggesting that this exercise regimen was detrimental to tendon development. After normalizing the exercise across all groups for a further 6 months, there was only limited ability for the tendons to recover, although there were changes associated with growth, in particular increases in hyaluronic acid and COMP. Thus, early exercise is potentially the most important determinant of tendon development.

In contrast, in the exercise study performed by Kasashima and colleagues,[64] COMP levels were not altered in the SDFT although significant rises were induced in the CDET. This further supports earlier work in miniature swine by Woo and colleagues[54] who demonstrated a significant change in tissue properties for digital extensor tendons and ligaments but not digital flexor tendons. It may be that the load 'history' over the 15 months of exercise was not sufficiently different between the two groups to induce a significant change in the digital flexor tendons.

Metabolic changes

TGF-β isoform expression was found both within and between fascicles in young tendon, mainly pericellular in location.[59] Interestingly, PCR analysis of TGF-β gene expression showed no growth factor expression after birth, except when the tendon was injured, suggesting that the tendon TGF-β stores are fixed and limited at birth.

These investigations suggest that tendon is able to respond to exercise during growth. However, this response appears to be dependent on the exercise regimes. In the study using Warmblood foals,[64] pasture (constant) exercise appeared to produce a better quality tendon than that resulting from either box rest (limited, low level, exercise) or enforced exercise with box rest (limited, but high level, exercise). Some, but not complete, recovery appeared to be possible between 5 and 11 months when the animals were allowed low-level free exercise. This study also confirmed that the 'window of opportunity' for tendon adaptation appeared to be early in the life of the animal.

The minimal changes induced by additional, albeit small, amount of treadmill exercise suggested that the natural exercise level at pasture may be optimal for tendon development. Certainly, the gamboling activities of foals at pasture would appear to be ideally suited for high strain rate controlled loading of the digital flexor tendons (Fig. 8.13). It may be that both time and intensity 'windows of opportunity' exist above or past which further augmentation of tendon properties can not be achieved.

Fig. 8.13
Gamboling activity of foals at pasture may be ideally suited to the development of tendons (courtesy of Dr Yoshinori Kasashima, Japan Racing Association).

Tendon injury and repair

Gross damage and mechanical failure

With the advent of clinical injury, the extent of the damage to the matrix varies from disruption of fibrillar cross-links (covalent and electrostatic), to individual fiber ruptures and ultimately failure of the entire tendon. This damage can be focal or generalized and one of the more common manifestations of superficial digital flexor tendinitis is a centrally located region of injury (so-called 'core' lesion seen ultrasonographically; Fig 8.14), usually with the most severe level being just below the midmetacarpal region but also extending throughout most of the length of the metacarpal extrasynovial tendon. Regions of the SDFT enclosed within a tendon sheath (carpal sheath proximally; digital sheath distally) are usually much less severely affected, although this can be relatively more common when the metacarpal region has been previously injured.

Desmitis of the accessory ligament of the DDFT can occur as an isolated injury or in conjunction with superficial digital flexor tendinitis. Its pathogenesis is therefore more related to the SDFT than the DDFT to which it attaches. While ponies rarely suffer strain-induced tendinopathy, they do have a relatively high incidence of desmitis of the accessory ligament of the DDFT.

The SL can fail at any site along its length, although certain areas are more common in horses used in different disciplines. Thus, race horses tend to suffer lesions of the body (and branches) of the SL, while sports horses more frequently have pathology centered within the proximal or branch regions of the ligament.

In contrast to the SDFT and SL, the deep digital flexor tendon (DDFT) is most frequently injured within the digital sheath. It is not known whether these injuries have a preceding phase of tendon degeneration but many are potentially due to single loading cycles which induce overstrain damage. Consequently, bilateral pathology is rarer. Two manifestations are seen clinically. The first arises within the substance of the tendon (although it may extend to the borders of the tendon), which is similar to other clinical manifestations of tendinitis. The second arises at the medial or lateral borders of the tendon, usually in the region of the metacarpo/metatarsophalangeal joint, with no, or limited, involvement of the internal substance of the tendon. These tendon 'tears' are thought to arise from 'bursting' pressures within the tendon when the metacarpo/metatarsophalangeal joint is overextended.

Other tendons can suffer from strain-induced injury, although much less commonly than that affecting the palmar soft tissue structures of the metacarpus. Ligament injuries tend to occur when the joint they span is loaded inappropriately to result in a degree of subluxation.

Repair processes in tendon

Once the tendon suffers clinical injury with disruption of the tendon matrix, there is intratendinous hemorrhage initially, usually followed rapidly by a pronounced inflammatory reaction. This inflammatory reaction results in an increase in blood flow, the development of edema, infiltration of neutrophils, macrophages and monocytes, and the release of proteolytic enzymes. While this is the earliest stage of repair, designed to remove damaged tendon tissue, the response is usually excessive, causing further damage to the tendon. This inflammatory phase is usually short lived but, within a few days, the reparative phase of repair begins. This results in a pronounced angiogenic response and the synthesis of scar tissue. This tissue has a different composition to tendon, having a higher ratio of collagen types III/I (~50% cf. 10% for normal tendon; Birch, personal communication), higher levels of glycosaminoglycans and much lower levels of COMP.[27]

The reparative phase of tendon healing merges with the remodeling phase when there is a gradual, but incomplete transformation of collagen type III to I as the scar tissue matures.[67] The new collagen fibrils become thicker and cross-linked. Even mature scar tissue tends to be less stiff as a material than tendon, but because large amounts are formed, the scarred tendon often becomes stiffer as a structure than the original tendon.[15]

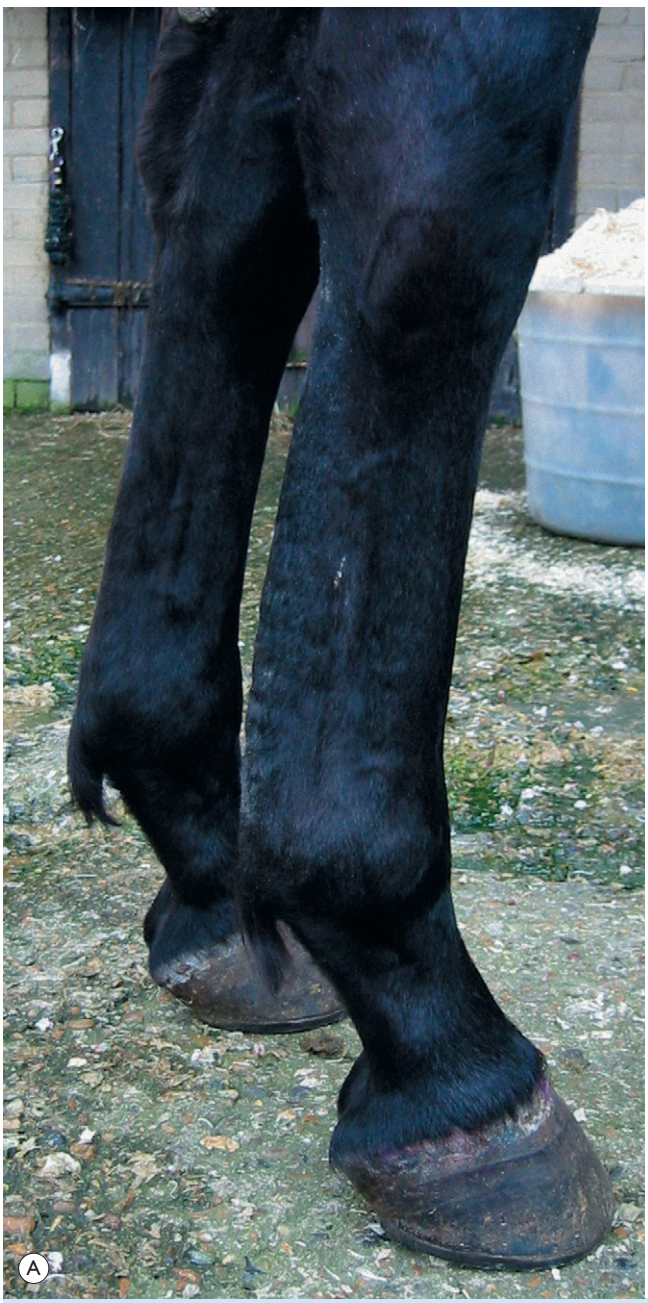
Diagnosis

Diagnosis of tendon injury is usually based on history (frequently a preceding bout of intense exercise) and the development of the signs of inflammation (pain, heat, swelling and lameness) over the affected structure (Fig. 8.14). Lameness may not always be present and tends to be related to the degree of inflammation rather than the degree of damage. In many cases, however, the onset of clinical tendinitis is associated with severe lameness.

The posture of the limb may be altered depending on the structure damaged and the severity of the injury. In the

case of severe superficial digital flexor tendinitis, resting metacarpophalangeal joint angle may be normal because of the action of the other supporters of this joint (SL and DDFT). However, when loading on the limb increases (e.g. when the contralateral limb is raised), the affected limb shows greater than normal overextension of the metacarpophalangeal joint. Severe damage to the SL will have greater effect on metacarpophalangeal joint extension.

For more subtle cases, careful palpation of the tendons in the limb should be made both with the limb weight bearing and



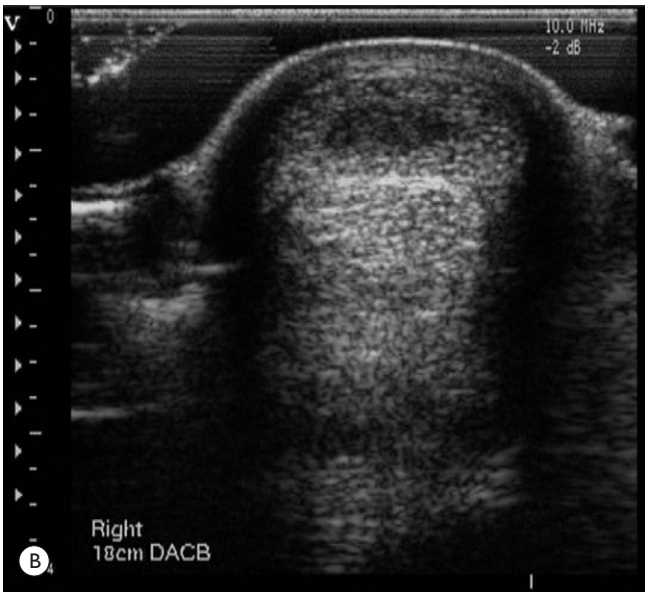


Fig. 8.14
(A) Clinical, (B) ultrasonographic, and (C) post-mortem appearance of the 'core' lesion – a common manifestation of superficial digital flexor tendinitis (SDFT).

raised. Careful attention should be made to pain response, subtle enlargement and consistency of the structure (soft after recent injury; firm after healing). The horse must be relaxed so that muscle activity does not tense the tendons and make them appear artificially firm. Careful visual assessment of 'bowing' of the palmar contour of the metacarpal region can help to identify subtle superficial digital flexor tendinitis.

Clinical examination, however, may not detect the most subtle injuries and assessment of the severity is limited by clinical examination alone. As prognosis is most dependent on the severity of the initial injury, it is prudent to evaluate the damaged area ultrasonographically and this is best carried out 4–7 days after the onset of the injury as many lesions expand during the initial few days. Modern ultrasound machines with a 7.5–10 MHz linear transducer produce excellent quality images of the flexor tendons and SL (see Chapter 20). While the metacarpal region can be evaluated ultrasonographically without clipping the hair, it is recommended to prepare the limb by clipping and washing (with a surgical scrub and spirit) to give the best-quality images. The horse should be standing square and both transverse and longitudinal images obtained in a methodical fashion throughout the length of the region containing the injured tendon. For the metacarpal region, the area is divided up into seven levels or zones, each with characteristic anatomy. Alternatively, the distance between the transducer and the accessory carpal bone can be recorded. The palmar soft tissue structures of the metacarpus can be evaluated satisfactorily from the palmar aspect of the limb, except for the SL branches which should also be evaluated from the medial and lateral aspects of the limb. Both limbs should *always* be examined as many cases of strain-induced tendon injury have bilateral components but with one limb more severely affected than the other.

Acute tendon pathology is manifest ultrasonographically by enlargement, hypoechogenicity (focal, e.g. 'core' lesion; see Fig. 8.14, or generalized), reduced striated pattern in the longitudinal images, and changes in shape, margin, or position. Chronic tendinopathy is associated with variable enlargement and echogenicity (often heterogeneous), and a reduced irregular striated pattern indicative of fibrosis.

Markers of tendon injury

When a tendon is injured, proteins are released from the tendon into either a surrounding synovial fluid (for intrathecal injuries) and/or the blood (for extrathecal injuries). It is potentially possible to detect these released proteins in either tendon sheath synovial fluid or blood which could then be used as a molecular marker of tendon disease.

The development of a specific assay for a molecular marker of tendon injury relies on one of two different approaches. One alternative is to identify a protein which is specific for tendon tissue and released into the bloodstream following injury. Studies on the molecular composition of tendon using 2D gel electrophoresis (Smith & Heinegård, personal communication) have demonstrated that there are many similarities between the proteins present in cartilage and tendon and few, if any, specific for tendon tissue, making this approach less viable at present.

The second alternative is to identify a protein that is not specific to tendon but whose distribution is restricted and/or whose fragmentation with injury is specific for tendon injury. One such protein is COMP, which has a restricted distribution to tendon, ligament, cartilage, intervertebral disk, and meniscus. Furthermore, COMP is particularly abundant in young midmetacarpal SDFT, the area most prone to injury. After skeletal maturity, the natural decrease in COMP levels within the metacarpal region of the SDFT can be accelerated by exercise.[12] These findings suggest that it might be a useful indicator of tendon damage if, once it is released from the metacarpal region of the SDFT, it gains access to the bloodstream and can subsequently be assayed. COMP is not significantly absorbed by the peripheral lymph nodes (cf. proteoglycan fragments; Frazer et al, unpublished data) and COMP fragments are found in the serum in humans.[68] While studies in man have demonstrated that COMP has potential usefulness as a marker of joint disease,[69] assay of the total amount of COMP in serum showed no significant alterations in COMP levels with tendon disease,[68] although there were significant increases associated with the commencement of training (Smith & Bathe, unpublished data). This assay quantifies COMP using a polyclonal antiserum that recognizes a number of epitopes on the COMP molecule. There is a normal significant background level of COMP in the serum (1–2 μg/mL), possibly representing the normal turnover of COMP from all tissues containing the protein. Certainly there are considerably higher levels of total COMP in the serum of growing horses compared to adults,[68] when COMP is being accumulated in the tissues. In addition, damage to cartilage in joint disease also contributes to the 'pool' of COMP in the serum and is therefore responsible for a reduction in the sensitivity of the assay for tendon disease itself.

However, COMP levels in digital sheath synovial fluid in horses with intrasynovial tendon injury demonstrated significant rises. We know from previous studies that there is < 1/100 the level of COMP in the digital sheath capsule,[27] so that rises observed in the digital sheath synovial fluid (approximately four times normal levels) suggest that COMP is lost from the intrasynovial tendon rather than the digital sheath. The COMP released within the digital sheath synovial fluid is composed of fragments which have been identified on SDS–PAGE after partial purification with ion exchange chromatography. This fragmentation pattern is different from that described for human joint diseases,[69,70] although may not be in the horse. These fragments represent ideal candidates for markers of tendon disease. Assay of these fragments, not normally present, would potentially enable a very sensitive assay to be developed.

In addition to proteins released after injury being useful for the detection of tendon damage, the healing process can also potentially be monitored using markers of protein synthesis. While serological markers of collagen synthesis (e.g. propeptide of collagen type I; PICP) were thought to be relatively specific for bone remodeling, recent studies have demonstrated significant rises of PICP following tendon injury.[71] Further work is necessary to determine if this molecular marker will be useful for the monitoring of tendon repair.

Review of current treatment strategies

Over the years, many treatment modalities have been tried with most showing equivocal or even deleterious effects. From our knowledge of the phases of tendon healing, the following have at least a rationale for treating tendinitis.[72]

Acute (inflammatory) phase

Physical therapy (rest, application of cold, and compression with bandaging) is the most important aspect of early management where the goal is to minimize inflammation and limit the action of proteolytic enzymes that continue to destroy tendon tissue (see Chapter 25). Pharmacologic interventions include short-acting steroids within the first 24–48 h (later application can inhibit the second phase of fibroplasia) and the use of polysulfated glycosaminoglycans, which have been shown to inhibit prostaglandin E2 production in vitro.[73] The intralesional use of steroids should be avoided as this has been associated, at least with depot preparations, with intratendinous calcification. Surgical treatment at this stage includes percutaneous tendon splitting, which has been shown to accelerate the resolution of the 'core' lesion seen ultrasonographically.[74] This can be done with a scalpel or, less invasively, performed with needle puncture, when it can be combined with intratendinous polysulfated glycosaminoglycan therapy. Desmotomy of the accessory ligament of the SDFT, often performed concurrently with percutaneous tendon splitting early on in the disease process, is suggested to reduce peak strains on the SDFT by bringing the superficial digital flexor muscle into play.[75] However, although initial data suggested a beneficial effect,[76] this has not been confirmed in other studies and has been suggested to contribute to a higher incidence of suspensory desmitis after its use.[77]

Subacute (fibroblastic) phase

Early and progressive mobilization and regular ultrasonographic monitoring aims to improve the quality of the forming scar tissue – the goal of this phase. If the cross-sectional area of the healing tendon increases by more than 10%, the exercise level should be reduced. The quality of the longitudinal fiber pattern when the animal returns to full work has been linked with the overall prognosis.[78] In an attempt to improve the quality of the scar tissue, β-aminoproprionitrile fumarate (BAPTEN™; no longer marketed for the treatment of tendon injuries) has been injected intratendinously 30–90 days after injury.[78] This drug inhibits lysyl oxidase, the enzyme that cross-links collagen molecules. In preventing the formation of cross-links, it is believed that collagen fibers will form with better longitudinal alignment under the stimulus of controlled exercise. When the drug wears off, cross-linking occurs and the scar increases in strength. Clinical trials in the USA indicated a benefit in the more severe cases.

Other drugs, such as sodium hyaluronate, have been used both intratendinously and peritendinously but studies have shown equivocal results. Some benefit in reducing adhesion formation in intrasheath tendon injuries has been demonstrated experimentally.

Newer treatments aimed at regenerating rather than repairing tendon represent the best hope for the future. Anabolic growth factors, such as IGF-1,[79] recombinant equine growth hormone,[80] and TGF-β have been tried empirically or in a collagenase model of tendon injury, but not comprehensively evaluated in the clinical situation, making interpretation of the benefits of these agents difficult. An important factor in assessing these new treatments is that they do actually generate tendon-like tissue rather than just increasing the amount of scar tissue produced, which will still compromise the outcome. One of the most exciting new developments is the use of mesenchymal stem cells (recovered from bone marrow)[81,82] although much work is still necessary to determine their effectiveness.

Chronic (remodeling) phase

A controlled ascending exercise program with regular ultrasonographic examinations encourages the further optimization of the scar tissue. In addition, ultrasound can enable the detection of early signs of reinjury to minimize the risk of catastrophic reinjury. Other methods aimed at preventing reinjury include desmotomy of the accessory ligament of the SDFT (see 'Acute phase' treatments) and the use of boots capable of providing significant support to the metacarpophalangeal joint. Traditional bandages fail to provide sufficient support under weight-bearing load, while novel designed boots have been shown to do so and potentially may help to prevent reinjury[83] (Fig. 8.15).

Specific therapies

Some tendon and ligament injuries have specific therapies in addition to those outlined above. DDFT tears within the digital sheath and SL tears into the metacarpo/metatarsophalangeal joint are best treated by tenoscopic/arthroscopic debridement. The outcome of hindlimb, but not forelimb, proximal suspensory desmitis appears to be improved (from 13% to 43%) by the use of extracorporeal shock wave therapy.[84,85] For those cases of hindlimb proximal suspensory desmitis also failing to respond to shock wave therapy, surgical neurectomy of the lateral plantar nerve combined with transection of the fascia overlying the proximal suspensory ligament provides an additional rational management technique. Both these latter two treatments are consistent with the hypothesis that hindlimb proximal suspensory desmitis is an example of a compartmental syndrome, unlike the forelimb (which carries a considerably better prognosis with conservative management alone).

Current concepts in prevention of tendinitis in the equine athlete

Strategies for the prevention of equine tendinitis

With the limitation of our ability with current treatments to return a horse with tendinitis to full work without danger of reinjury, prevention of the injury has to be considered as the most appropriate strategy. From our understanding of tendon physiology described in the preceding sections, four broad approaches for prevention can be considered.

Maximize the quality of the tendon prior to skeletal maturity

There is a large variation in the strength of the SDFT in a population of horses. Some of this variation may be due to specific genes. Either breeding out, or identifying horses with, those genetic variants associated with a genetic susceptibility to tendinitis would potentially lower the incidence of tendon injury. However, while the concept is simple, its achievement is considerably more difficult.

Skeletal tissues are much more able to adapt to the loads placed on them when they are immature and growing. This is certainly true for bone and muscle and we believe it to also be the case in tendon. Thus, carefully tailored exercise regimes during growth (0–2 years of age) would potentially improve the 'quality' of the tendon and minimize the effects of degeneration induced by training and racing after skeletal maturity (approximately 2 years of age in the horse) (Fig. 8.16). These exercise regimes must be within the 'windows of opportunity' of the right time and the right level. Growing tendon is also more susceptible to injury so these 'conditioning' programs have to induce adaptation suitable for subsequent racing without causing injury. However, the optimal prop-erty of equine tendon still needs to be deter-mined. Probably the most important characteristic would be fatigue resist-ance and, for any exercise regime in immature animals to be effective, it must demonstrate a reduction of tendon injuries within the subsequent athletic careers. The answers to these questions are not known but studies

Fig. 8.15
(A, B) Dalmar support boot capable of being used in the exercising horse and able to provide significant support to the metacarpophalangeal joint, unlike traditional bandages. This may provide a method of minimizing reinjury after rehabilitation (courtesy of the *Equine Veterinary Journal*, reproduced with permission).

are underwayto assess the effects of early exercise on musculoskeletal development.

Reduce the degeneration after skeletal maturity

Studies are turning towards investigating the mechanisms of aging in soft tissues, which may give therapeutic options for intervening in the aging process. At present, the only advice that can be given in this area is to avoid training solely aimed at the tendon in the adult horse. This will serve only to advance the rate of degeneration, which has to be considered an inevitable consequence of athleticism. Some forms of exercise may be more provocative of degeneration than others, but, at present, these are not known. However, high loading (i.e. fast speeds) is likely to be the most damaging.

Reduce the risk factors for tendinitis

The initiation of clinical tendinitis is provoked by sudden peak forces that overcome the strength of the (degenerated) tendon. This can obviously occur at any time, including out at pasture, but it is obviously most likely when the horse is loading its tendon maximally. This occurs when the horse is running fastest (hence the best horses are potentially more prone to tendon injury). Ground surface (which affects the horse's speed), fatigue (e.g. after longer races or in unfit horses), jumping, shoeing, and weight are all examples of factors that can increase the peak loading on the tendon and hence are risk factors for tendon injury. Some of these are rectifiable but others are a consequence of racing and not easily altered.

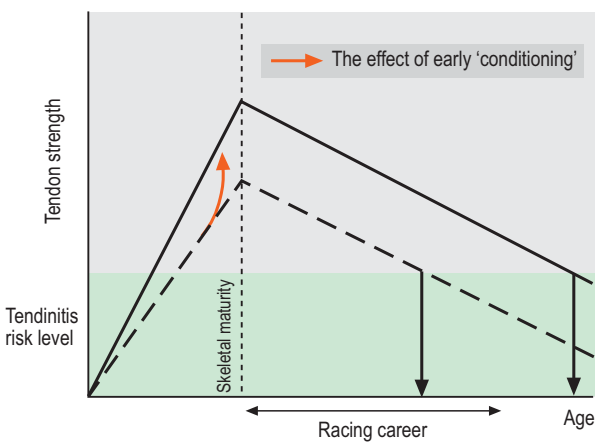


Fig. 8.16
Hypothetical response of tendons to the early introduction of exercise. The two lines refer to two different horses – one that develops poor-quality tendon during growth (dashed line) and one that develops good-quality tendon (solid line). Both accumulate damage within the tendon associated with postskeletal exercise and aging, which inevitably and progressively weakens the tendon. However, in the former, this weakening precedes the individual to clinical tendinitis within its racing career, whereas the latter is able to survive its racing career without suffering such injury. The imposition of 'appropriate' conditioning exercise during growth is hypothesized to improve the quality of the growing tendon, resulting in an individual more resistant to subsequent injury (courtesy of the *Journal of Comparative Biochemistry and Physiology*, reproduced with permission).

Early detection

This is not really a prevention strategy, as, by definition, a degree of tendon injury will already have occurred. However, if tendon injury can be detected very early, it is possible to prevent progression to more severe disease. Obviously, careful clinical inspection is vital in this area, but this is rather insensitive.

Ultrasonography has been the mainstay of tendon imaging and has advanced our knowledge and capabilities for management considerably. Ultrasonographic technology is still advancing and new machines have even better resolution. However, they are still relatively insensitive for predicting injury and the ideal time for a return to full work in the chronic stages. Furthermore, it is time-consuming and (frequently) requires the limbs to be clipped.

Future techniques in this area may rely on molecular markers of tendon injury. Fragments of proteins within the tendon, which are released with injury, can potentially be assayed for in the blood, which would give a practical test that would provide useful diagnostic, management, and prognostic information.

Recommendations for training of immature and mature animals

Pasture exercise early in life is essential for the development of digital flexor tendon that is likely to be most resistant to injury during adulthood. Additional imposed exercise may be able to augment this effect but the tendon is also more susceptible to injury at this age and so exercise levels have to be chosen with care. In addition, what about the other skeletal tissues? How do they respond to these exercise regimes? It would be pointless to develop a training regime beneficial for tendon but harmful to other tissues, such as bone and joints. However, different skeletal tissues mature at different times, thus potentially allowing different time 'windows of opportunity' for different tissues. We would suggest that tendon, ligament, and possibly cartilage are most responsive in the first year of life, while bone is more responsive at the yearling stage.

After skeletal maturity, training will have no effect on tendon adaptation and therefore training should be directed at muscular, respiratory, and cardiovascular fitness rather than the tendon.

References

1. Batson EL, Paramour RJ, Smith TJ, Birch HL, Patterson-Kane JC, Goodship AE. Are the material properties and matrix composition of equine flexor and extensor tendons determined by their functions? Equine Vet J 2003; 35:314–318.
2. Williams RB, Harkins LS, Hammond CJ, Wood JLN. Racehorse injuries, clinical problems and fatalities recorded on British racecourses from flat racing and National Hunt racing during 1996, 1997, and 1998. Equine Vet J 2001; 33:478–486.
3. Wilson JH, Robinson RA, Jensen RC, McArdle CJ. Equine soft tissue injuries associated with racing: descriptive statistics from American racetracks. In: Rantanen NW, Hauser ML, eds. Proceedings of the Dubai Equine International Symposium, 1996.
4. Pickersgill C. Epidemiological studies into orthopaedic conditions of the equine athlete. 2000 MVM thesis, University of Glasgow.
5. Gibbon WW, Cooper JR, Radcliffe GS. Sonographic incidence of tendon microtears in athletes with chronic Achilles tendinosis. Br J Sports Med 1999; 33:129–130.
6. Moller A, Astron M, Westlin N. Increasing incidence of Achilles tendon rupture. Acta Orthop Scand 1996; 67:479–481.
7. Houshian S, Tscherning T, Riegels-Nielsen P. The epidemiology of Achilles tendon rupture in a Danish county. Injury 1998; 29:651–654.
8. Maffulli N, Waterston SW, Squair J, Reaper J, Douglas AS. Changing incidence of Achilles tendon rupture in Scotland: a 15-year study. Clin J Sport Med 1999; 9:157–160.
9. Webbon PM. Post mortem study of equine digital flexor tendons. Equine Vet J 1977; 9:61–67.
10. Goodship AE, Birch HL, Wilson AM. The pathobiology and repair of tendon and ligament injury. Vet Clinics N Am: Equine Pract 1994; 10:323–349.
11. Jones AJ. Normal and diseased equine digital flexor tendon: blood flow, biochemical and serological studies. PhD thesis, University of London, 1993.
12. Smith RKW, Birch HL, Patterson-Kane J, et al. Should equine athletes commence training during skeletal development? Changes in tendon matrix associated with development, ageing, function and exercise. Equine Vet J 1999; Suppl 31:201–209.
13. Smith RKW, Birch HL, Goodman S, et al. The influence of ageing and exercise on tendon growth and degeneration – hypotheses for the initiation and prevention of strain-induced tendinopathies. Comp Biochem Physiol A Mol Integr Physiol 2002; 133:1039–1050.
14. Tsuzaki M, Guyton G, Garrett W, et al. IL-1 induces COX2, MMP-1, -3, and -13, ADAMTS-4, IL-1beta and IL-6 in human tendon cells. J Orthop Res 2003; 21:256–264.
15. Crevier-Denoix N, Collobert C, Pourcelot P, et al. Mechanical properties of pathological equine superficial digital flexor tendons. Equine Vet J 1997; Suppl 23:23–26.
16. McGuigan MP, Wilson AM. The effect of gait and digital flexor muscle activation on limb compliance in the forelimb of the horse *Equus caballus*. J Exp Biol 2003; 206: 1325–1336.
17. Wilson AM, McGuigan MP, Su A, van Den Bogart AJ. Horses damp the spring in their step. Nature 2001; 414:895–899.
18. Kraus-Hansen AE, Fackelman GE, Becker C, et al. Preliminary studies on the vascular anatomy of the equine superficial digital flexor tendon. Equine Vet J 1992; 24:46–51.
19. Strömberg B, Tufvesson G. Lesions of the superficial flexor tendons in racehorses. A microangiographic and histopathologic study. Clin Orthop 1969; 62:113–123.
20. Banes AJ, Donlon K, Link GW, et al. Cell populations of tendon: a simplified method for isolation of synovial cells and internal fibroblasts: confirmation of origin and biologic properties. J Orthop Res 1988; 6:83–94.
21. McNeilly CM, Banes AJ, Benjamin M, Ralphs JR. Tendon cells in vivo form a three dimensional network of cell processes linked by gap junctions. J Anat 1996; 189:593–600.
22. Kadler KE, Holmes DF, Graham H, Starborg T. Tip-mediated fusion involving unipolar collagen fibrils accounts for rapid fibril elongation, the occurrence of fibrillar branched networks in skin and the paucity of collagen fibril ends in vertebrates. Matrix Biol 2000; 19:359–365.
23. Canty EG, Kadler KE. Collagen fibril biosynthesis in tendon: a review and recent insights. Comp Biochem Physiol A Mol Integr Physiol 2002; 133:979–985.
24. Parry DAD, Craig AS, Barnes GRG. Tendon and ligament from the horse: an ultrastructural study of collagen fibrils and elastic fibres as a function of age. Proc R Soc London B Biol Sci 1978; 203:293–303.
25. Patterson-Kane JC, Parry DA, Birch HL, et al. An age-related study of morphology and cross-link composition of collagen fibrils in the digital flexor tendons of young thoroughbred horses. Connect Tissue Res 1997; 36:253–260.
26. Smith RKW, Gerard M, Dowling B, et al. Correlation of cartilage oligomeric matrix protein (COMP) levels in equine tendon with mechanical properties: a proposed role for COMP in determining function-specific mechanical characteristics of locomotor tendons. Equine Vet J 2002; Suppl 34:241–244.
27. Smith RKW, Zunino L, Webbon PM, Heinegård D. The distribution of cartilage oligomeric matrix protein (COMP) in tendon and its variation with tendon site, age, and load. Matrix Biol 1997; 16:255–271.
28. Rosenberg K, Olsson H, Mörgelin M, Heinegard D. Cartilage oligomeric matrix protein shows high affinity zinc-dependent interaction with triple helical collagen. J Biol Chem 1998; 273:20397–20403.
29. Rosenberg K. Cartilage oligomeric matrix protein (COMP): Functions in collagen binding and assembly. PhD thesis, University of Lund, Sweden, 2001.
30. Briggs MD, Hoffman SMG, King LM, et al. Pseudoachondroplasia and multiple epiphyseal dysplasia due to mutations in the cartilage oligomeric matrix protein gene. Nature Genetics 1995; 10:330–336.
31. Danielson KG, Baribault H, Holmes DF, et al. Targeted disruption of decorin leads to abnormal collagen fibril morphology and skin fragility. J Cell Biol 1997; 136:729–743.
32. Svensson L, Aszodi A, Reinholt FP, et al. Fibromodulin-null mice have abnormal collagen fibrils, tissue organization, and altered lumican deposition in tendon. J Biol Chem 1999; 274:9636–9647.
33. Svensson L. The role of leucine-rich repeat glycoproteins/proteoglycans in the assembly of collagen matrices. PhD thesis, University of Lund, Sweden, 1999.
34. Evanko SP, Vogel KG. Ultrastructure and proteoglycan composition in the developing fibrocartilagenous region of bovine tendon. Matrix 1990; 10:420–436.
35. Vogel KG, Koob TJ. Structural specialisation in tendons under compression. Int Review Cytol 1989; 115:267–293.
36. Batson EL, Smith RKW, Patterson-Kane JC, Goodship AE. Postnatal development initiates rapid tendon specific structural changes associated with a dramatic increase in cartilage oligomeric matrix protein (COMP). Transactions of the 49th Annual Meeting of the Orthopedic Research Society, 2003.

37. Screen HR, Lee DA, Bader DL, Shelton JC. Development of a technique to determine strains in tendons using cell nuclei. Biorheology 2003; 40:361–368.
38. Viidik A. Tensile strength properties of Achilles tendon systems in trained and untrained rabbits. Acta Orthop Scand 1969; 40:261–272.
39. Woo SL-Y. Mechanical properties of tendons and ligaments: I. Quasi-static and nonlinear viscoelastic properties. Biorheology 1982; 19:385–396.
40. Crevier N, Pourcelot P, Denoix JM, et al. Segmental variations of in vitro mechanical properties in equine superficial digital flexor tendons. Am J Vet Res 1996; 57:1111–1117.
41. Riemersma DJ, van den Bogert AJ, Jansen MO, Schamhardt HC. Tendon strain in the forelimbs as a function of gait and ground characteristics and in vitro limb loading in ponies. Equine Vet J 1996; 28:133–138.
42. Stephens PR, Nunamaker DM, Butterweck DM. Application of a Hall-effect transducer for the measurement of tendon strain in horses. Am J Vet Res 1989; 50:1089–1095.
43. Wilson AM, Goodship AE. Exercise-induced hyperthermia as a possible mechanism for tendon degeneration. J Biomech 1993; 27:899–905.
44. Birch HL, Wilson AM, Goodship AE. The effect of exercise-induced localised hyperthermia on tendon cell survival. J Exp Biol 1997; 200:1703–1708.
45. Gelberman R, Goldberg V, An K-N, Banes A. Tendon. In: Woo SL-Y, Buckwalter JA, eds. Injury and repair of musculoskeletal soft tissues. Park Ridge, IL, American Academy of Orthopaedic Surgeons; 1987:5–40.
46. Minetti AE, Ardigo LP, Reinach E, Saibene F. The relationship between mechanical work and energy expenditure of locomotion in horses. J Exp Biol 1999; 202:2329–2338.
47. Birch HL, Smith TJ, Lawes TJ, Goodship AE. Mechanical properties of equine flexor tendons show symmetry between right and left forelimbs within individuals but a wide variation in strength and stiffness between individuals. Proceedings of the XVIIth FECTS Meeting, Patras, Greece, 2000.
48. Maganaris CN. Tensile properties of in vivo human tendinous tissue. J Biomech 2002; 35:1019–1027.
49. Wilmink J, Wilson AM, Goodship AE. Functional significance of the morphology and micromechanics of collagen fibres in relation to partial rupture of the superficial digital flexor tendon. Res Vet Sci 1992; 53:354–359.
50. Patterson-Kane JC, Firth EC, Goodship AE, Parry DAD. Age-related differences in collagen crimp patterns in the superficial digital flexor tendon core region of untrained horses. Aust Vet J 1997; 75:39–44.
51. Patterson-Kane JC, Wilson AM, Firth EC, et al. Exercise-related alterations in crimp morphology in the central regions of superficial digital flexor tendons from young thoroughbreds: a controlled study. Equine Vet J 1998; 30:61–64.
52. Gillis C, Pool RR, Meagher DM, et al. Effect of maturation and aging on the histomorphometric and biochemical characteristics of equine superficial digital flexor tendon. Am J Vet Res 1997; 58:425–430.
53. Birch HL, McLaughlin L, Smith RKW, Goodship AE. Treadmill exercise-induced tendon hypertrophy: assessment of tendons with different mechanical functions. Equine Vet J 1999; Suppl 30:222–226.
54. Gillis C, Meagher DM, Pool RR, et al. Ultrasonographically detected changes in equine superficial digital flexor tendons during the first months of race training. Am J Vet Res 1993; 54:1797–1802.
55. Patterson-Kane JC, Wilson AM, Firth EC, et al. Comparison of collagen fibril populations in the superficial digital flexor tendons of exercised and nonexercised thoroughbreds. Equine Vet J 1997; 29:121–125.
56. Birch HL, Wilson AM, Goodship AE. Physical training induces alterations in tendon matrix composition which are structure specific. Proceedings of the British Orthopedic Research Society, 1997.
57. Birch HL, Bailey AJ, Goodship AE. Macroscopic 'degeneration' of equine superficial digital flexor tendon is accompanied by a change in extracellular matrix composition. Equine Vet J 1998; 30:534–539.
58. Cauvin ERJ. An investigation into the roles of transforming growth factor-beta (TGFβ) in the development, adaptation and repair of equine tendons. PhD Thesis, University of London, 2001.
59. Perez-Castro AV, Vogel KG. In situ expression of collagen and proteoglycan genes during development of fibrocartilage in bovine deep flexor tendon. J Orthop Res 1999; 17:139–148.
60. Wilson AM, Goodship AE. Exercise induced hyperthermia as a possible mechanism for tendon degeneration. J Biomech 1993; 27:899–905.
61. Archambault J, Tsuzaki M, Herzog W, Banes AJ. Stretch and interleukin 1beta induce matrix metalloproteinases in rabbit tendon cells in vitro. J Orthop Res 2002; 20:36–39.
62. Homandberg GA. Cartilage damage by matrix degradation products: fibronectin fragments. Clin Orthop 2001; 391:S100–S107.
63. van Weeren PR, Barneveld A. Study design to evaluate the influence of exercise on the development of the musculoskeletal system of foals up to age 11 months. Equine Vet J 1999; Suppl 31:4–8.
64. Kasashima Y, Smith RKW, Birch HL, et al. Exercise-induced tendon hypertrophy: cross-sectional area changes during growth are influenced by exercise. Equine Vet J 2002; Suppl 34:264–268.
65. Cherdchutham W, Becker C, Smith RKW, et al. Age-related changes and effect of exercise on the molecular composition of immature equine superficial digital flexor tendons. Equine Vet J 1999; Suppl 31:86–94.
66. Woo SL-Y, Gomez MA, Woo Y-K. Mechanical properties of tendons and ligaments. II. The relationships of immobilisation and exercise on tissue remodelling. Biorheology 1982; 19:397–408.
67. Watkins JP, Auer JA, Gay S, Morgan SJ. Healing of surgically created defects in the equine superficial digital flexor tendon: collagen-type transformation and tissue morphologic reorganisation. Am J Vet Res 1985; 46:2091–2096.
68. Smith RKW, Heinegård D. Cartilage oligomeric matrix protein levels in digital sheath synovial fluid and serum with tendon injury. Equine Vet J 2000; 32:52–58.
69. Saxne T, Heinegård D. Cartilage oligomeric matrix protein: a novel marker of cartilage turnover detectable in synovial fluid and blood. Br J Rheum 1992; 31:583–591.
70. Neidhart M, Hauser N, Paulsson M, et al. Small fragments of cartilage oligomeric matrix protein in synovial fluid and serum as markers for cartilage degradation. Br J Rheumatol 1997; 36:1151–1160.
71. Jackson BF, Smith RKW, Price JS. A molecular marker of type I collagen metabolism reflects changes in connective tissue remodelling associated with injury to the equine superficial digital flexor tendon. Equine Vet J 2003; 35:211–213.
72. Dowling BA, Dart AJ, Hodgson DR, Smith RKW. Superficial digital flexor tendinitis in the horse. Equine Vet J 2000; 32:369–378.
73. Frean SP, Lees P. Effects of polysulfated glycosaminoglycan and hyaluronan on prostaglandin E2 production by cultured equine synoviocytes. Am J Vet Res 2000; 61:499–505.
74. Henninger R, Bramlage LR, Schneider R. Short term effects of superior check ligament desmotomy and percutaneous tendon

splitting as a treatment of acute tendinitis. Proc Am Ass Equine Practitioners 1990; 36:539–540.
75. Bramlage LR. Superior check ligament desmotomy as a treatment for superficial digital flexor tendinitis. Proc Am Ass Equine Practitioners 1986; 32:365.
76. Bramlage LR, Rantanen NW, Genovese RL, Page LE. Long term effects of surgical treatment of superficial digital flexor tendinitis by superior check ligament desmotomy. Proc Am Ass Equine Practitioners 1988; 34:655–656.
77. Gibson KT, Burbidge HM, Pfeiffer DU. Superficial digital flexor tendinitis in thoroughbred race horses: outcome following non-surgical treatment and superior check desmotomy. Aust Vet J 1997; 75:631–635.
78. Reef VB, Genovese RL, Davis WM. Initial long term results of horses with superficial digital flexor tendinitis treated with intralesional beta-aminoproprionitrile fumarate. Proc Am Ass Equine Practitioners 1997; 43:301–305.
79. Dahlgren LA, van der Meulen MC, Bertram JE, et al. Insulin-like growth factor-I improves cellular and molecular aspects of healing in a collagenase-induced model of flexor tendinitis. J Orthop Res 2002; 20:910–919.
80. Dowling BA, Dart AJ, Hodgson DR, et al. Recombinant equine growth hormone on the biomechanical properties of healing superficial digital flexor tendon. Vet Surg 2002; 31:320–324.
81. Herthel DJ. Enhanced suspensory ligament healing in 100 horses by stem cells and other bone marrow components. Proc Am Ass Equine Practitioners 2001; 47:319–321.
82. Smith RKW, Korda M, Blunn GW, Goodship AE. Isolation and implantation of autologous equine mesenchymal stem cells from bone marrow into the superficial digital flexor tendon as a potential novel treatment. Equine Vet J 2003; 35:99–102.
83. Smith RKW, McGuigan MP, Hyde JT, et al. In vitro evaluation of non-rigid support systems for the equine metacarpophalangeal joint. Equine Vet J 2002; 34:726–731.
84. Dyson SJ. Proximal suspensory desmitis in the forelimb and the hindlimb. Proc Am Ass Equine Practitioners 2000; 46:137–142.
85. Crowe OM, Dyson SJ, Wright IM, Schramme MC, Smith RKW. Treatment of chronic or recurrent proximal suspensory desmitis using radial pressure wave therapy. Equine Vet J 2003; (in press).

CHAPTER 9

Joint physiology: responses to exercise and training

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Joint physiology and structure

The joint is an organ composed of synovium, articular cartilage and subchondral bone, with a local blood supply, innervation and fluid exchanges that function to maintain health and produce locomotion.[1] The joints are uniquely designed for rotary or hinge-like movement to permit limb and body movement. Joint tissues adapt to the magnitude and frequency of applied load which naturally occurs with exercise. Training (a forced exercise regimen) is designed to promote the adaptation of the joint structures and physiologic responses to permit high performance without joint compromise. The purpose of this chapter is to provide a comprehensive understanding of the consequences and complexities of physiologic and pathophysiologic changes that occur in the joint during training and exercise.

Basic anatomy and physiology

Tissues of the joint cavity have a specialized composition and three-dimensional anatomy which ultimately relate them to their specific biomechanical function. As such, the articular cartilage, whose ultimate function is to absorb and transfer loads, is a composite of collagen which provides tensile strength and highly charged proteoglycan subunits which provide compressive stiffness. In order to maintain cartilage composition and function, a slow but steady turnover of its components occurs, the rate of which is dependent on age, mechanical load and joint environment.[2–5] The building materials necessary for this turnover are provided through blood flow and exchanges from the synovial membrane and joint capsule, as well as through ultrafiltration and formation of synovial fluid, which provides the ultimate medium for these exchanges to occur.[6] The supply of nutrients to the avascular but metabolically active articular cartilage is provided by exchanges through the synovial microcirculation and transport in synovial fluid.

The synovial membrane is designed to provide a pathway for fluid exchanges, as well as a blood supply, and add to the composition of synovial fluid through hyaluronan synthesis. The synovial membrane is composed of an intima (also referred to as synovium), consisting of a luminal layer 1–5 cells deep, a capillary plexus which lies 6–11 μm beneath the intimal surface, a deeper network of lymph vessels and a subintima (or subsynovium) composed of adipose, areolar or fibrous tissue.[6] The intima is designed to favor exchanges between capillaries and the joint cavity: it lacks a basement membrane, intercellular gaps are present and intimal capillaries are fenestrated towards the joint cavity.[6] Furthermore, the synovial intima adopts a three-dimensional architecture which is dependent on its biomechanical environment. In areas of high biomechanical stress, the synovium is flat and rests on a fibrous, mechanically strong subintima. This is particularly true of synovium underlying tendons that cross over a joint, such as the extensor tendon overlying the metacarpophalangeal joint. In synovial recesses, the intima is thrown into a three-dimensional villous architecture. This network is more richly vascular and has been shown to be a preferential site of solute and macromolecule exchanges.[7] Hyaluronan synthesis is also greater in synovium from synovial villi.[8]

Intimal cells include synovial fibroblasts (or type B cells, approximately two thirds of cells) and bone marrow-derived mononuclear phagocytes (or type A cells, approximately one third of cells).[9] Light microscopy techniques are not a useful guide for assessing lineage, as subintimal macrophages are often elongated and intimal fibroblasts may take a rounded appearance.[9] These cells can be separated on the basis of cytochemical staining for uridine diphosphoglucose dehydrogenase, a marker for hyaluronan synthesis, and non-specific esterase, a macrophage marker.[10] These cells are also unique

as they are found in close association with specialized components of the intimal matrix, such as fibronectin, laminin, type IV collagen, type V collagen, entactin and sulfated glycosaminoglycans, which may serve to anchor the intimal cell layer to the underlying connective tissue.[11] The ability of the intima to maintain itself as a layer appears closely related to cell–matrix–cell interactions, through expression of adhesion molecules such as ICAM-1, VCAM-1, fibronectin, laminin and others and their integrin ligands are likely candidates.

With joint overuse and inflammation, the relative predominance of these cell types is altered, with subintimal macrophages forming 50–70% of cells in the intima. Integrin expression is also increased and the morphology of the cells is changed from small cells arranged parallel to the joint surface to a more superficial location arranged perpendicular to the joint cavity. These cells are also the dominant source of intimal vascular cell adhesion molecule (VCAM–1).[9] Expression of cell adhesion molecules by synovial intimal cells serves to direct leukocyte trafficking in disease. Most multinucleate cells within inflamed synovial intima carry macrophage lineage markers.[9] There is also evidence that synovial intimal cells could direct leukocyte trafficking in health and disease, through adhesion molecule expression.[9] Intimal fibroblasts proliferate in disease consistent with the synovial proliferation observed with chronic joint use and inflammation.[12]

Joint circulation

The synovial membrane functions to maintain articular homeostasis by providing a pathway for the exchange of nutrients and metabolic byproducts between blood and synovial tissues, including articular cartilage.[13,14] Optimal oxygen delivery to articular tissues serves to maintain normal synovial fluid composition,[15,16] chondrocyte metabolism and normal matrix composition and turnover.[17–19] The efficiency of exchange between the synovial membrane capillaries and joint cavity is dependent on capillary density, capillary depth and blood flow.[15,20]

Several tissues in the joint are provided with a rich vascular supply that responds to exercise and pathologic states. These include the joint capsule, synovial membrane, intra- and periarticular ligaments and subchondral bone. Articular cartilage is avascular. The articular blood supply of most diarthrodial joints is formed by small branches of the epiphyseal arteries running at the junction of the periosteum and the synovial membrane, forming an arterial circle. Larger branches penetrate the bone, whereas smaller branches remain at the periphery of the articular cartilage, forming the perichondral circulation. Subchondral bone blood supply is provided by the epiphyseal arteries, which travel in the epiphysis parallel to the articular cartilage, sending perpendicular branches which end in capillary loops at the deep surface of the calcified cartilage. Before physeal closure, this epiphyseal circulation is distinct from the metaphyseal circulation. The synovial membrane vascular supply is composed of capillaries which are very sparse in areas of high mechanical stress. The angle of reflection of the synovial membrane is composed of a rich vascular plexus and synovial villi are incompletely penetrated by a central arteriole.

The richest capillary density in the synovial membrane is within 25 μm of the joint surface. Capillary density is greatest in areolar or adipose synovium and lowest in fibrous synovium. Similarly, blood flow to synovium is greater than in the fibrous joint capsule and joint motion greatly affects intra-articular pressure and synovial blood flow (see intra-articular pressure below).[21] In addition, villous synovial membrane is more vascular than fibrous and preferential exchanges of small molecules such as albumin, as well as hyaluronan production, occur in synovial villi.[7] Health of the synovial villi is important to maintain viscous synovial fluid rich in hyaluronan.[22]

Factors that can acutely affect synovial blood flow include intra-articular pressure (IAP), local temperature, joint motion, vasomotor tone and reflexes and local release of vasoactive mediators. Exercise is the greatest activator of joint circulation. Cardiac output is concomitantly increased, as is blood flow.[23,24] Large arteries supplying the joint have intravascular pressure approaching systemic arterial pressure; however, blood flow and pressure are controlled at the arteriole and capillary level of the synovial membrane. Capillary pressure in the synovial membrane is low and local joint blood perfusion is strongly influenced by IAP. If effusion resulting in increased IAP is present, significant tamponade of the synovial blood flow occurs.[21] Intra-articular pressures of > 30 mmHg have been measured in fetlock joints of sound horses with effusion.[25] A significant decrease in blood flow to the synovial membrane was measured after an increased IAP of 30 mmHg.[21] Intra-articular acidosis develops at IAP of < 45 mmHg.[26]

Even in normal joint motion, as during exercise, regional blood flow will be arrested in accordance with high pressure profiles that occur within the compressed and highly tensed joint compartments.[27] As the joint moves from full extension to maximal flexion, a pumping action occurs, creating a pulsatile increase in blood flow.

Chronic joint disease, as seen in many active sports horses, can significantly decrease blood flow to the synovial membrane as the increased joint capsule fibrosis results in a concomitant decrease in capillary density and joint capsule compliance. Loss of joint capsule compliance increases IAP associated with joint effusion and motion.

Potential consequences of decreased articular blood flow include chronic ischemia and resultant synovial fibrosis and hypertrophy, generation of lactate and synovial fluid acidosis, and production of inflammatory mediators. Chronically hypoxic joints are more affected by exercise than normal joints, producing further hypoxia. A decreased blood supply could decrease drug delivery to the joint and decrease clearance of metabolites from the joint.

Morphometric and morphologic analyses of synovial vessels provide an insight into the contribution of synovial blood flow in disease.[28] Equine vessel anatomy contains a central arteriole and a helical venule descent from the tip to the base of the villus. The anatomical result is an

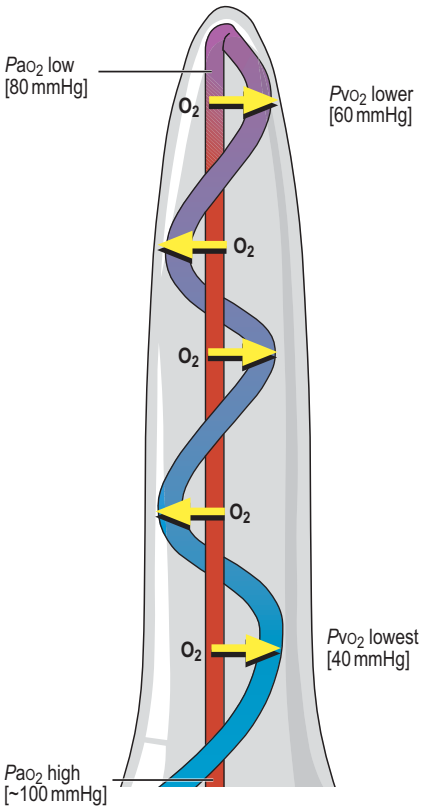


Fig. 9.1
Longitudinal section of an equine synovial villus. Note the central arteriole and helical venules that are anatomically appropriate for a countercurrent exchange mechanism and oxygen gradient from the arteriole to venules. The villus tip is susceptible to ischemia.

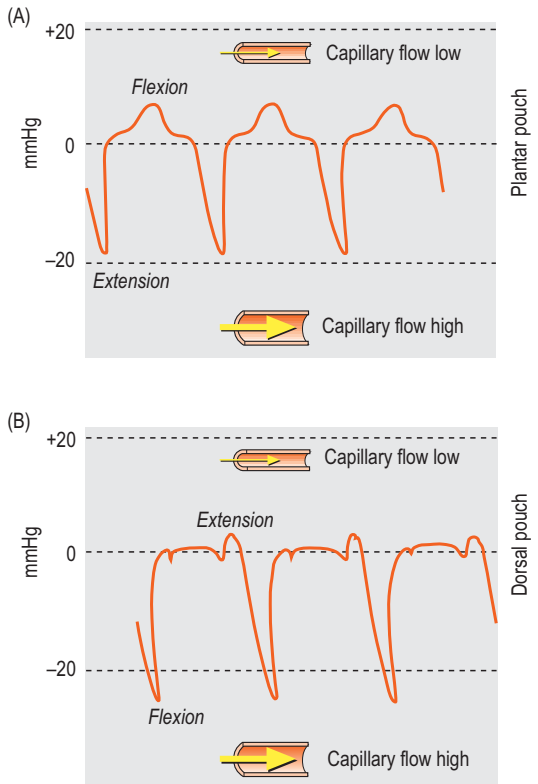


Fig. 9.2
Intra-articular pressure profiles of a normal exercising fetlock joint demonstrating the compartmentation and back-and-forth pulsatile blood flow in the capillaries of the synovial membrane. Capillary blood flow is higher during extension of the plantar pouch (A) and flexion of the dorsal pouch (lowest intra-articular pressure) (B) and lower during flexion of the plantar pouch (A) and extension of the dorsal pouch (highest intra-articular pressure) (B) .

arrangement that produces a countercurrent exchange system. These systems create ischemia at the tip of the susceptible villus[29] (Fig. 9.1). In normal synovial vessels, capillary flattening occurs with IAP greater than 25 mmHg.[28] In joint effusion and at phases of a normal stride, these IAP values are exceeded, resulting in decreased blood flow, decreased clearance and decreased lymph flow. These alterations are part of standard joint physiology in the horse in athletic training. In horses with chronic arthritis, decreased capillary density and increased intercapillary distance suggest altered trans-synovial fluid exchanges, as well as increased relative ischemia.

Data on joint physiology would suggest that in normal equine joints, an 'ebb and flow' of blood perfusion of synovial capillaries occurs from the back to the front of joints during exercise (Fig. 9.2). In joints with increased IAP (effusion) or decreased compliance (thickened stiff joint capsule), the reduction in blood flow will be even greater. The observation that synovial villi become blunted, shortened and clubbed with chronic joint overuse further supports the scientific evidence that the tips of the villi are most susceptible to hypoxia in the form of the typical ischemia reperfusion injury.[30] The fibrotic thickening of the villi may be stimulated by oxygen gradients created during tissue hypoxia.

Intra-articular pressure

Intra-articular pressure (IAP) is normally below atmospheric pressure in most joints at the 'angle of ease' and pressures between –2 to –12 mmHg have been reported. The 'angle of ease' is the most comfortable joint position and is typically a neutral position with the lowest IAP. Recordings of IAP in equine joints yielded similar subatmospheric values for the midcarpal and metacarpophalangeal joints.[25,28,31] Horses with healthy joints in active training will have 'tight' joints, i.e. no palpable effusion and a negative IAP. Maintenance of this negative pressure is thought to occur by joint motion, which enhances lymph flow from the interstitium, and by joint flexion which promotes fluid absorption by raising IAP.

The normal fluid balance is therefore maintained through two pumps in series, one that enhances fluid exchange to the interstitium and one that enhances lymph flow. Examination of pressure–volume curves in normal joints indicates that this relationship is sigmoid, with low articular compliance at normal subatmospheric pressures, an increased compliance at supra-atmospheric pressures up to 30 mmHg, and another increase in compliance at high IAP.[31] This relationship can be explained as a resistance to joint distension at IAP in the normal range, followed by accommodation of effusion at IAP up to 30 mmHg. This may prevent collapse of synovium capillaries and preserve joint blood flow. At IAP > 30 mmHg, the decreased compliance may counteract further effusion

and articular fluid accumulation. Rupture of the midcarpal joint capsule has been noted at IAP of > 80 mmHg in horses and this rupture was located in the palmar lateral pouch of the midcarpal joint, as has been observed clinically (Bertone, unpublished data, 1996).

The determinants of IAP include joint capsule compliance, joint angle, previous distension history, compliance of the joint capsule, muscle tension and joint load.[32,33] In addition, determination of pressure–volume relationships is also dependent on the type of infusate used for measurement.[31,34] Chronically inflamed joints have thickening and fibrosis of the joint capsule, resulting in decreased compliance. Joint flexion increases IAP. Slow distension–compression cycles result in progressive stress–relaxation of the joint capsule and a gradual increase in articular compliance. However, if rapid successive infusion–withdrawal cycles are performed, a progressive decrease in articular compliance can be measured. If the joint is distended with synovial fluid, an increased compliance is observed compared to infusion with saline, probably because of the lack of a fluid interface which increases surface tension and promotes joint collapse, confirming the importance of hyaluronan in joint lubrication during training and exercise.

The effect of joint history dependence on IAP and compliance explains the lack of correlation between the volume of effusion and pressure generated from the effusion. Long-term slowly accumulating joint effusion will have relatively low IAP compared to fast-developing effusions. In addition, pain due to effusion is caused by periarticular tension receptors; stress–relaxation may explain why rapidly forming effusions are more painful than slower forming ones.

Compartmentation of the joint is the functional separation of joint compartments at physiologic pressure and has been demonstrated in the rabbit stifle and the equine metacarpophalangeal joint.[27] During joint movement, synovial fluid flows from compartments of highest pressure to compartments of lowest pressure, producing an ebb and flow of synovial fluid over the articular cartilage. This process provides nutrients to the avascular cartilage, lubricates cartilage and keeps joint pressures from escalating excessively during joint movement. Movement of fluid through the synovium into the interstitium and lymphatics (termed conductance) is increased with exercise. Both a direct effect of increased IAP and a pumping action on the interstitium and lymphatics drive fluid resorption. Exercise increases this hydraulic conductance of fluid and improves clearance and turnover of joint fluid. This effect has been noted to continue for several hours after exercise. Normal exercise will not produce significant fluxes in IAP. These findings may be explained by the lower compliance of chronic diseased joints. In chronic joint effusion, pressures generated at rest but more remarkably at exercise are higher than capillary pressures, emphasizing the critical role of effusions on the generation of IAP.[35,36]

Synovial fluid dynamics

Understanding the pathophysiologic mechanisms behind synovial fluid turnover becomes important when one considers

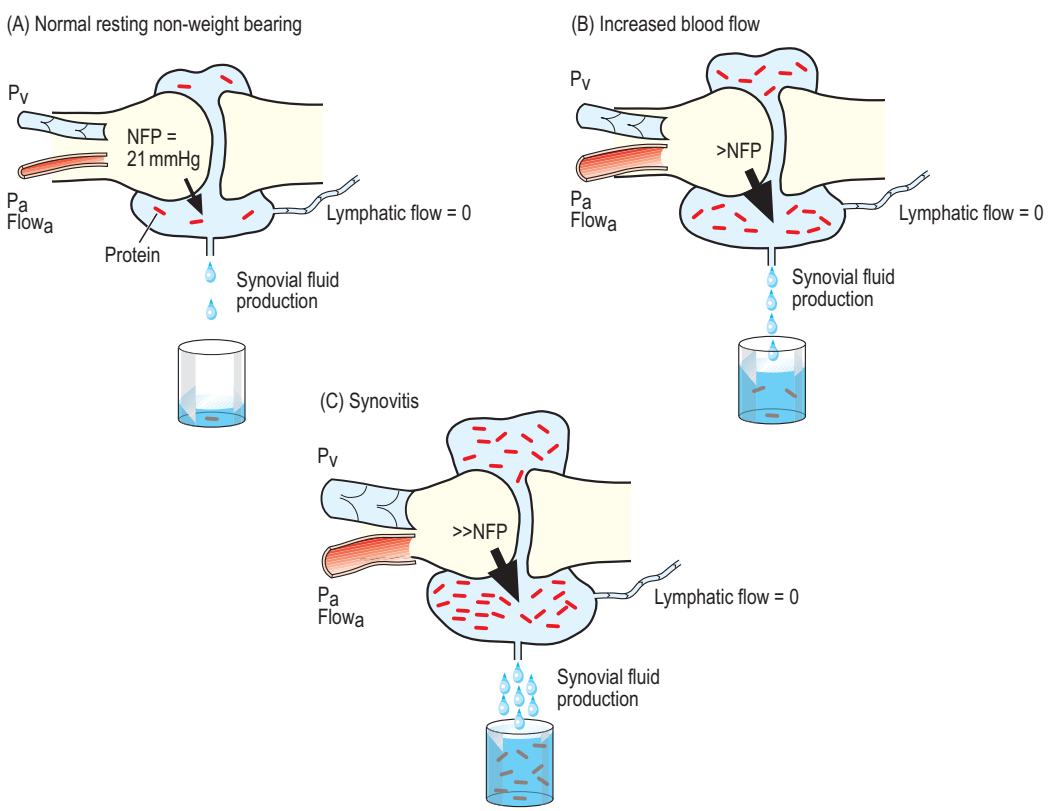


Fig. 9.3
Illustration of vascular and fluid forces in joints. (A) Normal joint at rest. (B) Normal joint during exercise with increased arterial blood flow. Arterial pressure and flow and trans-synovial flow are increased, but permeability is unchanged. (C) Abnormal joint with increased arterial blood flow such as occurs with synovitis. Arterial pressure (P_a) and flow ($Flow_a$) and trans-synovial flow are increased. Permeability, and therefore synovial fluid protein concentration, and interstitial edema are also increased. NFP = net filtration pressure, P_v = venous pressure.

the common concerns in actively training sports horses, including joint effusion, the potential clinical use of synovial fluid markers as indicators of exercise or disease state and progression[37,38] and the use of systemic or intra-articular medications in the treatment of joint disease (Fig. 9.3). The histology, ultrastructure and embryology of the synovium support the theory that the joint cavity is a third compartment of the interstitial space.[39] Interstitial and joint fluid is an ultrafiltrate of plasma to which hyaluronan is added. Fluid flow from the vascular space into the interstitium and joint space (third compartment space) and out into venules and lymphatics is tightly governed by Starling forces. Starling forces are a balance of arterial and venous pressures and colloid osmotic forces across the joint. The resultant fluid flow through the joint is modified by the permeability of the synovial membrane (osmotic reflection coefficient) and the vessel surface area available for fluid transport (filtration coefficient). Even in normal joints these forces are influenced by gravity (joint dependency), motion (exercise), and structure (joint compliance).[1,6,20,27,38,40,41] Horses are also somewhat unique in necessitating joint motion to maintain isogravimetric states of the joints (no fluid gain or loss). This is most notable in peripheral joints.[20] In normal stationary or standing equine limbs, lymphatic drainage from joints approximates zero until joint pressure exceeds 11 mmHg for the fetlock joint (transitional microvascular pressure). In standing animals without counterforces, such as motion or external bandages to increase lymph flow forces, gravitational pressures both increase arterial pressure to the joint and increase the venous and lymphatic pressure necessary for fluid to exit the joint. The result is the tissue edema and joint effusion known as 'stocking up', a physiologic imbalance of joint fluid flow leading to a positive isogravimetric state of the joint (gain of weight in the form of interstitial fluid).

Articular albumin and hyaluronan (synovial colloids) are molecules that play a role in oncotic pressures and drive joint fluid dynamics.[42] The half-life of the hyaluronan molecule in joints is relatively short (12–20 hours), suggesting that alteration in composition and molecular structure can quickly impact joint rheology. However, synovial fluid dynamics are dictated more by capillary permeability, IAP and protein concentration than hyaluronan concentration.[43]

Hyaluronan and joint lubrication

Hyaluronan is a non-sulfated glycosaminoglycan consisting of alternating units of D-glucuronic acid and N-acetyl-D-glucosamine. It exhibits polydispersity, but the average molecular weight is in the order of several million. In dilute solutions, each molecule behaves as a large coil but as the concentration of hyaluronan increases, entanglement of the coils occurs, eventually forming a uniform meshwork. Viscosity is non-linear and increases exponentially as the hyaluronan concentration increases, probably as a result of this three-dimensional framework.

The effect of hyaluronate on synovial fluid viscosity is proportional to chain length, protein concentration, pH, ionic composition and temperature. Viscosity decreases rapidly with increased shear rate, such as during sustained high motion in competitive events. Viscosity is variable between joints, being high in small joints. In a given joint, viscosity varies inversely with volume and joint effusion usually dilutes hyaluronan and viscosity. The hyaluronan molecule has been assigned a role in providing joint boundary lubrication while its viscoelastic and shear dependence properties have only been slowly accepted functions. It is apparent, however, that the nature and configuration of the molecule, and the existence of receptors to hyaluronan, provide some other insights as to the role of hyaluronan in vivo.

Hyaluronan solutions provide a barrier against water flow and may act as a barrier against rapid tissue weight changes. The meshwork may also act as a sieve to regulate transport of macromolecules and exclude macromolecules from space in the system.[44] In articular cartilage the hyaluronan-binding proteins, also referred to as hyaladherins, are aggrecan and link protein, which in combination with hyaluronan form the large proteoglycan aggregates of articular cartilage which provide the compressive stiffness necessary to accept loads such as occur in athletic events. Synovial fluid hyaluronan is also critically important to the mechanical properties ofthe joint cavity, enhancing the compliance of the joint capsule.[31]

Hyaluronan has also been shown to decrease joint pain with molecular weights of greater than 40 kDa. Hyaluronan of 860 kDa and 2300 kDa produced high-level and long-acting analgesia for 72 hours after injection. This effect was not related to binding to hyaluronan or bradykinin receptors.[45]

Joint pain

Joint pain is an important component of training any equine athlete as lameness is the greatest cause of morbidity in horses.[46] The physiology of joint pain primarily involves pain fibers found in the synovial membrane or subchondral bone. Joint pain can usually be attributed to joint inflammation, restrictive fibrosis and/or subchondral bone pain. Excessive joint strain during exercise can be in the form of a singular mishap or repetitive overstrain leading to joint inflammation. The joint is richly innervated with large myelinated afferent and efferent nerve endings and small unmyelinated C fibers. Sensory and motor innervation provide feedback that helps maintain joint stability, such that in the absence of these protective reflexes, severe arthropathy may develop if the joint is made unstable.[47] Activation of the peripheral nervous system can initiate the major features of acute inflammation, which include vasodilation, effusion and a lower threshold for pain.[48,49] The pain of arthritis is relayed by both C fibers and Aδ (delta) fibers. These fibers are activated by amines (serotonin, etc.) and neuropeptides (CGRP and substance P) that act synergistically to exert proinflammatory effects on the synovium. The presence of these neuropeptides has been documented in equine articular tissues.

Although acute inflammation is a necessary and appropriate response to initiate repair following tissue injury,

inadequate regulation of this response may lead to excessive tissue damage or chronic inflammation. A role of substance P in joint pain is supported by the clinical effectiveness of the substance P-depleting substance, capsaicin. Capsaicin (trans-8-methyl-N-vanillyl-6-nonenamide) is the pungent ingredient in hot paprika or chili peppers. It initially activates C fibers, resulting in substance P release and pain, but subsequently desensitizes or degenerates C fibers, suggesting a mechanism for pain alleviation with chronic use in articular inflammation.[50]

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in the treatment of articular inflammation and in the control of joint pain in athletic horses in training. The role of prostaglandins in pain is indirect, as they act to sensitize C fibers to subsequent stimulation. NSAIDs inhibit prostaglandin synthase enzymes (also known as cyclo-oxygenase) and diminish the formation of PGE_1, PGE_2, PGF and PGI from arachidonic acid. Corticosteroids inhibit phospholipase A2, thus preventing the formation of arachidonate, a substrate for the cyclo-oxygenase and lipoxygenase pathways. At high doses, corticosteroids also inhibit IL-1 and TNF, which can also sensitize pain nociceptors. These mechanisms may explain the analgesic effects of NSAIDs and steroids.

The role of neuropeptides in joint disease is currently under investigation and there appear to be differences in the contribution of neuropeptides to disease process in acute versus chronic inflammatory arthritis. In acute arthritis, loss of sensory nerves may contribute to inflammation, as demonstrated by increased edema formation in denervated limbs.[50] Similar results have been reported in an IL-1 induced model of acute inflammation in the horse, where increased edema and decreased permeability to macromolecules were observed in denervated limbs.[51] The role of innervation in chronic arthritis is complex. Staining for CGRP and substance P was increased in the sciatic nerve, dorsal root ganglia and periarticular tissues, but synovium staining was decreased. It appears that the role of neuropeptides in acute or chronic inflammation may vary as the distribution of sensory nerves is altered with the inflammatory response.

The therapeutic implications of the participation of neuroendocrine mechanisms in arthritis are many. Intramuscularly administered gold or topically applied capsaicin are agents that selectively destroy C fibers, thus lowering substance P levels, and have been found clinically useful. Capsaicin initially causes release of substance P from nerve endings, explaining the burning sensation felt upon initial application. NSAIDs (PGH_2 or cyclo-oxygenase inhibitors) decrease prostanoid production and intra-articular corticosteroids which inhibit the arachidonic acid cascade are effective in the treatment of inflammation and pain in arthritis.[52] In addition, stimulation of primary afferent nociceptive fibers causes release of glutamate and substance P from central spinal pathways. This nociceptive input can be inhibited by stimulation of proprioceptive and tactile type I and II fibers. Stimulation of these fibers can be accomplished by high-frequency, low-intensity transcutaneous neural stimulation, frequently used in physiotherapy.

Cartilage adaptation to training and exercise

Adaptation of cartilage to exercise is well established in horses and results in cartilage able to handle greater biomechanical stress, particularly in anatomical sites receiving high loads.[53–69] Joint stress and osteoarthritis are correlated in people and are empirically correlated in the equine athlete as well.[70] Overuse results in wear and tear when the stress of exercise exceeds the capability of the cartilage to adapt and structural damage occurs. Virtually all elite equine athletes with an extended career will have some degree of osteoarthritis. Exercise both increases and accelerates the development of biochemical articular cartilage heterogeneity.[55,58,65] These changes reflect the biodistribution of loading[53] and loading-induced changes in synovial fluid.[62] Use of intra-articular steroid medication in exercising horses has been shown to reduce the biomechanical supportive properties of the equine articular cartilage.[67]

Some of the differences in biomechanical and biochemical properties of articular cartilage result from species disparities, the characteristics of a particular joint or as a function of location within a joint. Differences in similar anatomic site locations in joints as a function of the level of exercise (i.e. non-strenuous as compared to strenuous) demonstrate that the history of loading undergone by the joint alters these biomechanical material properties. Indentation studies on equine articular cartilage from exercised and non-exercised horses demonstrated clear differences in biomaterial properties of the cartilage which were site specific. Sites of higher loading had greater changes, indicating an exercise adaptation. This was most dramatic for cartilage permeability (fluid conductance) in which exercise promotes water (fluid) flow out of the cartilage on loading. Fluid extrusion from articular cartilage on high-impact loading is a known mechanism for cartilage lubrication.[41] These biomechanical adaptations of cartilage correspond in a site-specific manner to alterations in cartilage metabolism with exercise. Chondrocytes increase their production and quality of proteoglycan to increase the compressive stiffness of cartilage. It takes longer than 3 weeks of training for the increase in proteoglycan synthesis to result in a measurable increase in total proteoglycan content.[54]

There is no consensus on the influence of exercise (beneficial[71] or neutral[72]) on the healing of injured articular cartilage, although assimilation of the studies would suggest that exercise during healing is beneficial as long as the impact trauma is below the level of repair tissue destruction.

Bone adaptation to training and exercise

In young horses put in training, bone is exposed to new stresses. During training bone rapidly remodels to decrease

bone porosity and increase bone trabecular width and mineralizing surface, thereby enhancing the bone's ability to withstand stress.[73] Younger horse bone (2 year olds) is less stiff and therefore greater strains (bone movement) have been measured during high-speed exercise as compared to older horses. These high strains seen in these young horses may lead to high-strain, low-cycle fatigue of the bone and subsequent bone pain (dorsal metacarpal cortex, sesamoid bones, caudal metacarpal condyle).[74] Computed tomography and histology have confirmed the presence of microcracks at these high-strain bone sites. Bone strain is even greater in the lead limb (the left limb in North American racing) correlating with the most common location of ultimate fracture (dorsal cortical fracture and condylar fracture).[75]

Immature cortical bone of horses is normally resorbing primary osteons during training and has greater resorption cavities and incompletely filled secondary osteons than that of older horses. This bone structure is more susceptible to fatigue microdamage resulting from training because of higher bone porosity, fewer completed secondary osteons and a lower proportion of circumferentially oriented collagen fibers.[76] Indeed, in racing Quarter Horses put in training, the bone density significantly decreased early in training and then increased later in training. Race horses experienced fewer bone-related injuries when they had greater cortical mass in areas of known high bone stress at the commencement of training.[77]

The metacarpus changes shape during maturation[78] and training[79,80] to lower strains during high-speed exercise. As an example, the dorsal cortex thickens during training, by production of periosteal new bone. This natural response to these demands on the bone enables bone to handle stress without developing microfractures or complete bone failure (fractures). Experimental exercise conditions confirm marked modeling (not remodeling) of the bone, particularly subperiosteal bone formation at the midshaft of the third metacarpal bone. Horses that complete a full training program have greater bone mineral content despite a lighter body weight, further demonstrating the principle of Wolfe's Law, summarized as the principle that bone is deposited in areas of increased bone stress demands.[81] Bone mineral density increases with age and exercise is critical for normal bone development.[82]

In summary, in horses in training, high bone strain can induce cyclic fatigue of bone, resulting in microdamage and ultimate bone failure. The less bone present at the start of training (immaturity or lack of musculoskeletal conditioning), the greater this risk. Bone responds by modeling but microfracture damage may develop and cause pain. Many (> 80%) 2-year-old racing Thoroughbreds[83] and Quarter Horses[84] demonstrate bone pain and it is estimated that ~12% go on to develop stress fracture, usually within 6 months to 1 year of showing pain.[78] Horses trained on harder surfaces (dirt as compared to wood fiber)[85] and faster horses[83] are at greater risk of developing bone pain and microfracture. It is proposed that the greater incidence of bone fatigue failure in Thoroughbreds, as compared to Standardbreds, is due to gait differences and resultant bone stresses during training and racing, not to inherent differences in the mechanical properties of the bone.[86]

References

1. Palmer J, Bertone AL. Joint structure, biochemistry and biochemical disequilibrium in synovitis and equine joint disease. Equine Vet J 1994; 26:263–277.
2. Morris EA, Treadwell BV. Effect of interleukin 1 on articular cartilage from young and aged horses and comparison with metabolism of osteoarthritic cartilage. Am J Vet Res 1994; 55:138–146.
3. Lane Smith R, Rusk SF, Ellison BE, et al. In vitro stimulation of articular chondrocyte mRNA and extracellular matrix synthesis by hydrostatic pressure. J Orthop Res 1996; 14:53–60.
4. Sah RL, Trippel SB, Grodzinsky AJ. Differential effects of serum, insulin-like growth factor-1, and fibroblast growth factor-2 on the maintenance of cartilage physical properties during long-term culture. J Orthop Res 1996; 14:44–52.
5. Buckwalter JA. Osteoarthritis and articular cartilage use, disuse, and abuse: experimental studies. J Rheumatol 1995; 22(suppl 43):13–15.
6. Levick JR. Blood flow and mass transport in synovial joints. The cardiovascular system IV: The microcirculation. In: Renkin EM, Michel CC, eds. Handbook of physiology. Bethesda, MD: American Physiological Society; 1984:917–994.
7. Hardy J, Bertone AL, Muir WW. Local hemodynamics, permeability and oxygen metabolism of innervated or denervated isolated equine joints. Am J Vet Res 1998; 59(10):1307–1316.
8. Myers SL, Christine TA. Hyaluronate synthesis by synovial villi in organ culture. Arthritis Rheum 1983; 26:764–770.
9. Edwards JCW, Winchester R, Henderson B, et al. Consensus statement. Ann Rheum Dis 1995; 54:389–391.
10. Athanasou N. Synovial macrophages. Ann Rheum Dis 1995; 54:392–394.
11. Revell PA, Al-Saffar N, Fish S, et al. Extracellular matrix of the synovial intimal cell layer. Ann Rheum Dis 1995; 54:404–407.
12. Zvaifler NJ. Macrophages and the synovial lining. Scand J Rheumatol 1995; 24(suppl 101):67–75.
13. Ghadially FN. Structure and function of articular cartilage. Clin Rheum Dis 1981; 7:3–27.
14. Hasselbacher P. Structure of the synovial membrane. Clin Rheum Dis 1981; 7:57–69.
15. Levick JR. Hypoxia and acidosis in chronic inflammatory arthritis; relation to vascular supply and dynamic effusion pressure. J Rheumatol 1990; 17:579–582.
16. Lund-Olsen K. Oxygen tension in synovial fluid. Arthritis Rheum 1970; 13:769–776.
17. Brighton CT, Lane JM, Koh JK. In vitro rabbit articular cartilage organ model. II. 35S incorporation in various oxygen tensions. Arthritis Rheum 1974; 17:245–252.
18. Clark CC, Tolin BS, Brighton CT. The effect of oxygen tension on proteoglycan synthesis and aggregation in mammalian growth plate chondrocytes. J Orthop Res 1991; 9:477–484.
19. Lane JM, Brighton CT, Menkowitz BJ. Anaerobic and aerobic metabolism in articular cartilage. J Rheumatol 1977; 4:334–342.
20. Bertone AL, Hardy J, Simmons EJ, Muir WW III. Vascular and trans-synovial forces of the stationary isolated joint. Am J Vet Res 1998; 59(4):495–503.
21. Hardy J, Bertone A, Muir W. Joint pressure influences synovial blood flow as determined by colored microspheres. J Appl Physiol 1996; 80:1225–1232.

22. Saari H, Konttinen YT, Tulamo RM, et al. Concentration and degree of polymerization of hyaluronate in equine synovial fluid. Am J Vet Res 1989; 50:2060–2063.
23. Amundsen BH, Wisloff U, Helgerud J, et al. Ultrasound recorded axillary artery blood flow during elbow-flexion exercise. Med Sci Sports Exerc 2002; 34:1288–1293.
24. Simkin PA, Huang A, Benedict RS. Effects of exercise on blood flow to canine articular tissues. J Orthop Res 1990; 8:297–303.
25. Strand E, Martin GS, Crawford MP, et al. Intra-articular pressure and elastance of the equine metacarpophalangeal joint in health and disease (abstract). Vet Surg 1994; 23:417.
26. Richman AI, Su EY, Ho G. Reciprocal relationship of synovial fluid volume and oxygen tension. Arthritis Rheum 1981; 24:701–705.
27. Macoris DDG, Bertone AL. Intra-articular pressure profiles of the cadaveric equine fetlock joint in motion. Equine Vet J 2001; 33(2):184–190.
28. Fitzgerald O, Soden M, Yanni G, et al. Morphometric analysis of blood vessels in synovial membranes obtained from clinically affected and unaffected knee joints of patients with rheumatoid arthritis. Ann Rheum Dis 1991; 50:792–796.
29. Izumisawa Y, Yamaguchi M, Bertone AL, et al. Equine synovial villi: distinctive structural organization of vasculature and novel nerve ending. J Vet Med Sci 1996; 58(12): 1193–1204.
30. Woodruff T, Blake DR, Freeman J, et al. Is chronic synovitis an example of reperfusion injury? Ann Rheum Dis 1986; 45:608–611.
31. Hardy J, Bertone AL, Muir WW. Pressure–volume relationships in normal equine midcarpal joints. J Appl Physiol 1985; 78:1977–1984.
32. Geborek, P, Moritz U, Wollheim FA. Joint capsular stiffness in knee arthritis. Relationship to intraarticular volume, hydrostatic pressure, and extensor muscle function. J Rheumatol 1989; 16:1351–1358.
33. Myers DB, Palmer DG. Capsular compliance and pressure–volume relationships in normal and arthritic knees. J Bone Joint Surg 1972; 54B:710–716.
34. Knight AD, Levick JR. Pressure–volume relationships above and below atmospheric pressure in the synovial cavity of the rabbit knee. J Physiol (Lond) 1982; 328:403–420.
35. Merry P, Williams R, Cox N, et al. Comparative study of intra-articular pressure dynamics in joints with acute traumatic and chronic inflammatory effusions: potential implications for hypoxic-reperfusion injury. Ann Rheum Dis 1991; 50:17–20.
36. Jayson MIV, Dixon ASJ. Intraarticular pressure in rheumatoid arthritis of the knee. III Pressures changes during joint use. Ann Rheum Dis 1970; 29:401.
37. Okumura M, Kim GH, Tagami M, et al. Serum keratan sulphate as a cartilage metabolic marker in horses: the effect of exercise. J Vet Med A Physiol Pathol Clin Med 2002; 49:195–197.
38. Bertone AL, Palmer JL, Jones J. Synovial fluid cytokines and eicosanoids as markers of joint disease in horses. Vet Surg 2001; 30:528–538.
39. Hadler NA. The biology of the extracellular space. Clin Rheum Dis 1981; 7:71–97.
40. Hardy J, Bertone AL, Weisbrode SE, et al. Cell trafficking, mediator release and articular metabolism in acute inflammation of innervated or denervated isolated equine joints. Am J Vet Res 1998; 59(1):88–100.
41. Palmer J, Bertone AL. Joint biomechanics in the pathogenesis of traumatic arthritis. In: McIlwraith CW, Trotter G, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 104–119.
42. Simkin PA, Benedict RS. Hydrostatic and oncotic determinants of microvascular fluid balance in normal canine joints. Arthritis Rheum 1990; 33:80–86.
43. Myers SL. Effect of synovial fluid hyaluronan on the clearance of albumin from the canine knee. Ann Rheum Dis 1995; 54:433–434.
44. Laurent TC, Laurent UBG, Fraser JRE. Functions of hyaluronan. Ann Rheum Dis 1995; 54:429–432.
45. Gotoh S, Onaya J-I, Abe M, et al. Effects of the molecular weight of hyaluronic acid and its action mechanisms on experimental joint pain in rats. Ann Rheum Dis 1993; 52:817–822.
46. Kaneene JB, Ross WA, Miller R. The Michigan equine monitoring system. II. Frequencies and impact of selected health problems. Prev Vet Med 1997; 29:277–292.
47. Vilensky JA, O'Connor BL, Brandt KD, et al. Serial kinematic analysis of the canine knee after L4–S1 dorsal root ganglionectomy: implications for the cruciate deficiency model of osteoarthritis. J Rheumatol 1994; 21:2113.
48. Muir WW III, Woolf CJ. Mechanisms of pain and their therapeutic implications. J Am Vet Med Assoc 2001; 219:1346–1356.
49. Basbaum AI, Levine JD. The contribution of the nervous system to inflammation and inflammatory disease. Can J Physiol Pharmacol 1991; 69:647.
50. Colpaert FC, Donnerer J, Lembeck F. Effects of capsaicin on inflammation and on the substance P content of nervous tissues in rats with adjuvant arthritis. Life Sci 1983; 32:1827.
51. Cambridge H, Brain SD. Calcitonin gene-related peptide increases blood flow and potentiates plasma protein extravasation in the rat knee. Br J Pharmacol 1992; 106:746.
52. Konttinen YT, Kemppinen P, Segerberg M, et al. Peripheral and spinal neural mechanisms in arthritis, with particular reference to treatment of inflammation and pain. Arthritis Rheum 1994; 37:965.
53. Palmer JL, Bertone AL, Litsky AS. Contact area and pressure distribution changes of the equine third carpal bone during loading. Equine Vet J 1994; 26:197–202.
54. Palmer JL, Bertone AL, Malemud CJ, et al. Site-specific proteoglycan characteristics of third carpal articular cartilage in exercised and nonexercised horses. Am J Vet Res 1995; 56(12):1570–1576.
55. Palmer JL, Bertone AL, Mansour J, et al. Biomechanical properties of third carpal articular cartilage in exercised and nonexercised horses. J Orthop Res 1995; 13(6): 854–860.
56. Brama PA, Tekoppele JM, Bank RA, et al. Development of biochemical heterogeneity of articular cartilage: influences of age and exercise. Equine Vet J 2002; 34:265–269.
57. van de Lest CH, Brama PA, van Weeren PR. The influence of exercise on the composition of developing equine joints. Biorheology 2002; 39:183–191.
58. Karaham S, Kincaid SA, Baird AN, Kammermann JR. Distribution of beta-endorphin and substance P in the shoulder joint of the dog before and after a low impact exercise programme. Anat Histol Embryol 2002; 31:72–77.
59. Murray RC, Birch HL, Lakhani K, Goodship AE. Biochemical composition of equine carpal articular cartilage is influenced by short-term exercise in a site-specific manner. Osteoarthritis Cartilage 2001; 9:625–632.
60. Murray RC, Smith RK, Henson FM, Goodship AE. The distribution of cartilage oligomeric matrix protein (COMP) in equine carpal articular cartilage and its variation with exercise and cartilage deterioration. Vet J 2001; 62:121–128.
61. Brama PA, Tekoppele JM, Bank RA, et al. The influence of strenuous exercise on collagen characteristics of articular

cartilage in Thoroughbreds age 2 years. Equine Vet J 2000; 32:551–554.
62. van den Hoogen BM, van de Lest CH, van Weeren PR, et al. Effect of exercise on the proteoglycan metabolism of articular cartilage in growing foals. Equine Vet J 1999; 31(suppl):62–66.
63. Brama PA, Tekoppele JM, Bank RA, et al. Influence of different exercise levels and age on the biochemical characteristics of immature equine articular cartilage. Equine Vet J 1999; 31(suppl):55–61.
64. van de Lest CH, van den Hoogen BM, van Weeren PR. Loading-induced changes in synovial fluid affect cartilage metabolism. Biorheology 2000; 37:45–55.
65. Murray RC, Janicke HC, Henson FM, Goodship AE. Equine carpal articular cartilage fibronectin distribution associated with training, joint location and cartilage deterioration. Equine Vet J 2000; 32:47–51.
66. Murray RC, Whitton RC, Vedi S, et al. The effect of training on the calcified zone of equine middle carpal articular cartilage. Equine Vet J 1999; 30(suppl):274–278.
67. Murray RC, DeBowes RM, Gaughan EM, et al. The effects of intra-articular methylprednisolone and exercise on the mechanical properties of articular cartilage in the horse. Osteoarthritis Cartilage 1998; 6:106–114.
68. Murray RC, Zhu CF, Goodship AE, et al. Exercise affects the mechanical properties and histological appearance of equine articular cartilage. J Orthop Res 1999; 17:725–731.
69. Little CB, Ghosh P, Rose R. The effect of strenuous versus moderate exercise on the metabolism of proteoglycans in articular cartilage from different weight-bearing regions of the equine third carpal bone. Osteoarthritis Cartilage 1997; 5:161–172.
70. Rogers LQ, Macera CA, Hootman JM, et al. The association between joint stress from physical activity and self-reported osteoarthritis: an analysis of the Cooper Clinic data. Osteoarthritis Cartilage 2002; 10:617–622.
71. Todhunter RJ, Minor RR, Wootton JA, et al. Effects of exercise and polysulfated glycosaminoglycan on repair of articular cartilage defects in the equine carpus. J Orthop Res 1993; 11:782–795.
72. Barr AR, Wotton SF, Dow SM, et al. Effect of central or marginal location and post-operative exercise on the healing of osteochondral defects in the equine carpus. Equine Vet J 1994; 26:33–39.
73. Young DR, Nunamaker DM, Markel MD. Quantitative evaluation of the remodeling response of the proximal sesamoid bones to training-related stimuli in Thoroughbreds. Am J Vet Res 1991; 52:1350–1356.
74. Nunamaker DM, Butterweck DM, Provost MT. Fatigue fractures in thoroughbred racehorses: relationships with age, peak bone strain, and training. J Orthop Res 1990; 8(4):604–611.
75. Davies HM, McCarthy RN, Jeffcott LB. Surface strain on the dorsal metacarpus of thoroughbreds at different speeds and gaits. Acta Anat (Basel) 1993; 146(2–3); 148–153.
76. Stover SM, Pool RR, Martin RB, et al. Histological features of the dorsal cortex of the third metacarpal bone mid-diaphysis during postnatal growth in thoroughbred horses. J Anat 1992; 181:455–469.
77. Neilsen BD, Potter GD, Morris EL, et al. Changes in the third metacarpal bone and frequency of bone injuries in young Quarter Horses during race training – observations and theoretical considerations. J Equine Vet Sci 1997; 17:541–545.
78. Nunamaker DM. Metacarpal stress fractures In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996:195–199.
79. Sherman KM, Miller GJ, Wrondki TJ, et al. The effect of training on equine metacarpal bone breaking strength. Equine Vet J 1995; 27(2):135–139.
80. Davies HM, Gale SM, Baker ID. Radiographic measures of bone shape in young thoroughbreds during training for racing. Equine Vet J 1999; 30(suppl):262–265.
81. McCarthy RN, Jeffcott LB. Effects of treadmill exercise on cortical bone in the third metacarpus of young horses. Res Vet Sci 1992; 52(1):28–37.
82. Cornelissen BP, van Weeren PR, Ederveen AG, Barneveld A. Influence of exercise on bone mineral density of immature cortical and trabecular bone of the equine metacarpus and proximal sesamoid bone. Equine Vet J 1999; 31(suppl):79–85.
83. Boston RC, Nunamaker DM. Gait and speed as exercise components of risk factors associated with onset of fatigue injury of the third metacarpal bone in 2-year-old Thoroughbred racehorses. Am J Vet Res 2000; 61(6):602–608.
84. Goodman NL, Baker BK. Lameness diagnosis and treatment in the quarter horse racehorse. Vet Clin North Am Equine Pract 1990; 6(1):85–108.
85. Moyer W, Spencer PA, Kallish M. Relative incidence of dorsal metacarpal disease in young Thoroughbred racehorses training on two different surfaces. Equine Vet J 1991; 23(3):166–168.
86. Nunamaker DM, Butterweck DM, Black J. In vitro comparison of Thoroughbred and Standardbred racehorses with regard to local fatigue failure of the third metacarpal bone. Am J Vet Res 1991; 52:97–100.

CHAPTER 10

Imaging of the musculoskeletal system in horses

Jean-Marie Denoix and Fabrice Audigié

Introduction

During recent decades, diagnostic imaging has considerably progressed in human and veterinary medicine. Horses have benefited from the tremendous technological progress made in different imaging modalities. Because of this improvement in our diagnostic capabilities, significant advances in equine medicine, and especially in the knowledge of musculoskeletal diseases, were made and many new clinical entities previously unknown were identified and documented.

In the 1980s, radiography was the only technique used by the equine practitioner. Now several imaging procedures are available, at least in referral centers. According to their use, indications and complexity, imaging techniques can be divided as basic procedures, easily used in practice (such as radiography and ultrasonography), topographical modalities giving information on the location of pathologic processes (such as thermography and nuclear scintigraphy), and advanced, more sophisticated cross-sectional and multiplanar techniques (such as computed tomography and magnetic resonance imaging).

Basic techniques

Radiography

Conventional radiography is the classic technique of diagnostic imaging. It provides high-definition image quality, especially when single emulsion film is used. This procedure is well known, simple to use, and allows examination of every part of the horse body and limbs. Radiographic

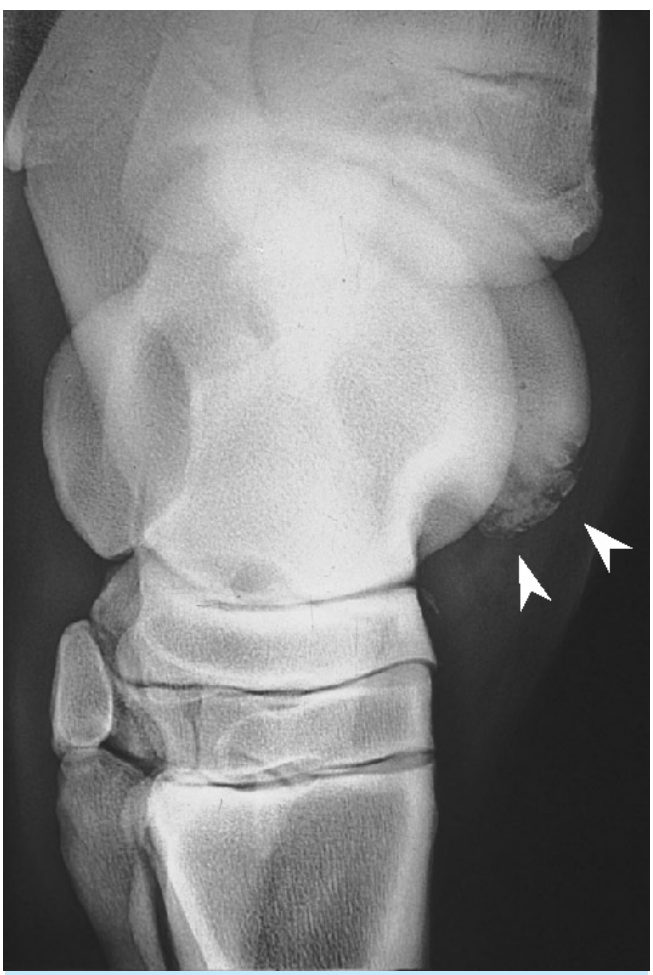


Fig. 10.1
Nineteen-month-old French Trotter colt. Dorsomedial–plantarolateral oblique projection of the left hock. Osteochondral fragmentation of the lateral trochlear ridge of the talus (arrowheads).

interpretation requires a good knowledge of anatomy, geometry of the radiographic projections,[1] and the different manifestations of tissue alterations. It features an excellent imaging representation of bones. Identification of bone injuries is based on changes in density (bone lysis or bone sclerosis) and bone architecture (sclerosis of the spongious bone and lysis of the compact or subchondral bone) as well as changes in shape and contour.[2]

Many osteoarticular conditions can be diagnosed with radiography.[3,4] This modality allows diagnosis and documentation of most of the osteochondral lesions, such as articular surface or periarticular osteochondral fragmentation (Fig. 10.1) and subchondral bone cysts (Fig. 10.2) in young and adult horses. Radiography is the first technique used for the diagnosis and documentation of complete fractures (Figs 10.3, 10.4) as well as fatigue fractures (Fig. 10.5). This technique is also essential for the diagnosis of degenerative joint disease (Fig. 10.6), based on the presence of lysis or sclerosis of the subchondral bone, periarticular osteophytes and, in some cases, thinning of the 'joint space', which represents the two opposite articular cartilage layers in synovial joints. Lysis of the compact bone (in short bones) or cortical bone associated with sclerosis of the adjacent cancellous bone is

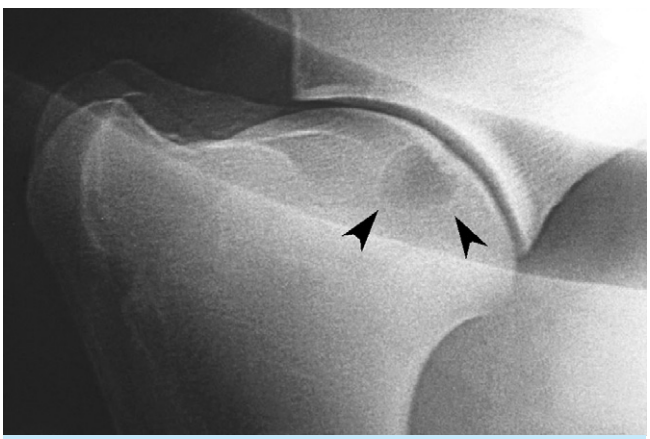


Fig. 10.2
Two-year-old French Trotter colt. Mediolateral projection of the right shoulder. Subchondral bone cyst of the humeral head (arrowheads).

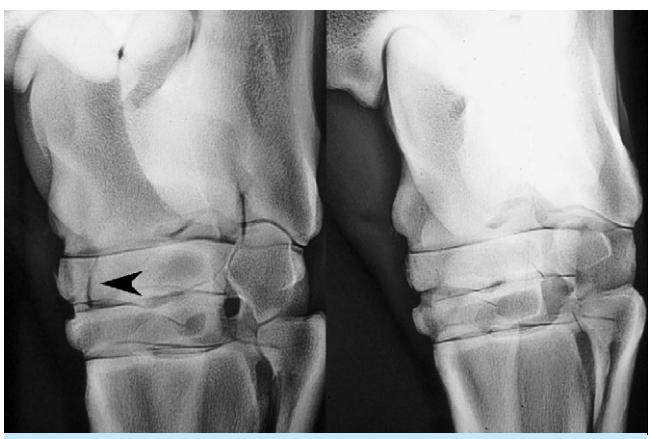


Fig. 10.3
Four-year-old French Trotter male. Dorsolateral–plantaromedial oblique projection on the left hock. Biarticular fracture of the central tarsal bone (arrowhead). Note that a slightly different projection (on the right) does not show the fracture line.

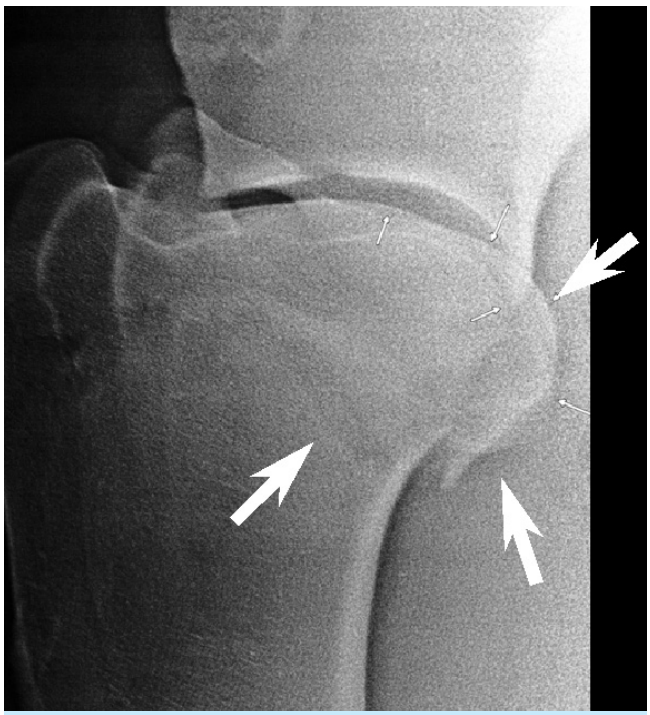


Fig. 10.4
Two-year-old Selle-Français colt. Mediolateral projection of the right shoulder. Traumatic fracture of the caudomedial part of the humeral head (arrows).

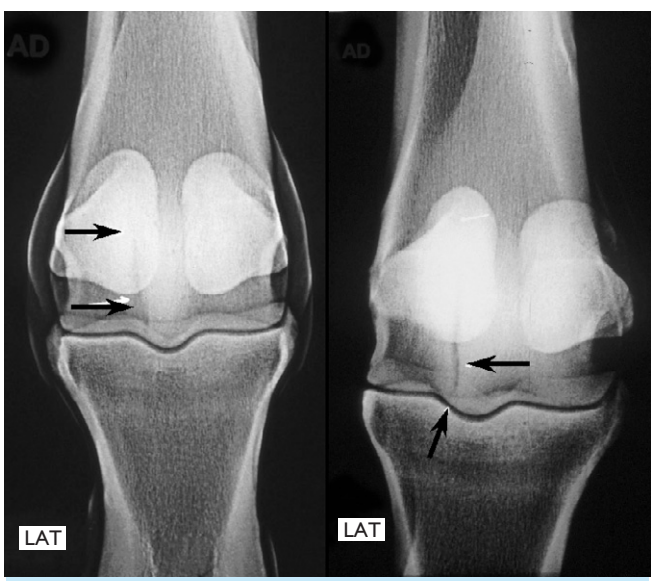


Fig. 10.5
Two-year-old Thoroughbred filly. Dorsopalmar projections of the right front fetlock. Lateral parasagittal fatigue fracture of the metacarpal condyle. Note that the fracture line is clearer on a slightly oblique projection (right).

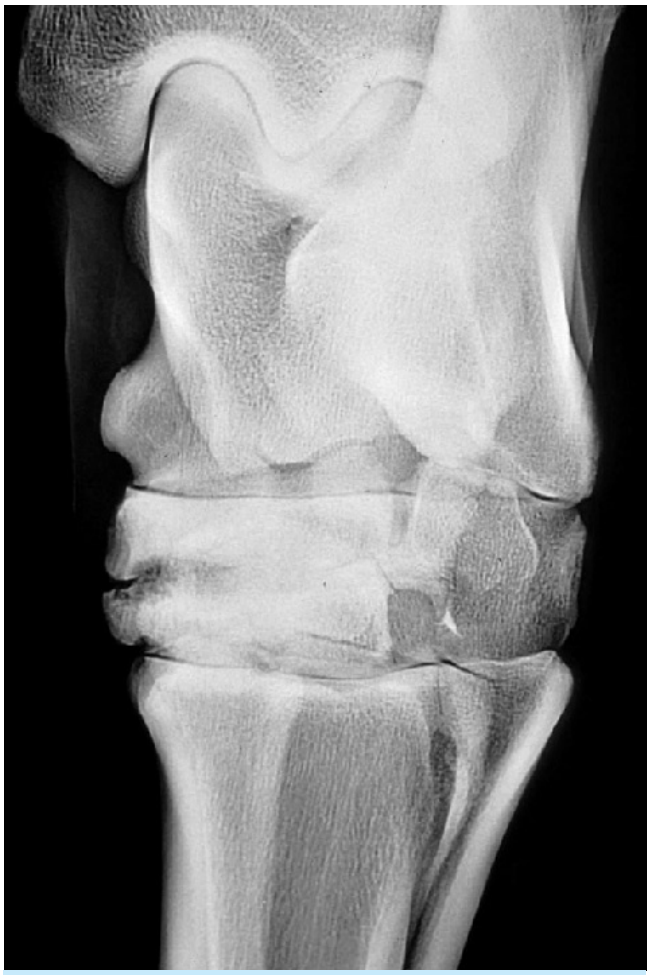


Fig. 10.6
Six-year-old Selle-Français gelding.
Dorsolateral–plantaromedial oblique projection on the left hock. Degenerative joint disease of the distal intertarsal joint with severe suchondral bone lysis of the central and third tarsal bones. Note the sclerosis of the spongious bone of Tc and T3.

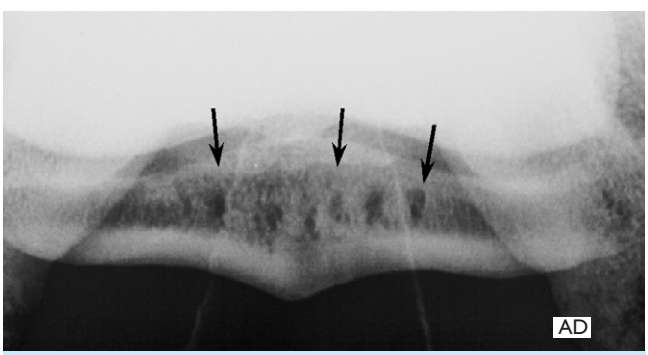


Fig. 10.7
Sixteen-year-old Selle-Français gelding.
Proximopalmar–distodorsal oblique (sky-line) projection of the distal sesamoid (navicular) bone. Severe lysis of the compact bone of the distal sesamoid bone flexor surface and sclerosis of the cancellous bone between the enlarged distal synovial fossa (arrows).

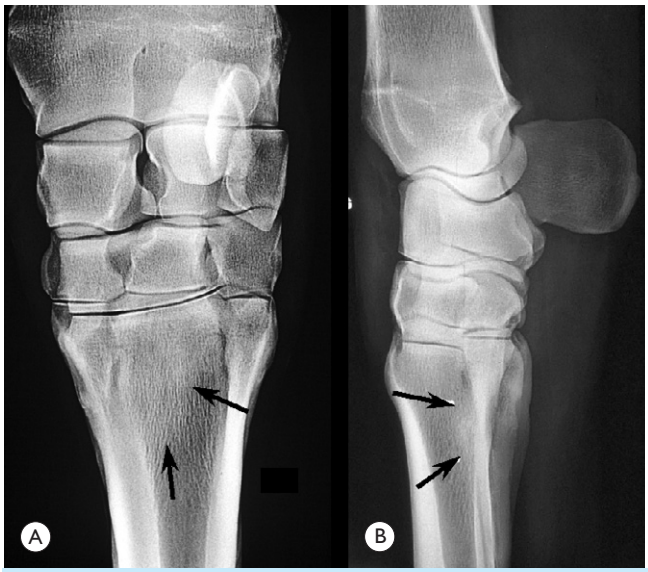
always indicative of advanced bone remodeling in pathologic processes (Fig. 10.7). In conjunction with ultrasonography, radiography is also very useful for the detection of enthesopathies, providing information on the insertion surface of ligaments and tendons (Fig. 10.8). As this technique does not have any regional limitation (depending on the power of the machine), many neck, back, and pelvic problems can be diagnosed with radiography. Cervical lesions including malformation, malalignment (Fig. 10.9), stenosis of the vertebral canal (Fig. 10.10), osteochondral fragmentation of the articular processes, fractures, and degenerative intervertebral disk lesions are easily assessed with portable machines, especially in young horses. In the thoracic spine, the diagnosis of kissing spines in the midthoracic region (Fig. 10.11) and in the withers (Fig. 10.12) can also be achieved with portable machines. Conversely, lesions involving the articular processes (Fig. 10.13) and vertebral bodies (Fig. 10.14) can be diagnosed only with non-portable powerful machines, which are only available in equine referral hospitals. In our patients, osteoarthrosis of the synovial joints between the articular processes of the lumbar and thoracic spine is a significant condition responsible for poor performance in sport and race horses.

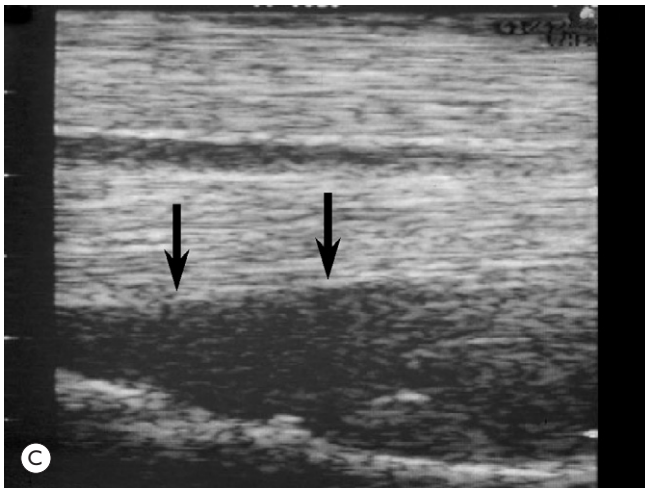
Besides the anatomopathologic information, radiography allows a functional evaluation through the assessment of joint angulation and congruency. Stress radiographs can be performed to assess joint stability, and to identify localized reduction of the cartilage thickness. Contrast radiography is an invasive technique whose indications have been reduced since the use of ultrasonography.[5]

Contrary to other techniques, such as magnetic resonance imaging (MRI) or computed tomography, most of the joints can be examined with radiography, including the proximal joints and intervertebral joints. As radiography is the older imaging technique used in diagnostic imaging, its limitations are well known. They include:

- evaluation of complex anatomic regions, because of the superimposition of multiple soft tissue and bony structures
- lack of identification of contour, size and shape changes when the structure evaluated is not profiled by the X-ray beam
- failure to identify changes in radiopacity for moderate changes in mineral content
- the lack of differentiation of soft tissues that present a similar density
- the lack of information on cartilage architecture that does not permit detection of early lesions. Thinning of cartilage is recognized only late in the disease process. Moreover, imaging techniques such as MRI and scintigraphy have demonstrated the limitations of radiography in the identification of some bone injuries such as stress fractures, bone contusion, and bone edema.

With computed and digital radiography, differentiation of the soft tissues is improved.[6] Manipulation of the density and contrast parameters allows a better evaluation of the





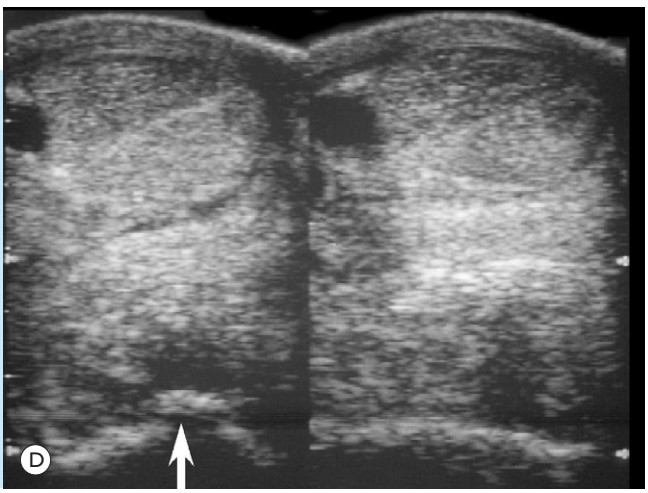


Fig. 10.8
Three-year-old French Trotter filly. Proximal third interosseous enthesopathy. (A) Dorsopalmar projection of the proximal metacarpus. Note the heterogeneous density of the proximal third metacarpal bone (arrows). (B) Lateromedial projection of the proximal metacarpus. Note the sclerosis of the spongious bone at the origin of the suspensory ligament (arrows). (C) Sagittal ultrasound scan of the proximal metacarpus. The suspensory ligament is enlarged and hypoechogenic (arrows) and its insertion surface is irregular. (D) Transverse ultrasound scans of the proximal metacarpus. The suspensory ligament is enlarged and hypoechogenic and an enthesophyte is imaged on the left scan (arrow).

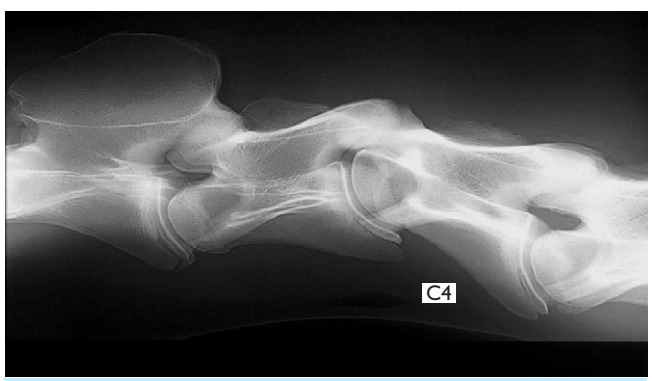


Fig. 10.9
Eighteen-month-old Anglo-Arabian colt. Lateral projection of the cranial cervical spine. Malalignment of the third (C3) and fourth (C4) cervical vertebrae with hypoplasia of the ventral part of the vertebral head of C4 inducing a C3–C4 stenosis of the vertebral canal.

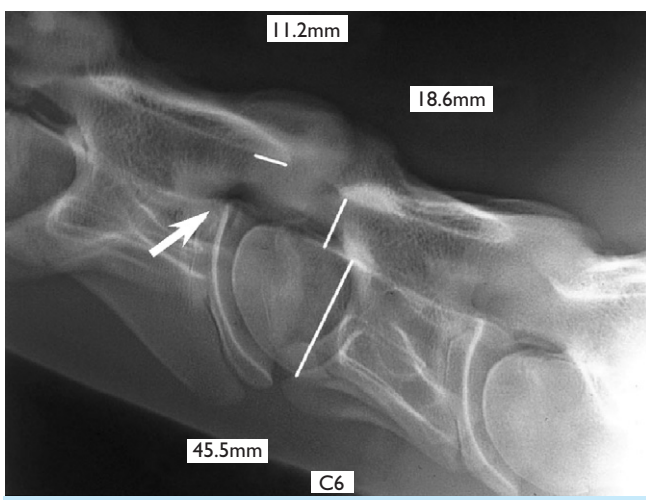


Fig. 10.10
Four-month-old Thoroughbred filly. Lateral projection of the caudal cervical spine. Stenosis of the vertebral canal of the sixth cervical vertebra (C6) and caudal lengthening of the vertebral arch of the fifth cervical vertebra compatible with static and dynamic spinal cord compression. There is also hypertrophy of the articular processes between C5 and C6, a ski-jump deformation of the vertebral fossa of C5 (arrow) as well as a malalignment between C6 and C7.

different anatomical components of the area examined. Small structures such as joint spaces can be enlarged and direct measures (such as thickness, angulation) can be easily done (see Fig. 10.10). Both duplication of the images and communication are considerably improved for dissemination of the diagnostic information.

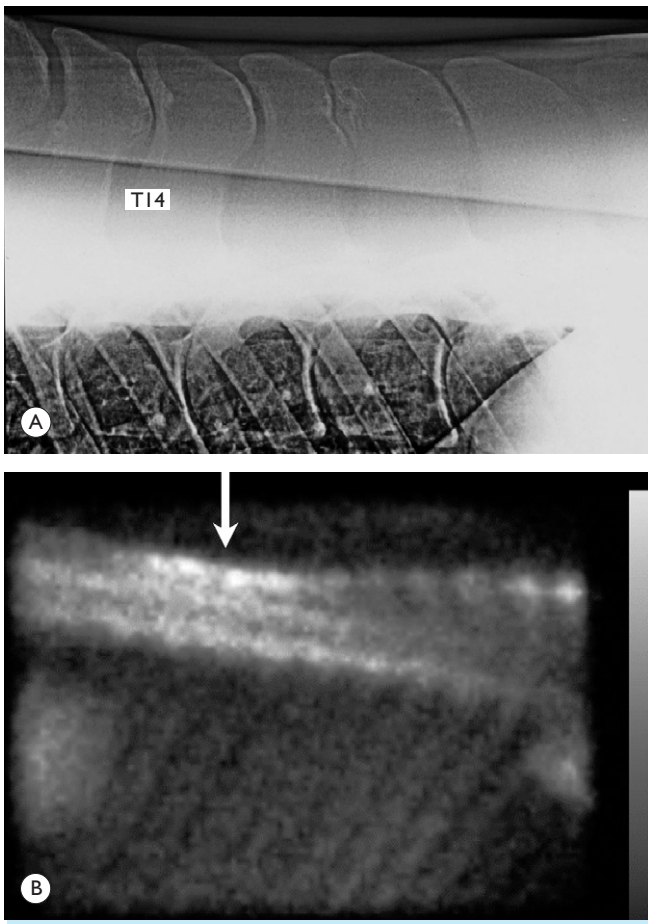


Fig. 10.11
Ten-year-old Grand Prix show jumper, Selle-Français male. Kissing spines in the thoracic vertebral column. (A) Lateral radiographic projection on the standing horse showing contact and bone remodeling between the spinous processes from T12 to T17 (cranial to the left). (B) Scintigram of the thoracic vertebral column showing increased radioisotope uptake in the spinous processes of the same area (cranial to the right).

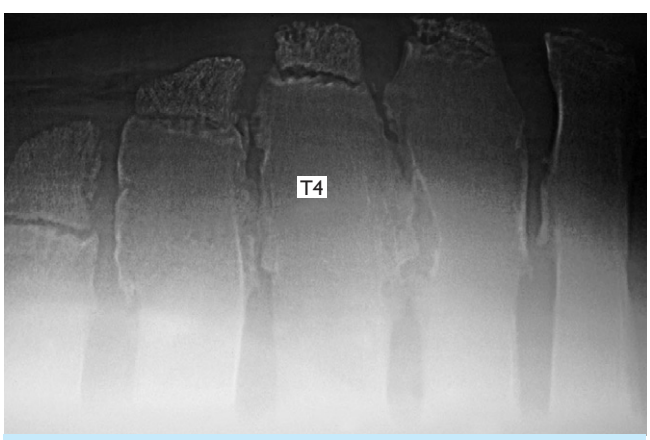
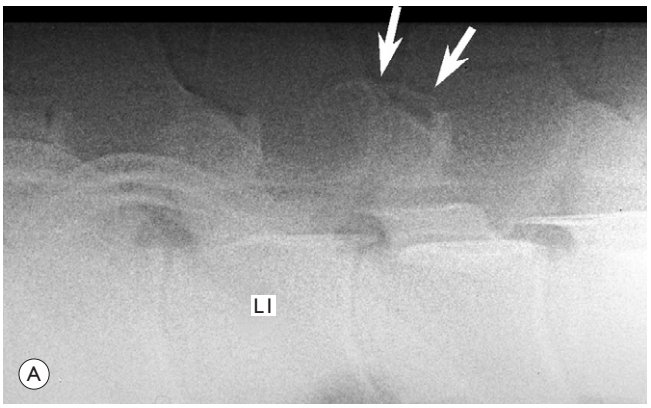


Fig. 10.12
Six-year-old Selle-Français female. Lateral projection of the spinous processes of the withers. Kissing spines between the second and sixth thoracic vertebrae (T4 = fourth thoracic vertebra).



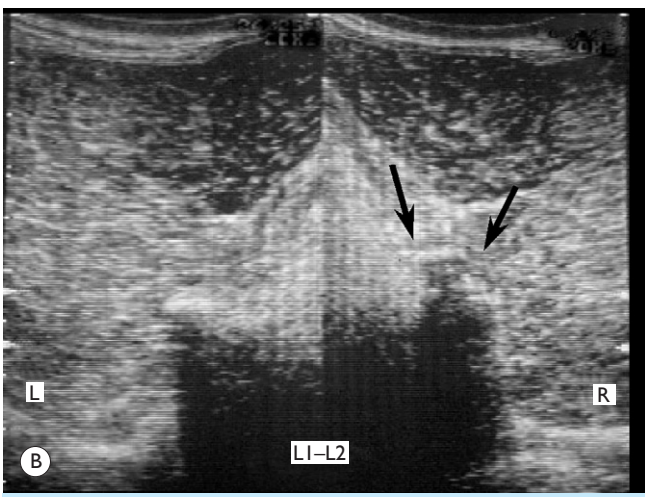


Fig. 10.13
Three-year-old French Trotter filly. (A) Lateral projection of the lumbar spine on the standing patient. Periarticular bone proliferation (arrows) between the first (L1) and second (L2) lumbar vertebrae indicative of osteoarthrosis of the synovial joints between the caudal and cranial articular processes. (B) Transverse ultrasound scan of the back of the same patient at the junction between L1 and L2 (L1–L2) showing that the periarticular osteophyte (arrows) is mainly located on the right side (right scan).

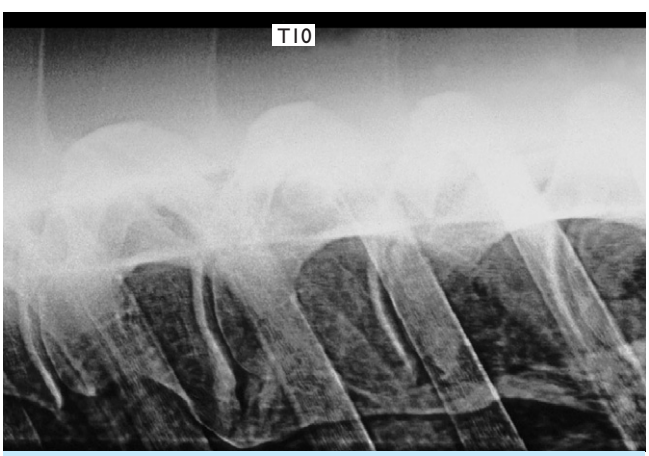


Fig. 10.14
Fourteen-year-old Grand Prix show jumper, Hanoverian male. Lateral projection of the thoracic vertebral column showing an extensive ventral spondylosis between the ninth and twelfth thoracic vertebrae (T10 = tenth thoracic vertebra).

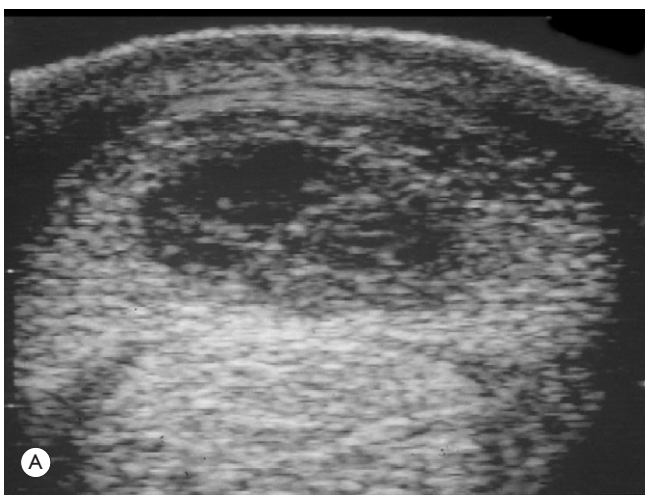
Despite the development of new imaging modalities, radiography remains essential in the management of sport and race horses. Extensive evaluation of the four limbs, back and neck can be made easily with this technique, allowing the detection of clinical, subclinical or silent bone or osteoarticular lesions. This information is useful in the management of high level athletic horses as treatment can be anticipated and preventive measures can be instituted with an adequate shoeing program and adaptation of the physical exercise program.

Ultrasonography

The use of ultrasonography for diagnosis and management of disease in athletic horses began in the 1980s with the assessment of tendon injuries and heart problems. It was considerably extended during the 1990s in the field of exercise physiology, internal medicine, and in the diagnosis of lameness with the application of ultrasonography in the diagnosis of joint injuries.[5]

Providing imaging of soft tissues, and being easy to use, ultrasonography represents an excellent complementary technique to radiography in equine practice. On multiple joints it allows a good representation of ligaments, capsule, synovial membrane and fluid, articular cartilage and subchondral bone. Identification of tendon, ligament and capsule lesions is based on modification of size (thickening and more rarely thinning) and shape as well as modification of echogenicity and architecture (alteration of the fiber pattern).

One of the main applications of ultrasonography in athletic horses is the diagnosis and follow-up of tendon injuries in the metacarpal and metatarsal areas[7–9] as well as in the pastern region.[10,11] The diagnosis of recent lesions is based on the presence of thickening and hypoechogenic areas with altered fiber pattern (Fig. 10.15). These changes are indicative of edema, hemorrhage and rupture of tendon fibers. In old and completely healed lesions, the tendon remains thickened (Fig. 10.16). Although it recovers an echogenicity close to normal, the fiber pattern remains altered, with shorter linear fibers than in uninjured parts of the tendon (Fig. 10.17A). Realization of oblique cross-sections highlights the contrast between the normal parts of the tendon and the scar tissue which remains echogenic because of the non-uniform alignment of its fibers (Fig. 10.17B). Thanks to its real-time capability, ultrasonography is useful for evaluation of dynamic events such as flexor tendon behavior during mobilization of the fetlock.[12] The diagnosis and documentation of enthesopathies has been considerably improved since the combined use of radiography and ultrasonography (see Fig. 10.8). In these conditions, abnormal findings are present in the tendon itself and on the bone insertion surface (the enthesis) where remodeling, lysis and enthesophytes can be seen.



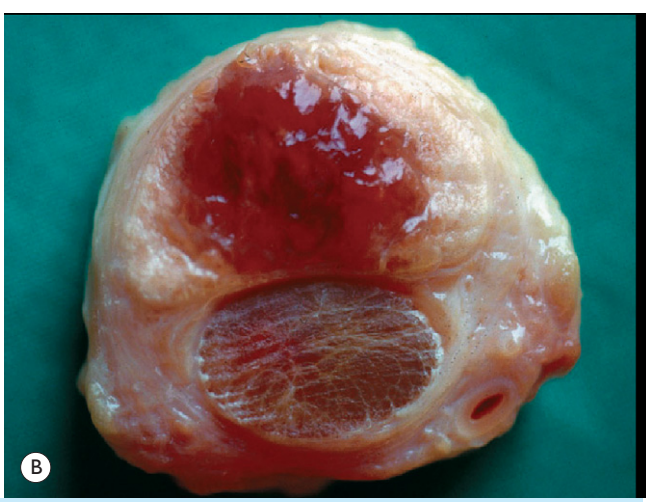


Fig. 10.15
(A) Seven-year-old three-day event Selle-Français gelding. Transverse ultrasound scan of the metacarpal area. Acute hypoechogenic core lesion of the superficial digital flexor tendon. (B) Transverse section of an anatomopathologic specimen showing a typical recent core lesion of the superficial digital flexor tendon.

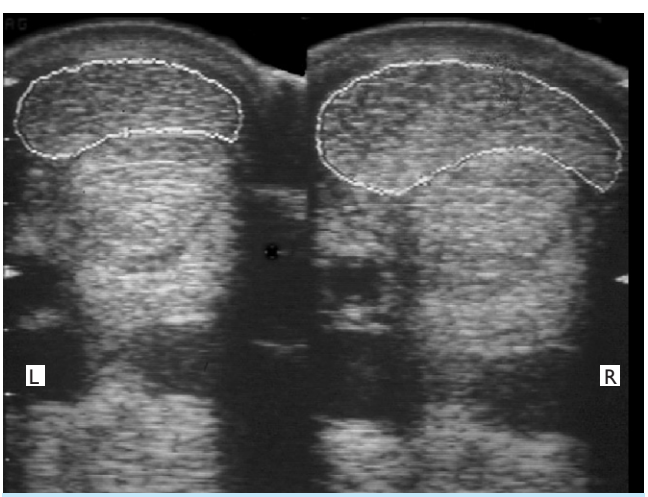


Fig. 10.16
Eight-year-old Grand Prix show jumper, Hanoverian male. Transverse sections of the left (left image) and right (right image) metacarpal areas. Old lesion of the right superficial digital flexor tendon. Note the thickening of the right tendon compared to the left one.

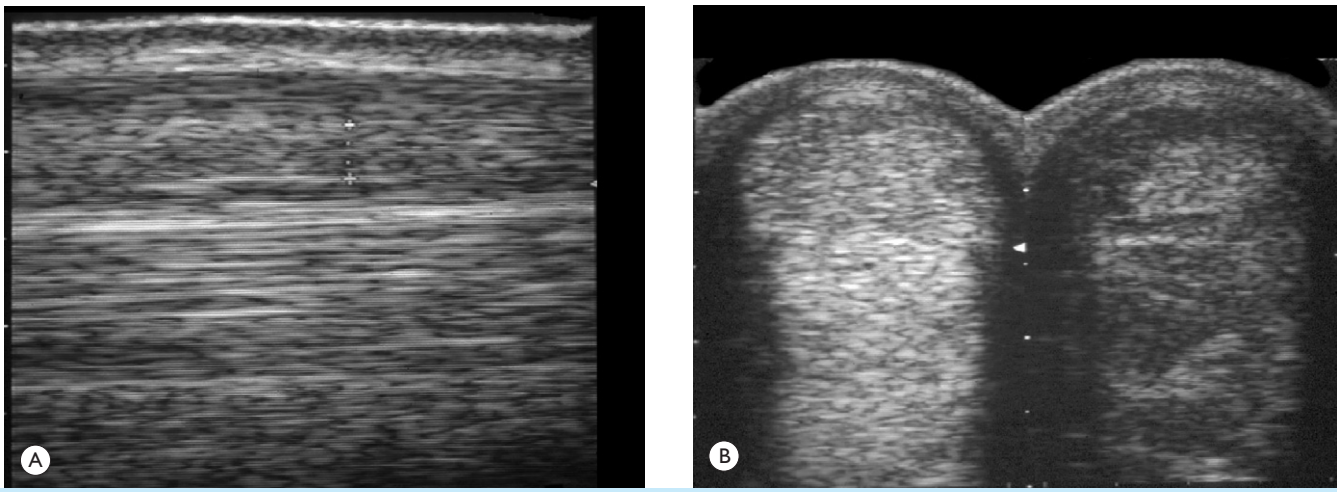
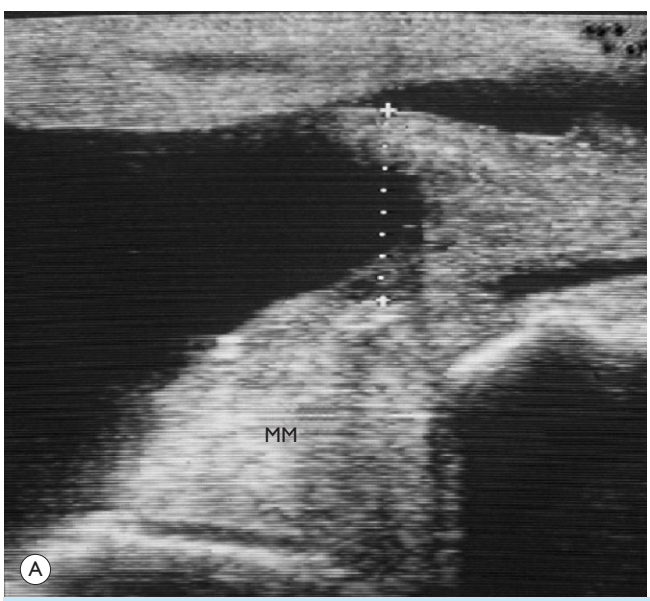


Fig. 10.17
Eight-year-old three-day event Thoroughbred gelding. Old core lesion of the superficial digital flexor tendon. (A) Longitudinal section showing central scar tissue with shorter linear pattern than in the rest of the tendon. (B) Transverse sections. The left scan is made with the ultrasound beam perpendicular to the tendon; the scar tissue and normal tendon present small difference in echogenicity and architecture. On the right scan, the ultrasound beam is oblique and only the scar tissue is echogenic because of the lack of uniform orientation of its fibers. This technique allows better tissue differentiation within the tendon.

Ultrasonography is a well-tolerated technique allowing non-invasive imaging of most of the soft tissues in joints including ligaments.[5,13–15] Complete ligament rupture can easily be diagnosed with this technique (Fig. 10.18A).[16] In



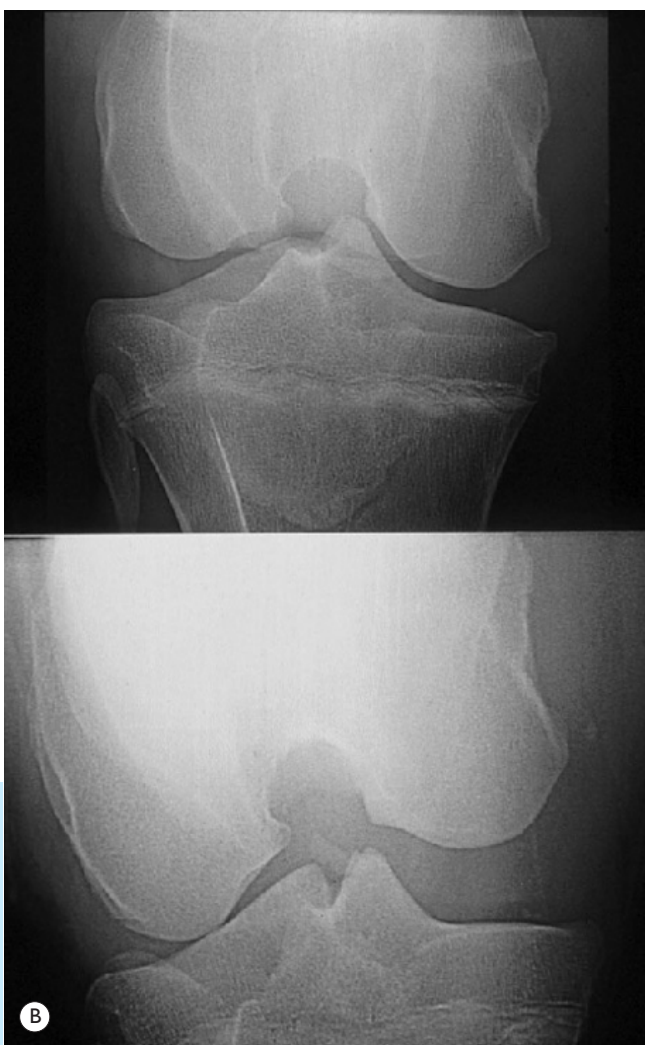


Fig. 10.18
Two-year-old Selle-Français colt that was recently kicked by another horse on the left stifle. (A) Longitudinal ultrasound scan at the medial aspect of the stifle (proximal to the left). Complete intrasynovial rupture (crosses) of the medial collateral ligament of the femorotibial joint. (B) Caudocranial radiographic projections of the same stifle. The lower view was performed after the ultrasound scanning, the limb being gently abducted to demonstrate joint instability. MM, medial meniscus.

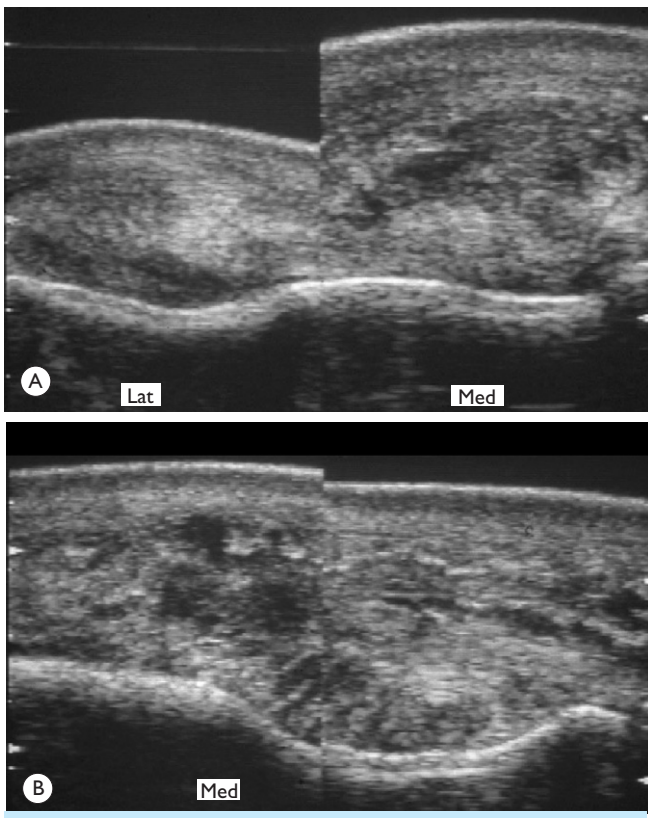


Fig. 10.19
Four-year-old French Trotter filly. Severe chronic desmopathy of the medial collateral ligament of the right hind fetlock. (A) Transverse section of the normal lateral (left) and injured medial (right) collateral ligaments of the affected fetlock. (B) Longitudinal section of the injured medial collateral ligament (proximal to the left). The superficial layer of the ligament is tremendously thickened with a very heterogeneous echogenicity and loss of fiber pattern.

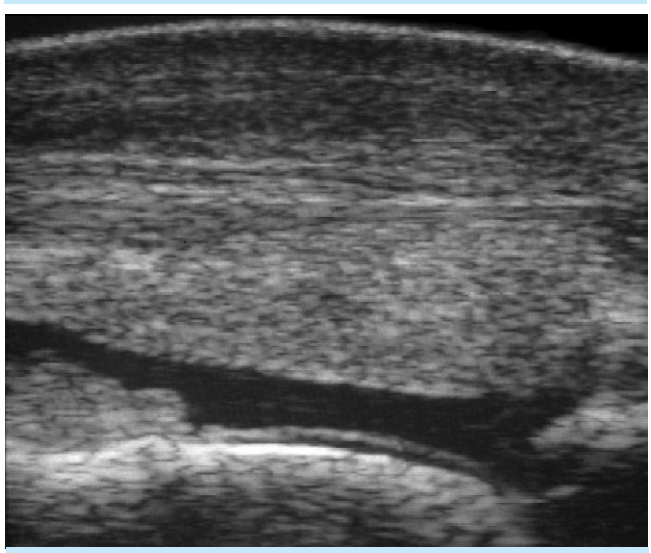


Fig. 10.20
Six-year-old Selle-Français female. Sagittal section of the dorsal aspect of the fetlock (proximal to the left). Mild synovial fluid distension of the dorsal recess of the metacarpophalangeal joint allowing a nice representation of the proximodorsal synovial fold and metacarpal articular cartilage of the fetlock joint.

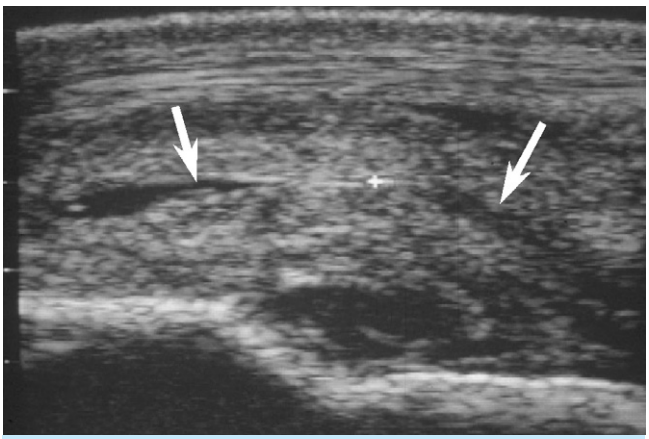
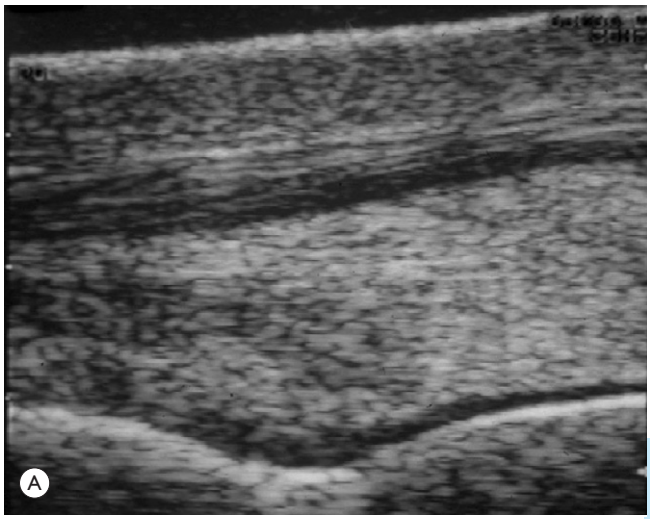


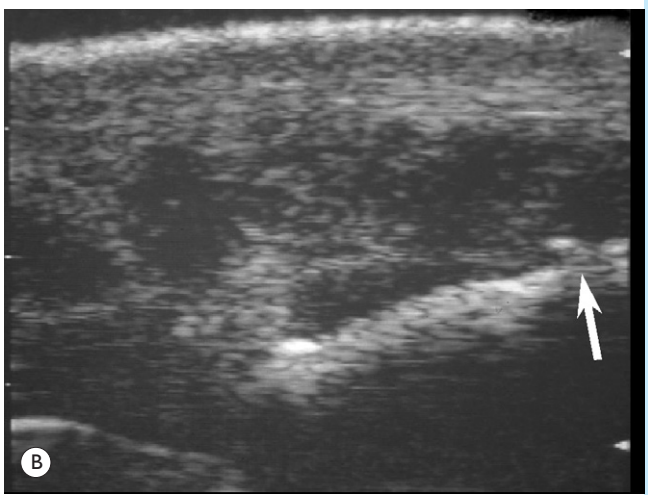
Fig. 10.21
Four-year-old French Trotter male. Sagittal section of the dorsal aspect of the fetlock (proximal to the left). Severe chronic proliferative synovitis of the proximodorsal synovial fold (arrows) of the fetlock joint.

this particular condition, joint instability can be demonstrated with both ultrasonography and radiography (Fig. 10.18B). Acute as well as chronic desmopathies are common in race and sport horses and were often underdiagnosed when diagnostic imaging was limited to radiography. Now with ultrasonography these lesions can be identified (Fig. 10.19) and their healing can be documented.

Many other joint conditions have benefited from the more generalized use of ultrasonography. Synovial fluid distension, often associated to acute or chronic synovitis, can easily be identified with this technique and the presence of fluid highlights the other structures of the joint such as the articular cartilage and synovial plica or villi (Fig. 10.20). Chronic proliferative synovitis at the dorsal aspect of the fetlock no longer requires contrast radiography to be diagnosed, as ultrasonography is much more informative on the architecture of the lesion (Fig. 10.21) and is non-invasive.[5] Capsule lesions also are common, especially in race horses, and again underestimated if imaging is limited to radiography. Their ultrasonographic diagnosis is based on the same criteria used for tendon lesion and enthesopathies (Fig. 10.22). Ultrasonography has also demonstrated the frequent occurrence of meniscal injuries in sport and race horses.[5] These lesions can be found alone or concomitantly with other femorotibial lesions such as subchondral bone cysts, collateral desmopathies or cruciate desmopathies. With reference to the normal appearance of uninjured menisci (Fig. 10.23) several types of lesion can be seen, such as tears (Fig. 10.24), deformation (Fig. 10.25), collapse, prolapse, dystrophic mineralization, and bone metaplasia.[5]

Articular margins, cartilage, and subchondral bone lesions can be shown with ultrasonography, which represents a very valuable complementary technique to radiography for a more complete assessment of joint injuries.[5,13] This technique is very sensitive to any periarticular bone remodeling and osteophyte formation (see Fig. 10.13). Articular cartilage can only be examined when the joint surface is exposed to the ultrasound beam (Table 10.1; Fig. 10.26). Ultrasonography provides





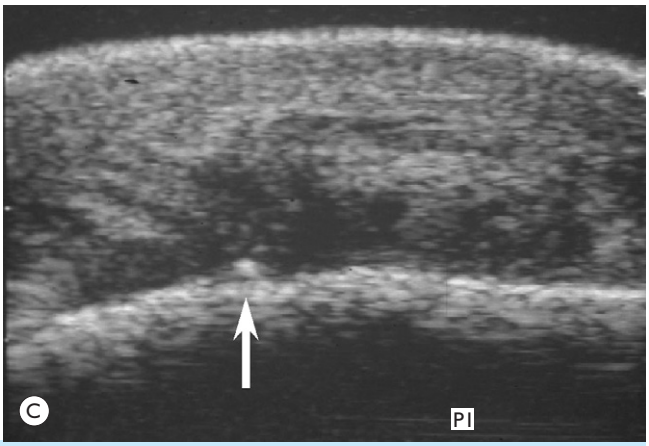


Fig. 10.22
Four-year-old French Trotter male. Sagittal section of the dorsal aspect of the fetlock (proximal to the left). Capsulitis of the fetlock joint. (A) Sagittal section dorsal to the metacarpal condyle. The capsule has a normal appearance. (B) Sagittal section dorsal to the metacarpophalangeal joint space and proximal aspect of the proximal phalanx. The capsule is thickened and hypoechogenic with alteration of its fiber pattern; a small enthesophyte can be seen on the dorsal aspect of the proximal phalanx (arrow). (C) Transverse section at the level of the enthesophyte (arrow) on the dorsal aspect of the proximal phalanx, showing thickening and hypoechogenicity of the capsule. P1, proximal phalanx.

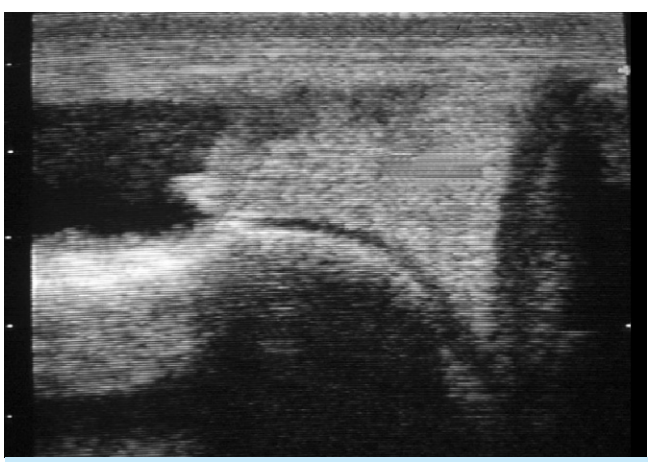


Fig. 10.23
Five-year-old French Trotter male. Reference transverse ultrasonographic image of the medial meniscus obtained from a longitudinal scan performed at the medial aspect of the stifle (proximal to the left). The meniscus presents a triangular echogenic appearance between the medial femoral (left) and tibial (right) condyles.

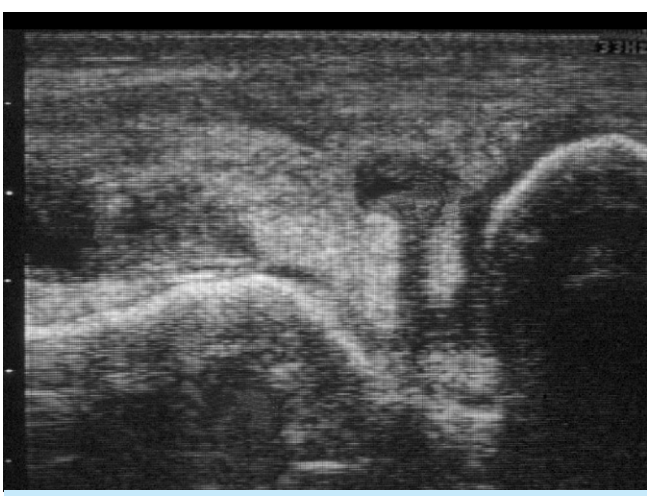


Fig. 10.24
Eight-month-old French Trotter filly. Longitudinal ultrasonographic scan performed at the medial aspect of the stifle (proximal to the left). Severe acute tears of the medial meniscus demonstrated as hypoechoic horizontal and vertical lines dividing the meniscus into three parts.

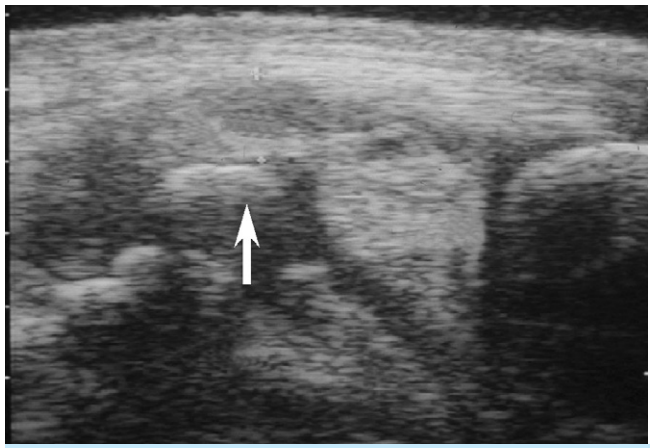


Fig. 10.25
Ten-year-old show jumper, Selle-Français female. Longitudinal ultrasonographic scan performed at the medial aspect of the stifle (proximal to the left). Severe periarticular remodeling of the medial femoral condyle. Compare to the shape of the condyle in Fig. 10.23.

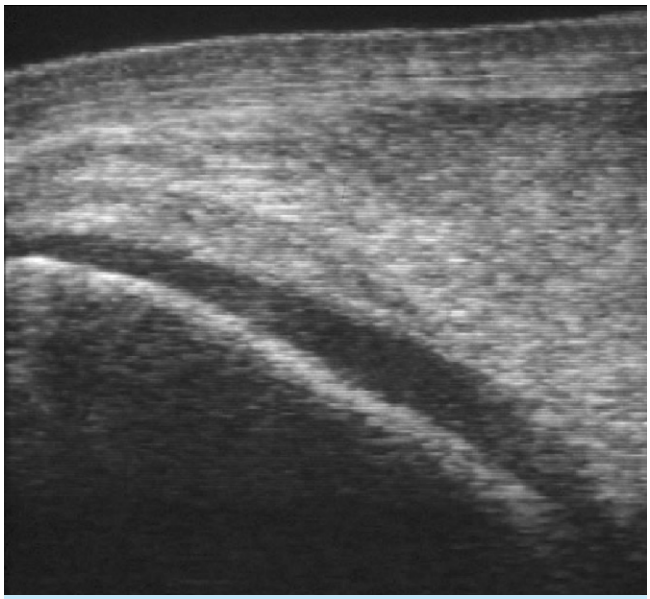


Fig. 10.26
Ten-year-old Thoroughbred gelding used in flat racing. Reference parasagittal ultrasound image of the medial femoral condyle, made on the flexed stifle (proximal to the left). The hypoechogenic articular cartilage separates the articular capsule and the regular hyperechogenic subchondral bone surface.

diagnostic information on the cartilage surface (fibrillation, defect), the deep limit with the subchondral bone (defect of ossification, subchondral osteolysis), and the structure of the cartilage in surfaces where it is thick enough (e.g. femoral trochlea and condyles). With high-definition probes, the cartilage thickness can be measured, and complete, as well as partial, defects can be documented. A cartilage lesion must be considered if ultrasonographic examination reveals the presence of periarticular osteophytes, joint distension with synovitis or echogenic spots in the synovial fluid.

Table 10.1 Ultrasonographic access to articular surfaces in horses

Joints	Weight bearing	Flexion	Main limitations
Fetlock joint	Dorsal aspect of the metacarpal condyle	Distal aspect of the metacarpal condyle	• Proximal surface of proximal phalanx • Articular surface of the proximal sesamoid bones • Plantar aspect of the metacarpal/tarsal condyle
Antebrachiocarpal joint	Articular margins	Most of the distal surface of the radius	Proximal surface of the proximal row of the carpus
Middle carpal joint	Articular margins	Most of the proximal surface of C3	Distal surface of the proximal row of the carpus
Shoulder	Articular margins and peripheral part of the humeral head	Flexion and adduction: lateral part of the humeral head	Distal surface of the scapula Medial part of the humeral head
Tarsocrural joint	Dorsal aspect of the trochear ridges of the talus	Plantar aspect of the trochear ridges of the talus	Distal surface of the tibia
Femoropatellar joint	Trochear ridges of the femur	No more	Articular surface of the patella
Femorotibial joint	Articular margins and abaxial surfaces of the femur and tibia	Femoral condyles	Tibial condyles

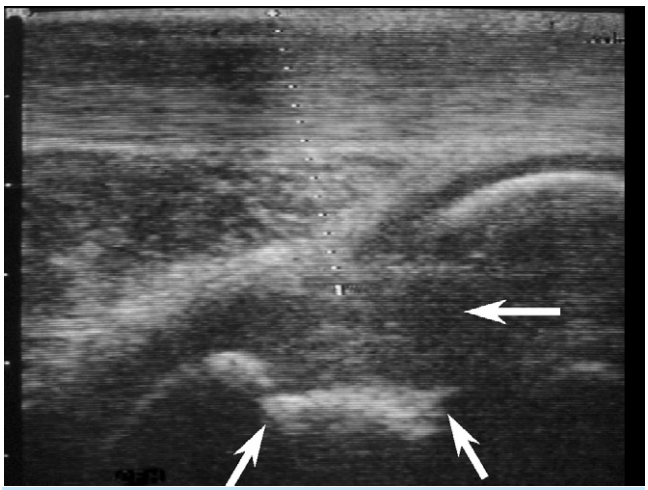


Fig. 10.27
Two-year-old Thoroughbred colt. Parasagittal ultrasound scan showing a large subchondral cyst (arrows) of the medial femoral condyle. The dotted line was drawn to measure the depth of the lesion.

The normal subchondral bone surface is imaged as a regular hyperechogenic line.[5,17] This line is interrupted by subchondral bone cysts, which are imaged as subchondral bone depressions (Fig. 10.27). Sensitivity of utrasonography to detect subchondral bone defects is high, and is often superior to radiography. This technique is also very sensitive to subchondral bone lysis (Fig. 10.28). In the proximal regions of the limbs, the diagnosis of bone fracture is easier with ultrasonography than with radiography, especially in field practice. Transrectal examination of the medial aspect of the acetabulum allows diagnosis of acetabular fracture (Fig. 10.29) on the standing horse avoiding the need for a radiographic examination in dorsal recumbency under general anesthesia, which presents a risk for the patient.

Ultrasonography brought new significant knowledge in the causes of lameness and poor performance in horses involving the foot, back and pelvis.[18,19] In the foot, the diagnosis of suprasesamoidean deep digital flexor tendinopathy, as well as distal enthesopathy of this tendon on the flexor surface of the distal phalanx, can be acheived with adequate probes and technique (Fig. 10.30).[15,18] Distal impar sesamoidean desmopathy and enthesopathy can also be diagnosed with a distal approach of the foot through the frog (Figs 10.31, 10.32). Routine

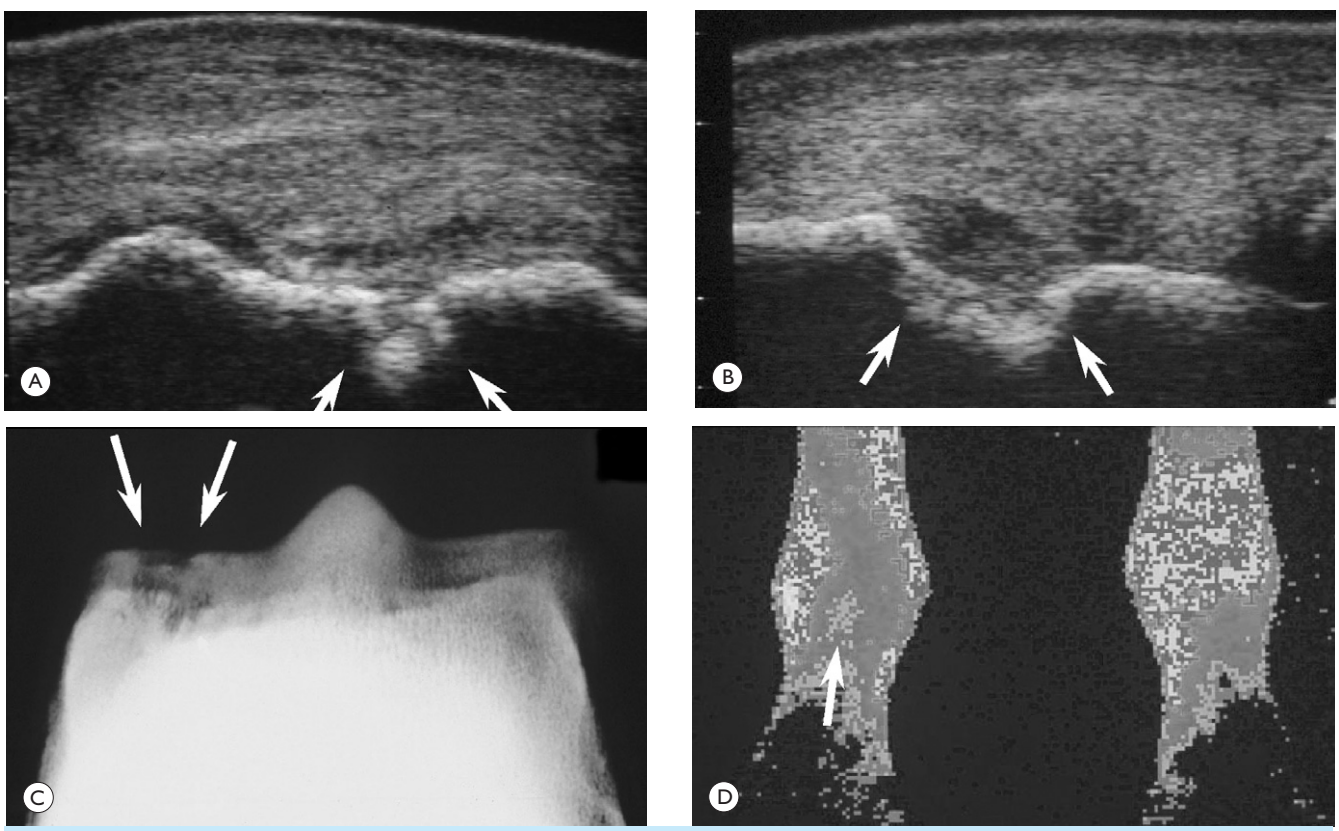


Fig. 10.28
Five-year-old French Trotter gelding. Subchondral osteolysis of the medial metacarpal condyle of the right fetlock. (A) Transverse ultrasound scan of the metacarpal condyle showing a focal subchondral osteolysis of the medial condyle (arrows). (B) Parasagittal ultrasound scan of the medial metacarpal condyle confirming the subchondral osteolysis (arrows). (C) Subsequent proximodistal radiographic projection of the flexed fetlock demonstrating the severe subchondral osteolysis of the medial metacarpal condyle (arrows). (D) Thermographic image demonstrating a colder area over the medial metacarpal condyle of the right fetlock.

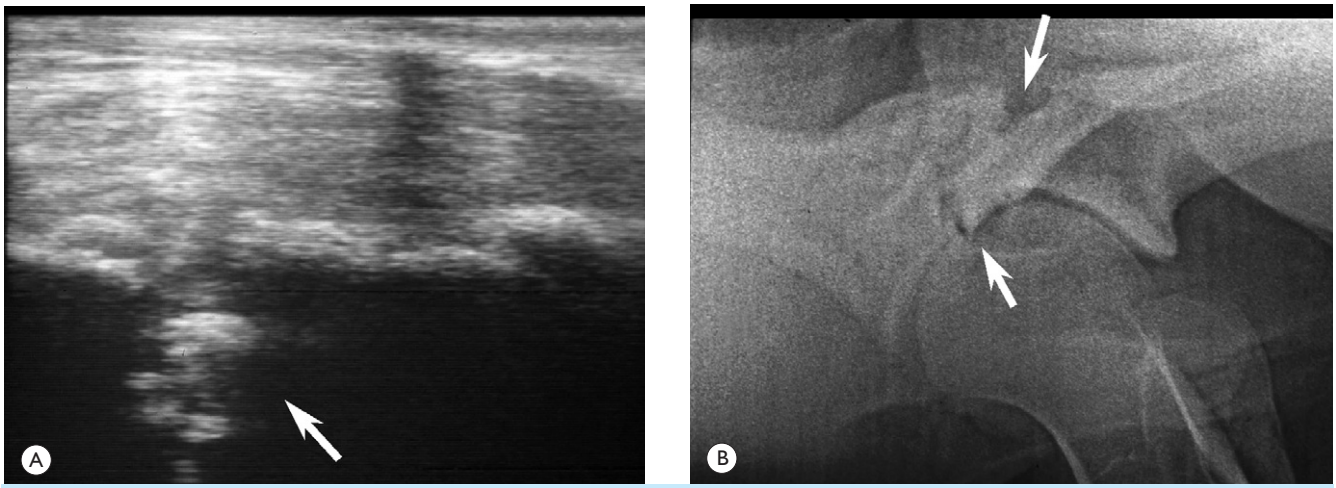


Fig. 10.29
Two-year-old French Trotter filly. (A) Transrectal ultrasound scan of the medial aspect of the acetabulum showing an echogenic fracture line (arrow) interrupting the bone surface of the coxal bone. (B) Subsequent radiographic examination of the hip area on the standing patient demonstrating the acetabular fracture and moderate displacement of the bone fragments (arrows).

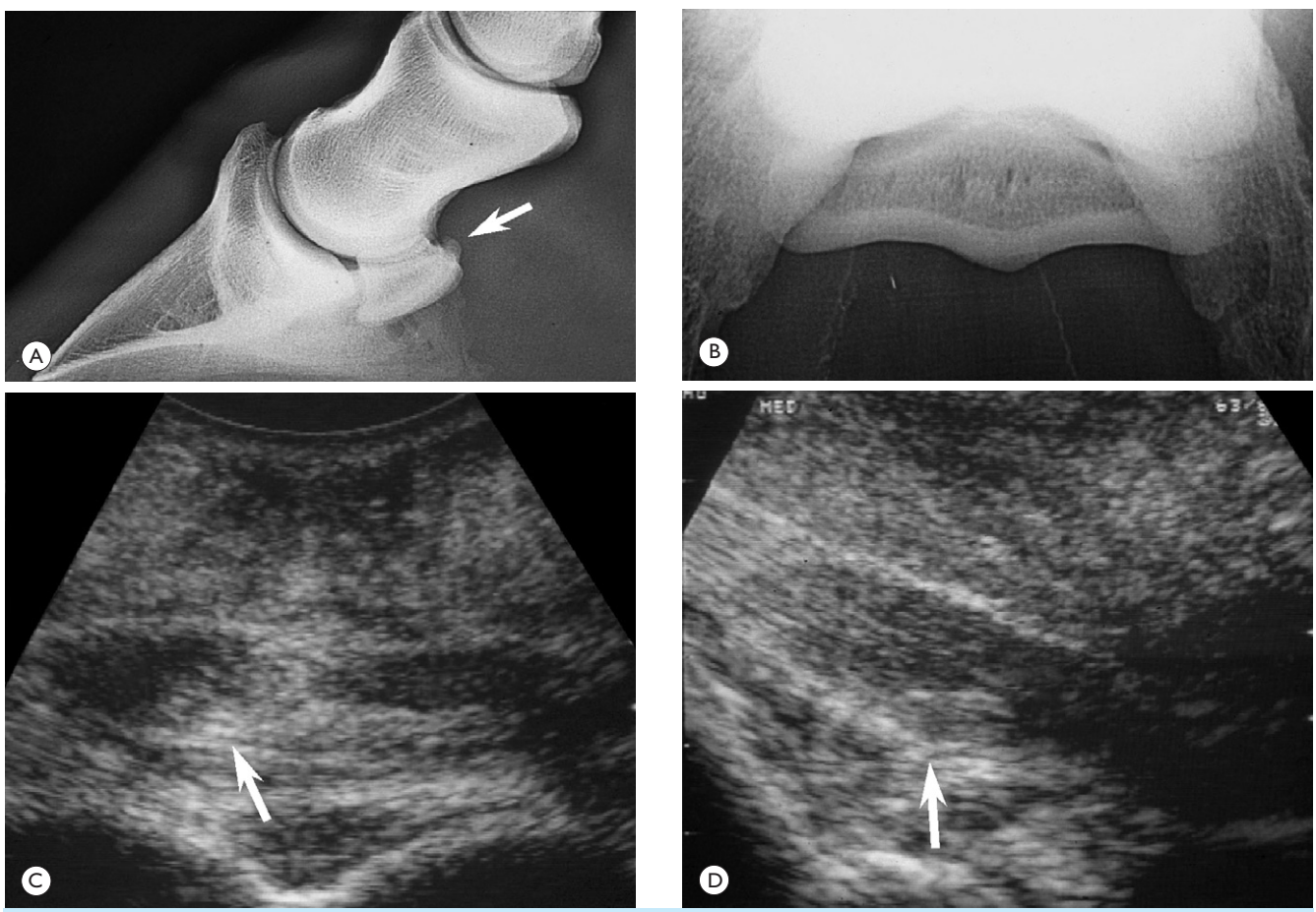


Fig. 10.30
Ten-year-old show jumper, Selle-Français stallion. Suprasesamoidean tendinopathy of the deep digital flexor tendon (DDFT). (A) Lateromedial radiographic projection of the affected foot showing remodeling of the proximal border of the distal sesamoid bone (arrow). (B) Proximopalmar–distodorsal radiographic projection of the distal sesamoid bone showing a normal flexor surface. (C) Transverse ultrasound scan of the DDFT using a proximopalmar approach of the navicular apparatus, the probe being placed at the most distal aspect of the pastern. The medial part of the DDFT (on the left) is thickened (compare to the lateral part, on the right) and presents deep abnormal echogenic material indicative of dystrophic mineralization (arrow). (D) Medial parasagittal ultrasound scan of the DDFT using a proximopalmar approach of the navicular apparatus. The medial part of the DDFT is thickened (its two borders are convex) and presents deep abnormal echogenic material indicative of dystrophic mineralization (arrow).

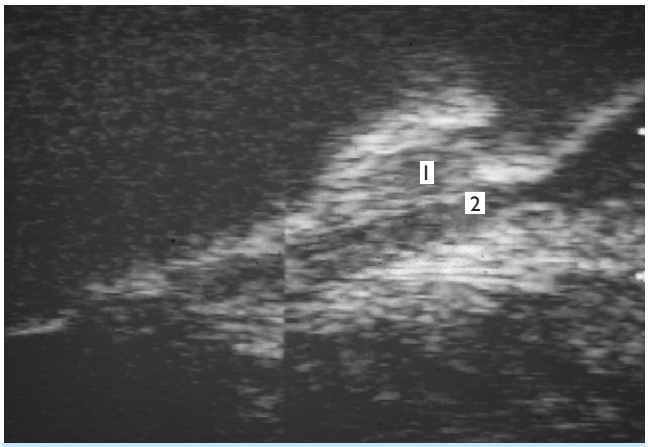


Fig. 10.31
Four-year-old French Trotter gelding. Reference ultrasound scan of the distal aspect of the navicular apparatus imaged through the frog. The distal impar sesamoidean ligament (1) is more echogenic than the deep digital flexor tendon (2).

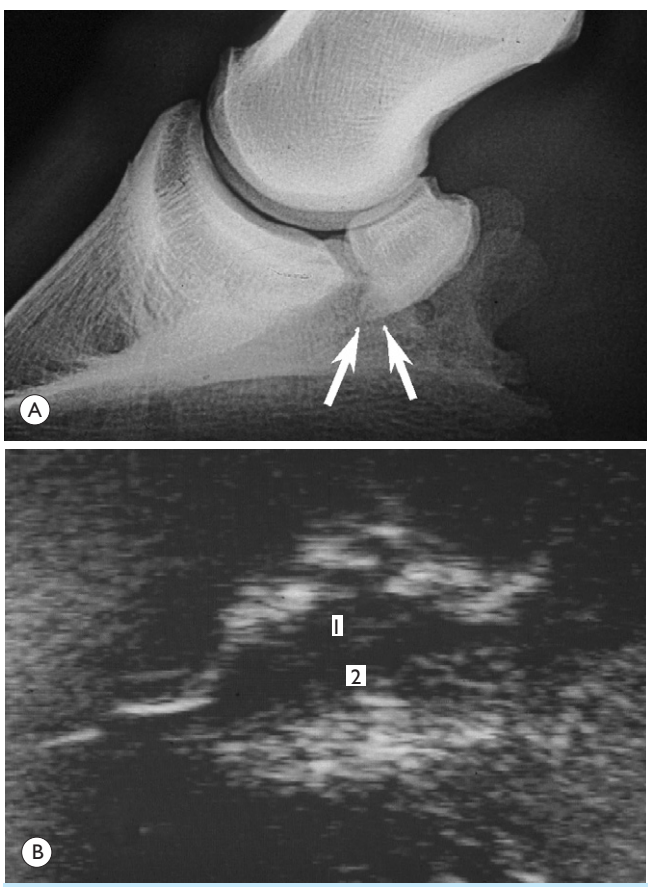


Fig. 10.32
Eleven-year-old show jumper, Selle-Français gelding. Desmopathy and enthesopathy of the distal impar sesamoidean ligament (DISL). (A) Lateromedial radiographic projection of the affected foot showing remodeling and osteolysis of the distal border of the distal sesamoid bone (arrows). (B) Ultrasound scan of the distal aspect of the navicular apparatus imaged through the frog. The DISL (1) is completely anechogenic and severe bone remodeling is present at its proximal and distal attachments (2).

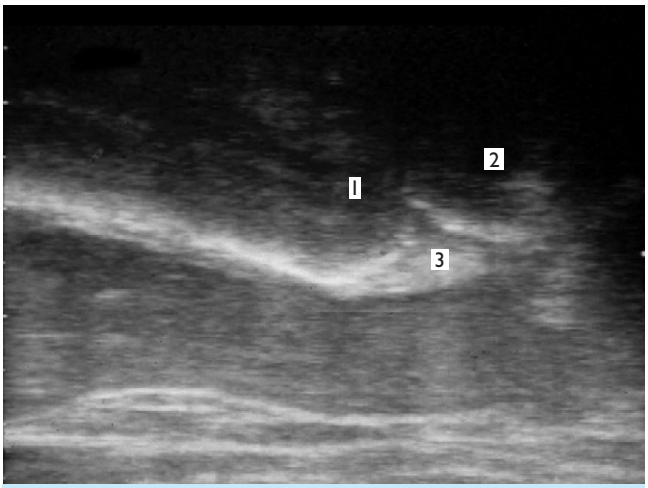


Fig. 10.33
Six-year-old French Trotter gelding. Reference transrectal ultrasound scan of the ventral aspect of the sacroiliac joint. The articular margins of the sacrum (1) and ilium (2) are smooth and regular and the ventral sacroiliac ligament is echogenic (3).

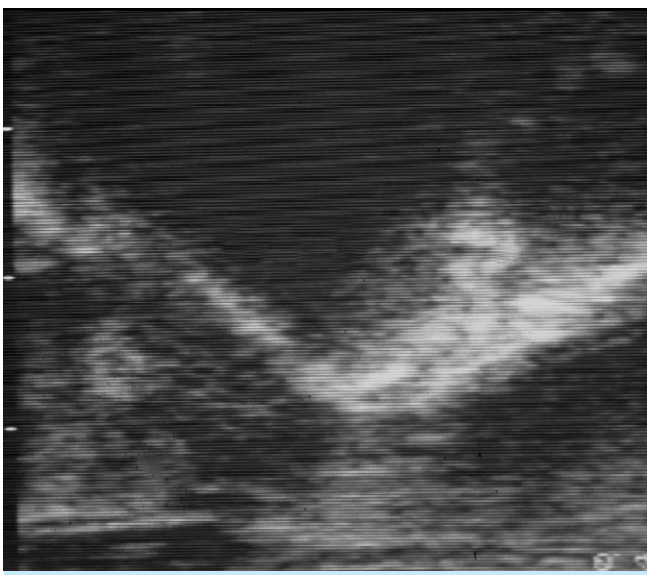
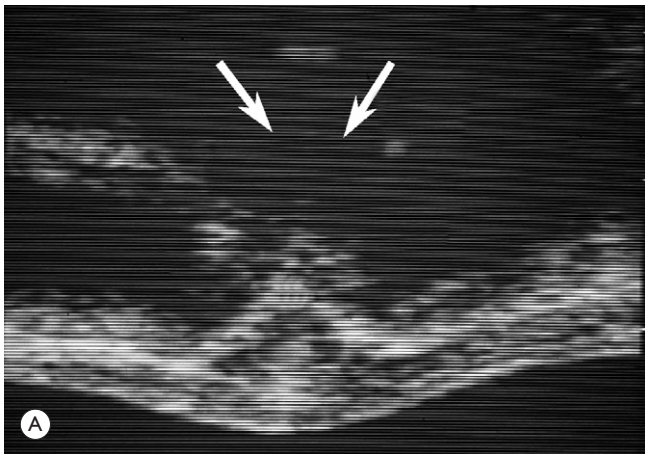


Fig. 10.34
Six-year-old Selle-Français stallion. Transrectal ultrasound scan of the ventral aspect of the sacroiliac joint. There is marked remodeling and elevation of the articular margins of the joint indicative of sacroiliac degenerative disease.

transrectal ultrasonographic examination of the lumbosacroiliac area provides valuable diagnostic information on the causes of hind limb gait irregularities and poor performance in athletic horses.[19] Sacroiliac degenerative lesions can be demonstrated (Figs 10.33, 10.34). Lumbosacral disk degenerative lesions have been diagnosed in clinical cases and documented in horses subsequently examined post-mortem (Fig. 10.35).[18] Other abnormal findings observed in athletic horses include lumbosacral ankylosis, disk dystrophic mineralization, bone lesion involving the vertebral fossa of the last lumbar vertebra and lumbosacral subluxation (Fig. 10.36).



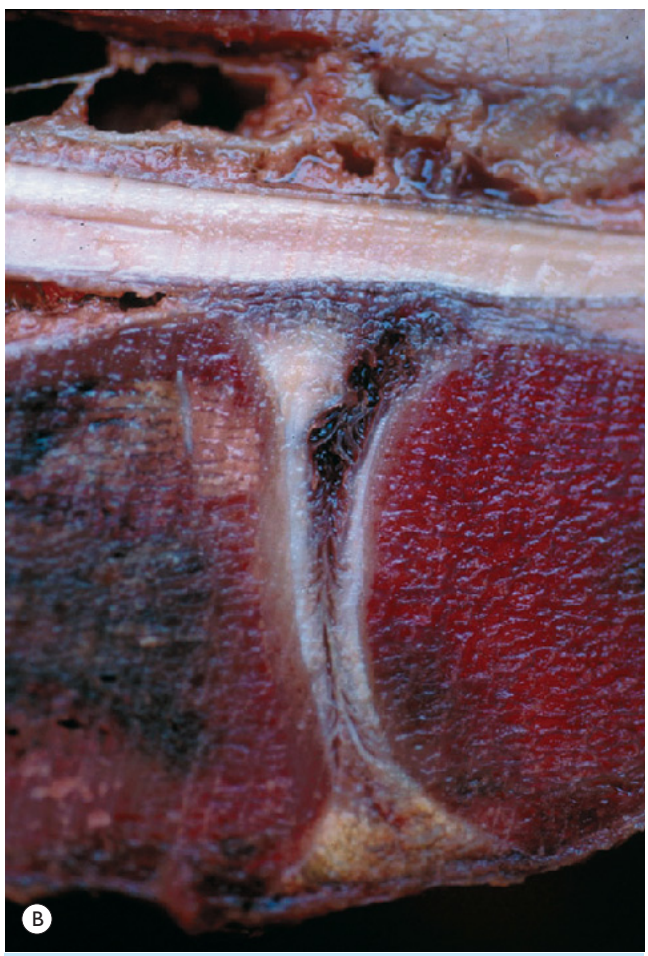


Fig. 10.35
Six-year-old French Trotter female. Severe lumbosacral intervertebral disk degeneration. (A) In vivo median transrectal ultrasound scan of the ventral aspect of the lumbosacral joint. Only the ventral part of the disk is echogenic; the dorsal part is completely anechogenic (arrows). (B) Post-mortem frozen specimen of the same intervertebral disk imaged on a median section. There is disruption of the disk fibers with fluid accumulation in the dorsal part of the disk.

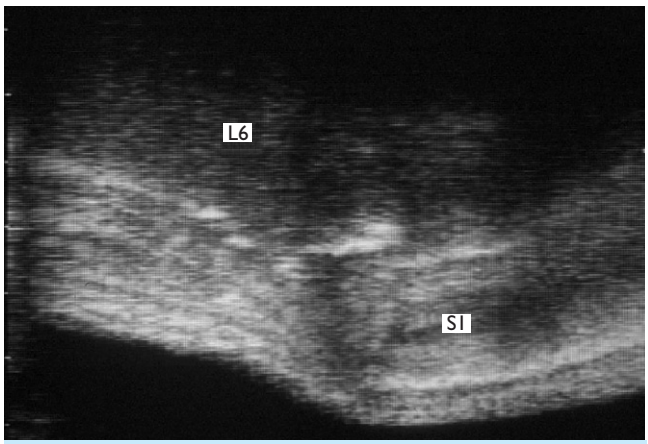


Fig. 10.36
Three-year-old French Trotter female. Lumbosacral subluxation (spondylolisthesis). There is ventral displacement of the sacrum (S1, on the right) relative to the sixth lumbar vertebra (L6, on the left).

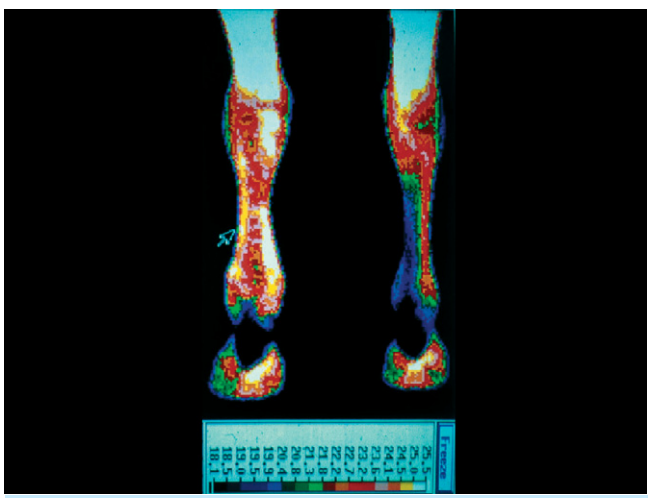


Fig. 10.37
Palmar aspect of the forelimbs of a 7-year-old French Trotter female with an acute episode of suspensory desmitis on the left limb. The palmar aspect of the left metacarpal area is approximately 4°C warmer than the right one.

Ultrasonography requires considerable knowledge of soft tissue anatomy[15,17] as well as a precise and rigorous technique. As there are many breed and individual variations in the size of anatomical structures, each specific element must be compared with the equivalent one on the opposite limb or with the more cranial and caudal ones in the neck and back. If a lesion is suspected it must be demonstrated on longitudinal and transverse sections, and the findings must be different from the equivalent unaffected structure when the same approach is made.

The acoustic impedance of bone and air is responsible for the main limitations of ultrasonography. Because of that, the deep internal architecture of bones and lungs cannot be imaged and the access to abdominal viscera is incomplete. Regarding the musculoskeletal system, ultrasonography is limited for a complete representation of the internal structures of the foot, the medial aspect of the shoulder, the cruciate ligaments within the intercondylar fossa of the femur, the

interosseus sacroiliac ligament and the interosseus ligaments of the carpus and tarsus. Limitations of ultrasonography in the evaluation of the articular cartilage include: the limited access to articular surfaces in congruent and low mobile joints (see Table 10.1); the lack of precise information on architectural changes and the need for high-definition probes for evaluation of thin articular cartilage such as in the distal part of the metacarpal condyle.

Today, for the assessment of equine musculoskeletal diseases, ultrasonography must be used in conjunction with radiography on most of the clinical cases requiring an imaging evaluation. With the constant technological improvement of ultrasound imaging equipment, the use of this modality will be applied to new anatomic areas with new approaches. Therefore, this technique will continue to advance the progress in equine veterinary diagnosis and science and will expand its use for the management of athletic horses.

Topographical techniques

Two techniques, thermography and nuclear scintigraphy, can be used in conjunction with the clinical examination in an attempt to identify the location of pathological processes.

Thermography

Using infrared cameras, complete thermal imaging of the horse body or a focused evaluation of a precise area is easy to perform.[20] In all cases, image acquisition must be done under standardized conditions. As interpretation is mainly based on the comparison of symmetrical areas, the horse limbs must be placed symmetrically, without lateral or medial rotation. During image acquisition of the axial regions, the horse must stand square while the camera is strictly placed in the median plane.

Much emphasis has been placed on the detection of acute inflammatory processes (Figs 10.37, 10.38) and this procedure seems useful in the detection of early changes in the flexor tendons in horses in training or competition.[20] In

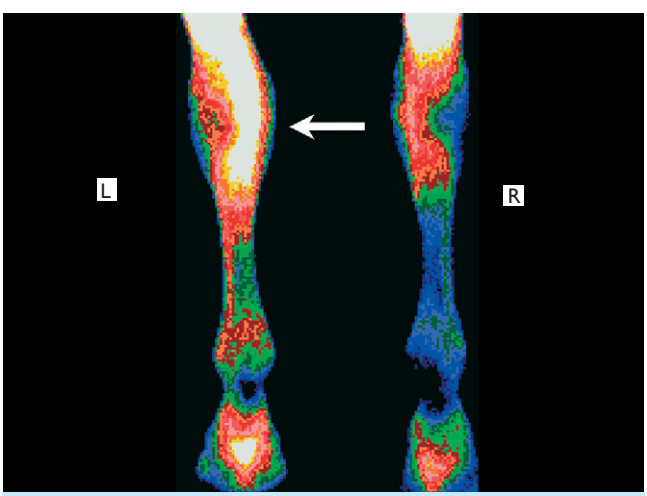


Fig. 10.38
Palmar aspect of the forelimbs of an 8-year-old show jumper, Selle-Français male with a recent left front limb lameness and a mild swelling at the palmaromedial aspect of the carpus. This area presents an increased skin temperature compared to the opposite (arrow). Utrasonographic examination showed that the horse had a rupture of the flexor retinaculum.

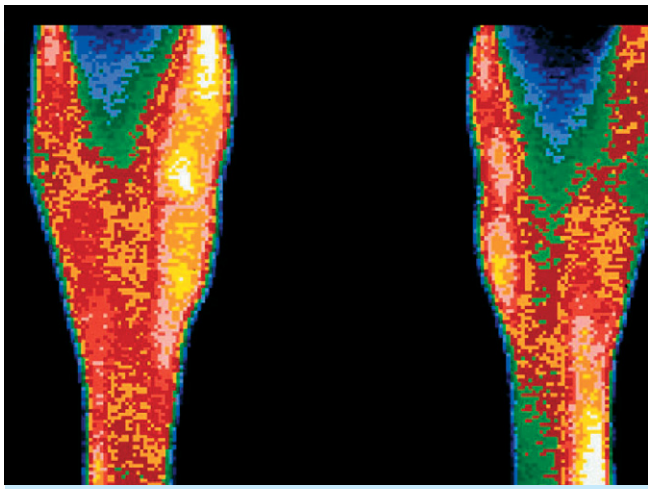


Fig. 10.39
Plantar aspect of the hind limbs of a 14-year-old Grand Prix show jumper, Selle-Français gelding with a chronic proximal enthesopathy of the left suspensory ligament. The plantaromedial aspect of the left hock and proximal metatarsal area is mildly warmer than the opposite ones (same horse as Fig. 10.47).

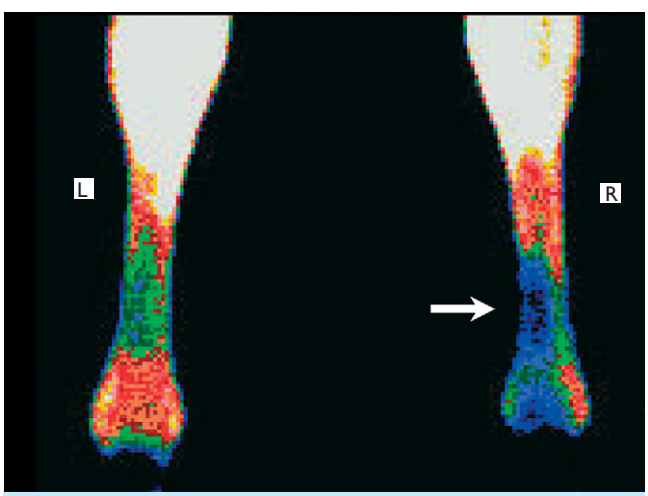


Fig. 10.40
Palmar aspect of the forelimbs of a 6-year-old steeplechaser Thoroughbred gelding who presented a severe right superficial digital flexor tendinitis 12 months before this image was made. The skin temperature of the right tendon region is colder than the opposite one (arrow) indicating a good tolerance of the exercise level of activity during the reconditioning program.

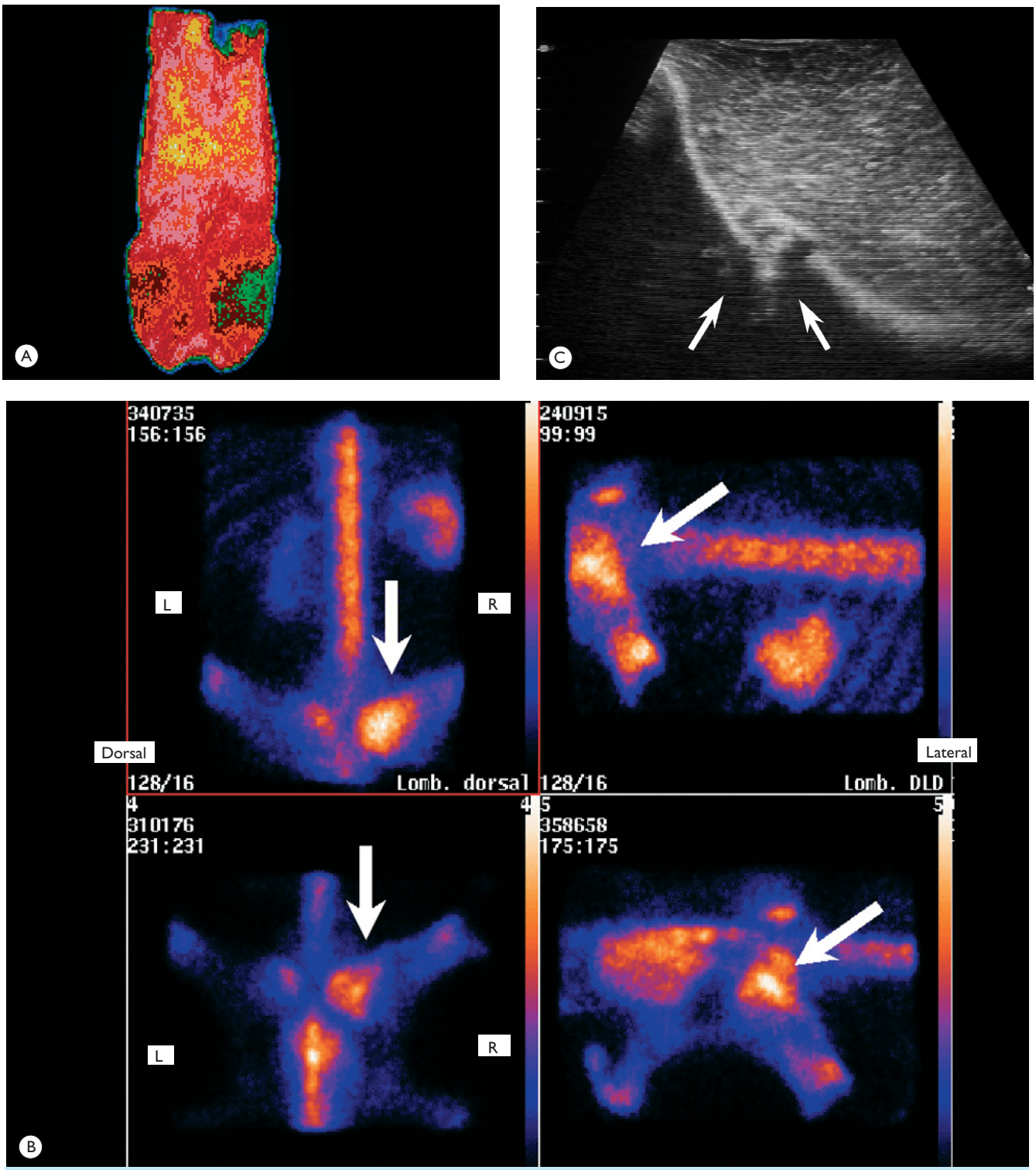


Fig. 10.41
Imaging documentation of a 6-year-old Thoroughbred gelding who presented an acute and severe lameness of the right hind limb during a flat race 10 days before the examination. (A) Dorsal aspect of the back and pelvis showing a cold area over the right side of the croup. (B) Bone phase scintigraphic image of the dorsal aspect of the pelvis. Increased radioisotope uptake is observed over the right ilial wing close to the sacroiliac joint (arrows). (C) Transverse ultrasound scan of the right side of the croup showing a sagittal fatigue fracture (arrows) with callus formation of the ilial wing. The cold cutaneous area observed on the thermogram (A) can be related to sympathetic reflex in the affected region as well as disuse of the painful structures.

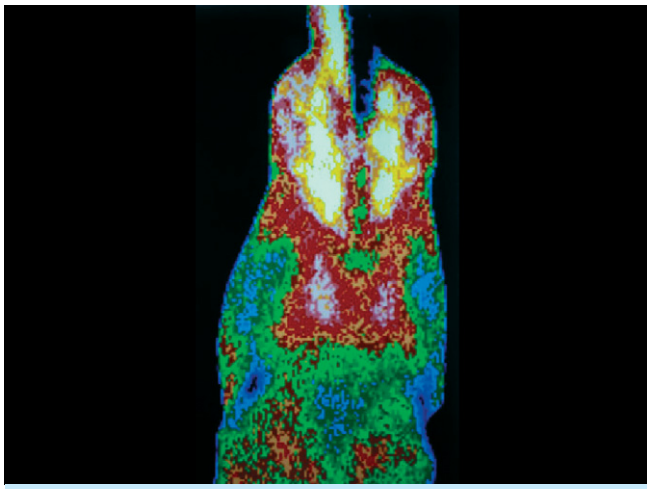


Fig. 10.42
Thermogram of the dorsal aspect of the back and neck of a 10-year-old show jumper, Selle-Français female with severe osteoarthrosis in the caudal cervical spine. A symmetric hot area can be seen in the withers receiving the ultimate endings of the dorsal rami of the caudal cervical spinal nerves.

chronic processes, the diagnostic value of thermography is more limited (Fig. 10.39), and in many cases, cold spots can be seen over the injured areas (see Fig. 10.28D). Thermography is useful for follow-up of horses returning to training after suffering tendinopathies (Fig. 10.40). Alteration of the skin temperature may also be induced by nerve reflex (Fig. 10.41) or nerve irritation or injury (Fig. 10.42).

Thermography is completely non-invasive and easy to use. Thermograms are real-time images, easy to read and understand by horse owners. This method is useful for documentation of a lesion and presents a pedagogical point-of-interest to support the discussion of the pathophysiology of a disease process.

The diagnostic value of this method has been actively promoted in the veterinary market during the last 10 years. Nevertheless, thermography presents some limitations, including the lack of sensitivity to deep lesions and chronic processes, and a lack of specificity because of interference, with many artifacts. Therefore, interpretation of the images must be done carefully to avoid false-negative and false-positive diagnoses.

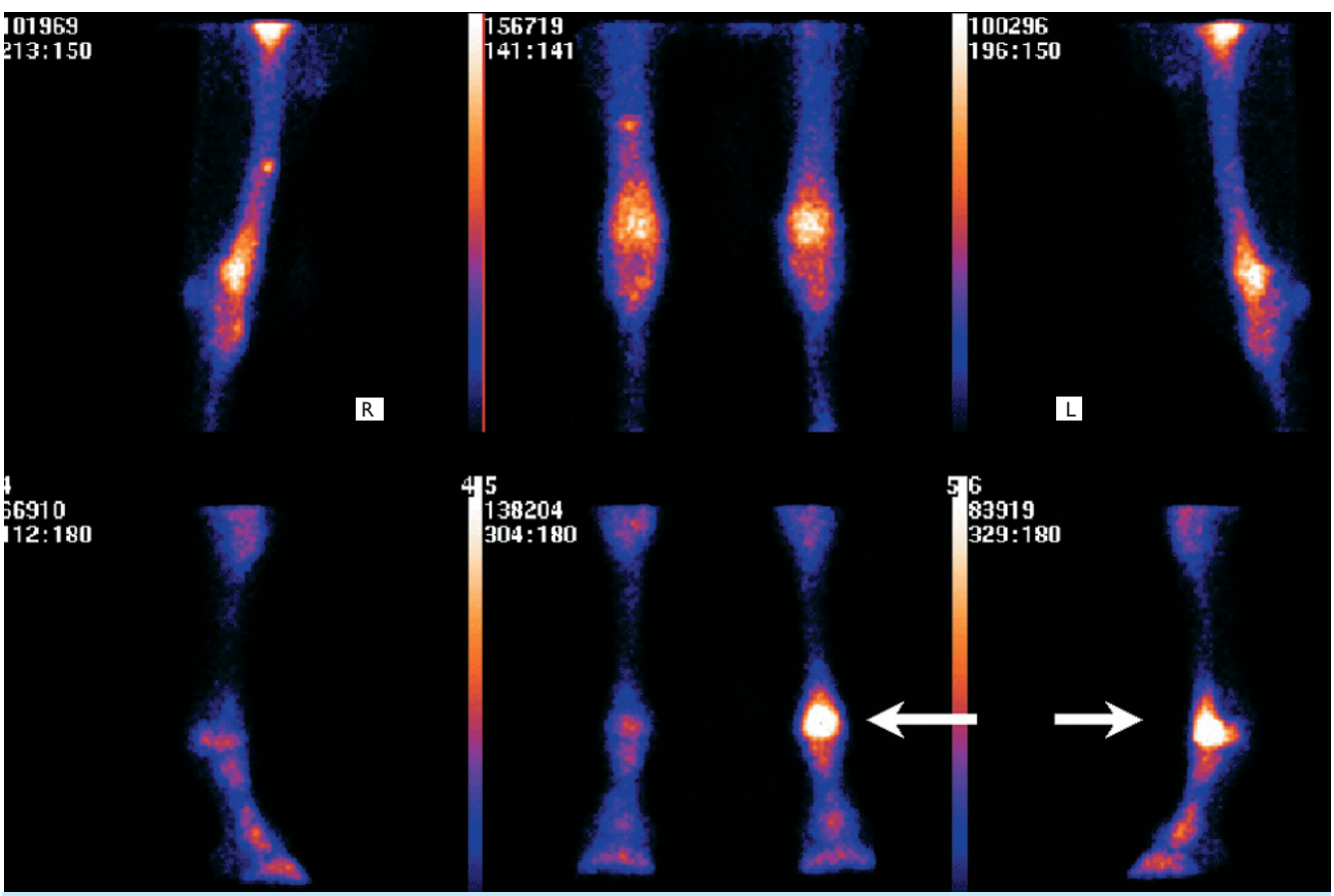


Fig. 10.43
Five-year-old French Trotter male presenting a chronic right front limb lameness at low and high speeds, improved after analgesia of the proximal suspensory ligament. There is intense radioisotope uptake in the metacarpal condyle of the left front fetlock (arrow), which was interpreted as a secondary compensating change induced by functional overload.

Nuclear scintigraphy

Bone scintigraphy is based on the detection of the fixation of polyphosphonate molecules labeled with technetium on bone sites undergoing active remodeling.[21] The bone tracer binds on the hydroxyapatite crystals of newly forming bone. The detection of bone radiation activity is made using a gamma camera.

Scintigraphy is indicated in many clinical situations, the two most common indications being a complete whole-body scan ('locomotor check-up') in horses presented because of poor performance without obvious lameness, and investigation of a specific lameness that is difficult to diagnose. Other common indications include detection of mutiple sites of pain, identification of back and pelvis osteoarticular injuries, investigation of non-blockable lameness and examination of hind limb (or front limb) lamenesses in dangerous horses.

After injection of the radiolabeled phosphonate, complete osteoarticular scintigraphic examination consists of three phases.[22,23] The vascular phase occurs immediately after injection. Because of this, the camera must be placed against the most clinically interesting region before performing the injection. The second phase is the soft tissue phase and images must be made within 10 to 15 min after injection. Soft tissue phase scintigraphy provides information regarding injuries such as tendinitis,[23] synovitis, or bursitis.[24] The bone phase examination, the third phase, is usually performed 3 h after injection.

The technique of image acquisition and interpretation has been described in several papers[21,23] and only specific comments are made in this chapter. Physical exercise before injection of the marker is highly recommended to increase distribution of the marker in the distal and middle parts of the limbs as well as in the regions presenting lesions or compensating stresses. Longeing for 15 min is effective for sport horses.[25,26] In race horses, and especially in Trotters, exercise on the track is preferable because it reproduces the biomechanical conditions responsible for the athletic problems of the patient.

Interpretation of the scintigraphic images is based mainly on the detection of radiopharmaceutical uptake ('hot spots'). The distribution and intensity of bone uptake is dependent on the individual horse, age, conformation,[26] locomotion as well as the discipline in which the horse is used.[27] Therefore, it is critical to compare carefully the radioisotope uptake pattern of homologous limbs and symmetric areas of the same patient to appreciate the significance of each site. To do that, it is important to get absolutely symmetric images during image acquisition (same frame, same 3D orientation, same distance). Positioning of the horse, of the limb (or back), and placement of the camera must therefore be standardized.

The amount of radiation detected by the camera is dependent on morphologic parameters (bone size), physiologic parameters (bone remodeling), and the thickness of overlying soft tissues. The amount of radioisotope uptake of a particular location depends on the blood distribution (bone perfusion) of the radiopharmaceutical and on the degree of bone remodeling of this site. Therefore, scintigraphy provides physiopathologic information. Bone remodeling increases

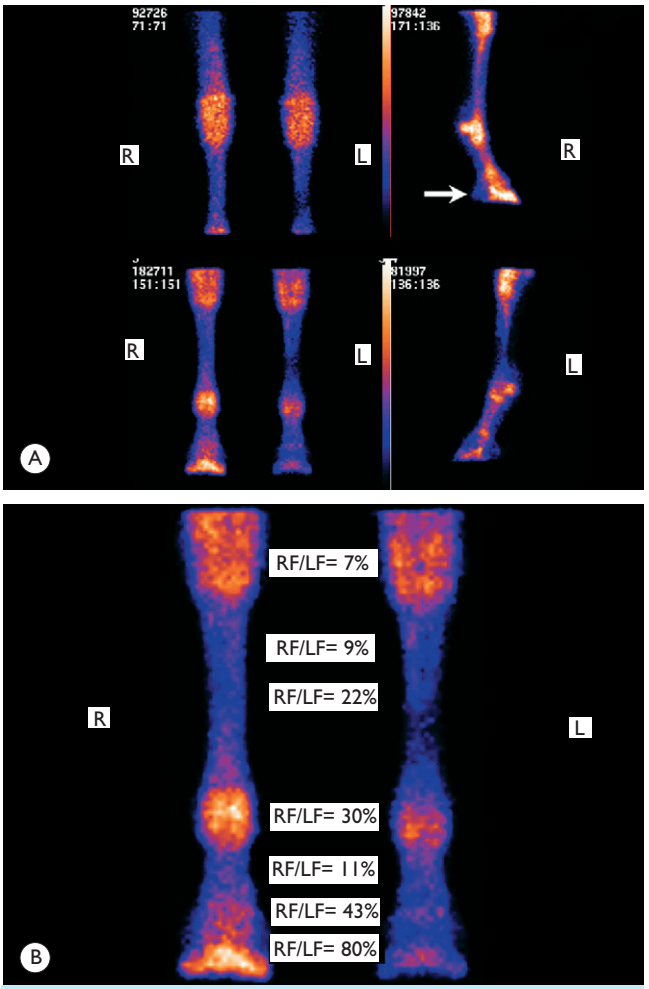


Fig. 10.44
Five-year-old Trackener male used for dressage presenting a right front limb lameness with clinical, radiographic, ultrasonographic and MRI findings (same horse as Fig. 10.50) of podotrochlear syndrome (navicular disease). (A) There is increased radioisotope uptake in the navicular area of the right limb (arrow), but all the more proximal regions are more active than their left equivalent regions. (B) Quantification allows determination that the ratio of relative activities of right versus left regions is higher in the foot than in the more proximal regions.

under physiologic conditions (exercise level, increased biomechanical stresses) and pathologic conditions such as active bone lesions. Presence of a painful area in a limb induces higher stresses on the opposite limb. Because of that, higher radioisoptope activity can be detected in the sound limb (Fig. 10.43) compared with the lame limb (compensation on the opposite limb). When an inflammatory process is responsible for the lameness (Fig. 10.44) the increased blood supply delivers more radiopharmaceutical to this limb (increased perfusion in the same limb).[27] These physiopathologic factors must be considered in the interpretation of the scintigraphic scans to avoid misdiagnosis. Identification of these factors and interpretation of the uptake distribution underline the need for a precise clinical examination, which must be done before and after the scanning procedure.

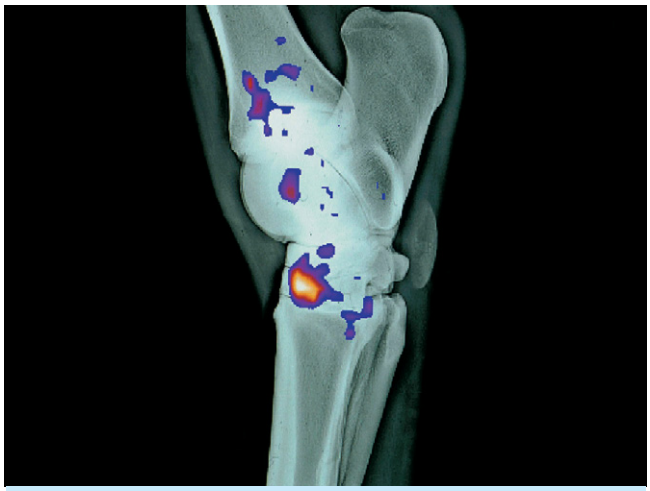


Fig. 10.45
Four-year-old French Trotter female. Scintigraphic image of the right hock superimposed on a lateromedial radiographic projection. Increased radioisotope uptake is present in the third tarsal bone (T3). There were no radiographic abnormalities found on a complete study. This observation was indicative of bone stress of T3.

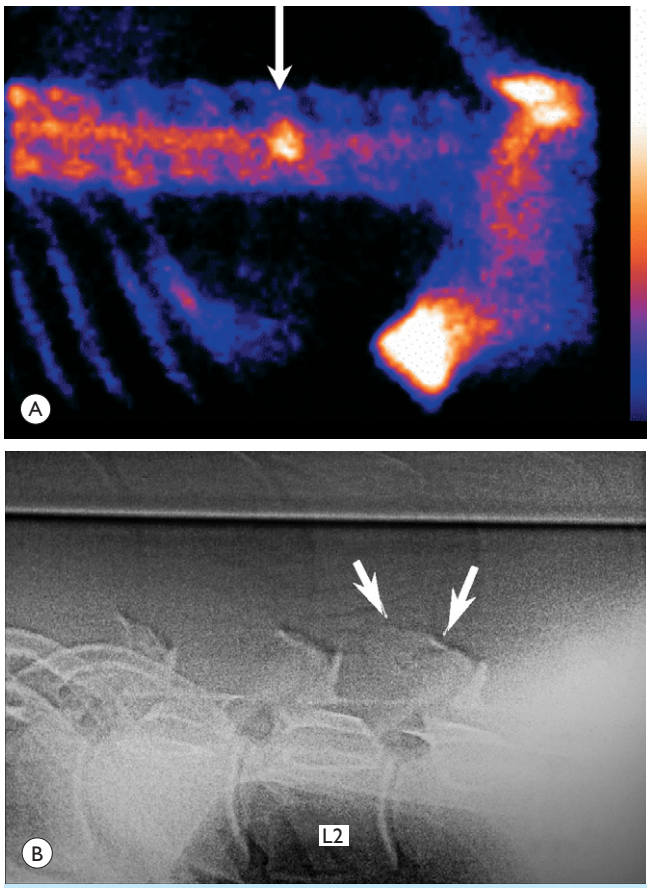


Fig. 10.46
Ten-year-old Grand Prix show jumper, Selle-Français stallion presenting an active osteoarthrosis of a synovial intervertebral joint and articular processes in the lumbar area. (A) Oblique scintigraphic image of the lumbar area. Intense radioisotope uptake is observed in the articular processes of the intervertebral joint between the second (L2) and third (L3) lumbar vertebra (arrow). (B) Radiographic image of the lumbar area of the same horse. An extensive periarticular bony proliferation can be seen over the articular processes of the L2–L3 joint space (arrows).

Identification of lesions is based on increased radioisoptope uptake due to the more intense remodeling taking place in bone injuries such as fractures, stress fractures,[28,29] enthesopathies[30] or osteophyte production. This interpretation can be done subjectively or objectively using software designed for quantification of the radiation activity (e.g. Hermes, from Nuclear Diagnostics, Gravesend, UK).[26] Correct interpretation of the scintigrams requires precise anatomic and topographic landmarks of the region examined, especially for deep structures.[31] Besides, not every region of increased uptake is necessarily correlated to pain (false-positive information). Conversely, it is likely that some chronically painful areas, such as in the back, do not show significant uptake because of attenuation by overlying muscle (false-negative information).

Although skeletal muscle damage has been diagnosed with scintigraphy,[32] this technique is especially useful for identification of bone trauma (contusion, stress, microfractures) without or with discrete radiographic manifestation.[29] These lesions can be seen in the cuboidal bones of the carpus and tarsus (Fig. 10.45) as well as in epiphyses such as the distal metacarpal or metatarsal condyles and distal radial condyle. In race horses, this procedure is also very useful for the detection of cortical bone stress fracture such as in the third metacarpal and metatarsal bones, tibia, radius and humerus. In the pelvis, complete fracture may be difficult to diagnose without scintigraphy (see Fig. 10.41). Some subchondral bone cysts can present very intense radiosotope uptake, especially in the medial femoral condyle, proximal radius and distal epiphysis of the proximal phalanx.

Scintigraphy is also indicated for the detection of osteoarthrosis in low-motion joints (distal tarsus, proximal interphalangeal joint, back) where the involvement of the subchondral bone is often essential (Fig. 10.46). In the distal tarsus, when several joints (tarsometatarsal, distal intertarsal, proximal intertarsal joints) present concomitantly abnormal radiographic findings, scintigraphy allows determination of which site is undergoing the most active remodeling process. In the thoracolumbar spine, scintigraphy is useful in establishing the clinical significance of abnormal radiographic findings involving the spinous processes (see Fig. 10.11), the articular processes (Fig. 10.46) or the vertebral bodies (spondylosis). Many recent or chronic enthesopathies demonstrate an increased radioisotope uptake in the bone insertion surface. This has been observed in the proximal and distal insertions of the suspensory ligament (third interosseus muscle) in both the front and hind limbs (Fig. 10.47) as well as in the insertion surface of collateral ligaments in several joints.

Quantification of the radiation activity (Fig. 10.48) provides objective data on the remodeling intensity during the follow-up of specific lesions. It allows evaluation of the efficacy

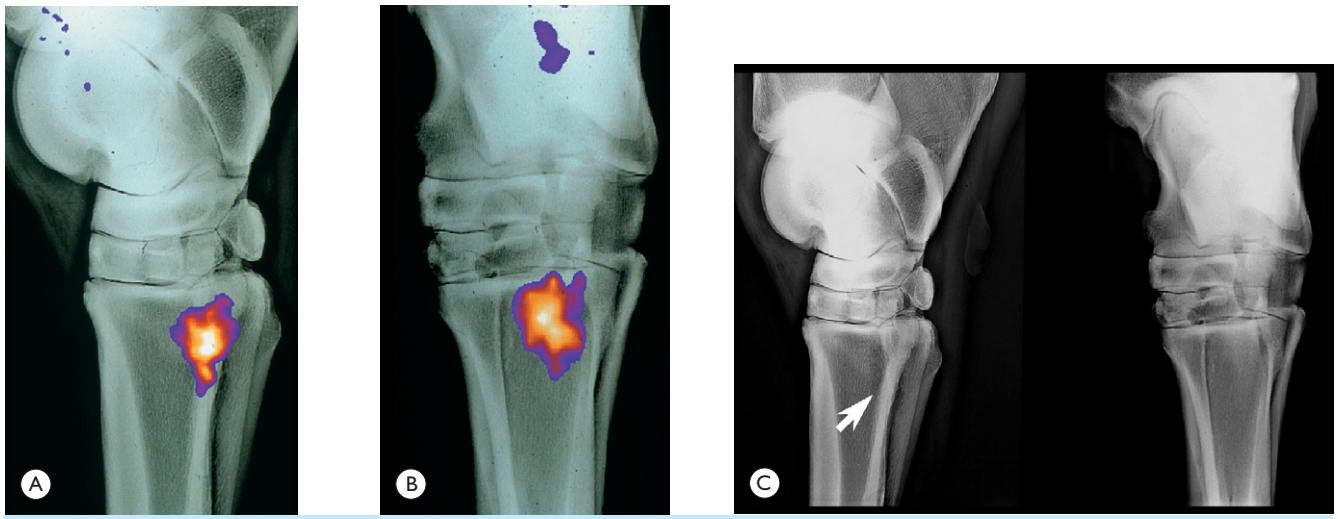


Fig. 10.47
Fourteen-year-old Grand Prix show jumper Selle-Français gelding with a chronic left hind limb lameness (same horse as Fig. 10.39). Superimposition of the radiographic and scintigraphic images of the left hock. (A) Lateromedial radiographic projection and lateral scintigram. (B) Dorsoplantar radiographic projection and plantar scintigram. (C) Lateromedial and dorsoplantar radiographic projections demonstrating mild thickening of the plantar cortex of the proximal third metatarsal bone. Based on these findings, the result of ultrasonographic examination and local analgesia, a diagnosis of chronic proximal enthesopathy of the left suspensory ligament was established.

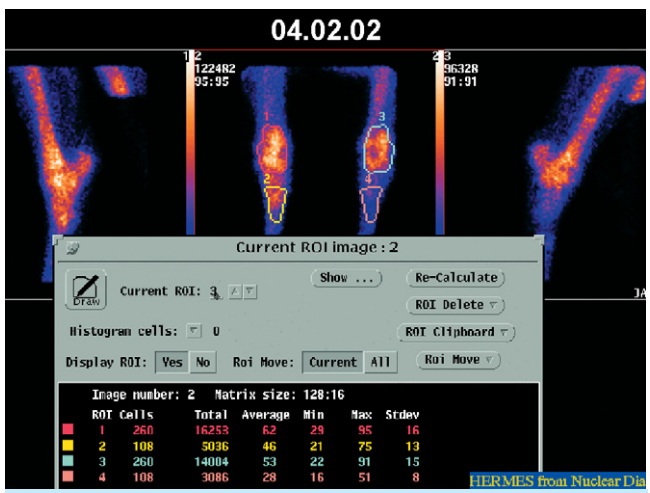


Fig. 10.48
Nine-year-old Grand Prix show jumper, Selle-Français stallion presenting a bilateral proximal enthesopathy of the suspensory ligament in the hind limbs. Scintigram of the plantar aspect of both hocks. Marked increased radioisotope uptake is present in the right proximal metatarsus and mild uptake is seen on the left proximal metatarsus. Uptake quantification was used to monitor the response to treatment and to manage the horse's level of physical activity.

of treatments and to provide recommendations regarding the physical exercise level of activity of the affected horse.

Scintigraphy presents specific advantages compared to other imaging techniques. It permits a complete screening of the whole body of the horse and detection of lesions that cannot be identified by other methods. There is no regional limitation with this technique, except the access to the medial aspect of the limbs and deep structures such as the pelvic symphysis.

Apart from its cost, the main limitation of bone scintigraphy is the low sensitivity to soft-tissue injuries, although incidental radioisotope uptake may be observed in damaged tendons or skeletal muscles. It is likely that the uptake of deep vertebral lesions such as spondylosis and vertebral osteoarthrosis between the articular processes is attenuated by the thick dorsal epiaxial muscles of the horse. Besides, this procedure seems to have a quite poor sensitivity to old or chronic osteoarticular problems such as periarticular osteochondral fragmentation. It must be also recognized than some 'silent' lesions could be painful and have a clinical significance. Therefore, scintigraphy does not replace a good clinical examination, which remains essential for interpretation of the scintigrams. The conclusions of the clinical and scintigraphic examinations must be assessed using diagnostic analgesia techniques. Besides, the definitive diagnosis of the lesion and determination of its severity requires the use of other imaging techniques such as radiography, ultrasonography as well as CT and MRI when indicated and available.

Advanced techniques

Computed tomography

Because of the limited access of the horse body in machines designed for human patients, computed tomography (CT scanning) has the same anatomic limitations as MRI.

In a specific region of interest, the image is produced after quantification by a series of detectors of an X-ray beam passing through a slice of the examined anatomical area.[33–35] The different anatomic tissues, presenting specific X-ray

absorption, are imaged on sequential slices of the scanned region. The ability of the technique to detect slight difference in X-ray absorption within tissues[36] and manipulation of the CT gray-scale provides a much better differentiation of soft tissues than with conventional radiography. CT images can be selectively displayed to highlight either bone structures or soft tissues by adjusting window width and level as necessary (bone or soft tissue display windows).

Because of the cross-sectional characteristics of this imaging modality, superimposition or overlapping of different tissues do not occur and this allows a real isolation ('dissection') of the lesion directly exposed without covering layers, and therefore permits detection of small lesions inside a volume. Digital assembling of adjacent tomographic images allows reconstruction of new images in different anatomical planes as well as 3D representation of bone and joint surfaces.[35]

CT provides an exceptional imaging representation of bone and joints. With this technique, detection of radiographically occult fractures in the distal phalanx[37,38] or in fourth metacarpal bone[35] has been achieved. CT presents an extreme ability to detect variations of bone density,[34,38,39] such as sclerosis and lysis of the subchondral bone,[40] as well as cancellous bone. The sensitivity of CT to subchondral bone cysts[34,35] and bone stress (fatigue fractures) is now well established. Moreover, this technique can provide an excellent spatial representation of fractures.[41] Bone shape and contour are precisely imaged allowing diagnosis of enthesophytes and periosteal proliferative lesions.[35]

CT may also provide useful information on soft tissues, especially in the foot where lesions involving the deep digital flexor tendon such as abnormal shape, dystrophic mineralization and enthesophytes can be identified. Because of the capabilities of ultrasonography and MRI, the use of CT for examination of soft tissues elsewhere than in the foot is questionable. In humans, 3D CT angiography with volume-rendering technique is now used for evaluation of intracerebral aneurysms.[42] In the future, it is likely that this technique will allow evaluation of blood vessels in the foot, such as in laminitic horses.

Magnetic resonance imaging

MRI represents the gold standard technique in human orthopedics, sport medicine and neurology.[28,43–46] This technique is based on the analysis of magnetic properties of the tissues, All tissues are imaged on the MRI scans. It provides excellent anatomic information on cross-sections in different planes. As a cross-sectional imaging modality, every isolated slice can be imaged separately, thereby allowing identification of small lesions, avoiding superimposition and hiding of deep layers by superficial tissues.

In most applications of MRI, horses are examined using devices designed for human patients.[35,36,47,48] With open machines,[47] more areas can potentially be examined than with tunnel machines and the positioning of the horse is more flexible. High-magnetic-field machines (e.g. 1.5 T field machine) provide better definition and quicker image acquisition than low-field equipment (e.g. 0.2 to 0.5 T fields), without significantly affecting a difference in diagnostic capabilities. With the use of human machines adapted to equine patients, the procedure requires general anesthesia of the horse and is time consuming. The cost and maintenance of the facility is expensive and, above all, examination is currently limited to the distal and intermediate parts of the limbs (from the foot to the carpus/tarsus) as well as to the head and cranial part of the neck in adult horses. Equipment that may image distal limbs while the horse is standing is currently

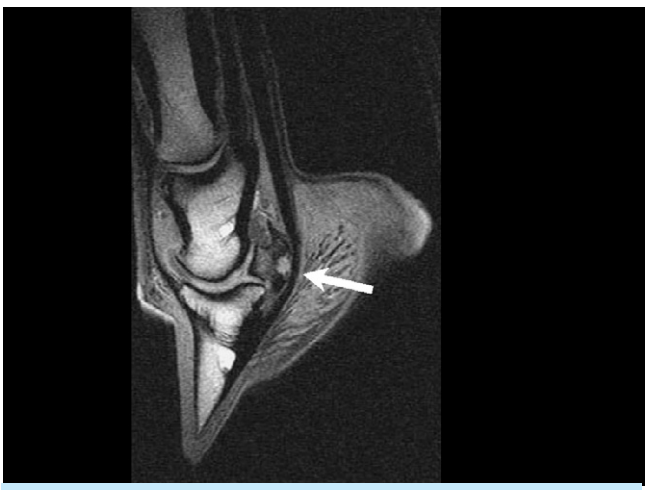


Fig. 10.49
Eight-year-old dressage Selle-Français gelding presenting a chronic bilateral front limb lameness for 3 years. Sagittal T1-weighted MRI scan of the left foot showing a focal area with high signal in the palmar compact bone of the distal sesamoid (navicular) bone (arrow). The horse also had clinical, radiographic, and ultrasonographic findings of podotrochlear syndrome (navicular disease).

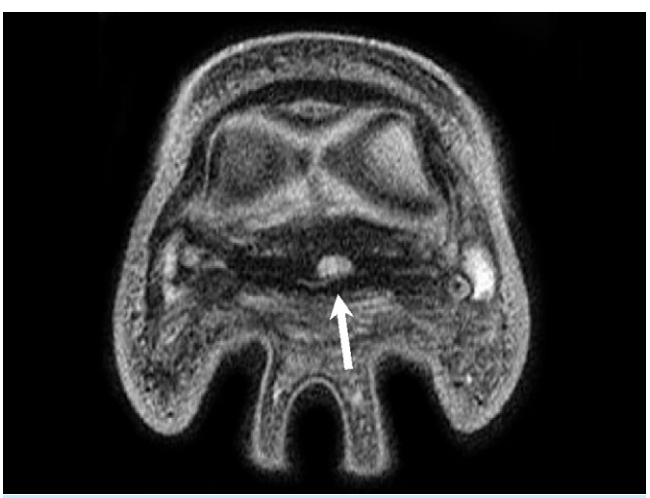
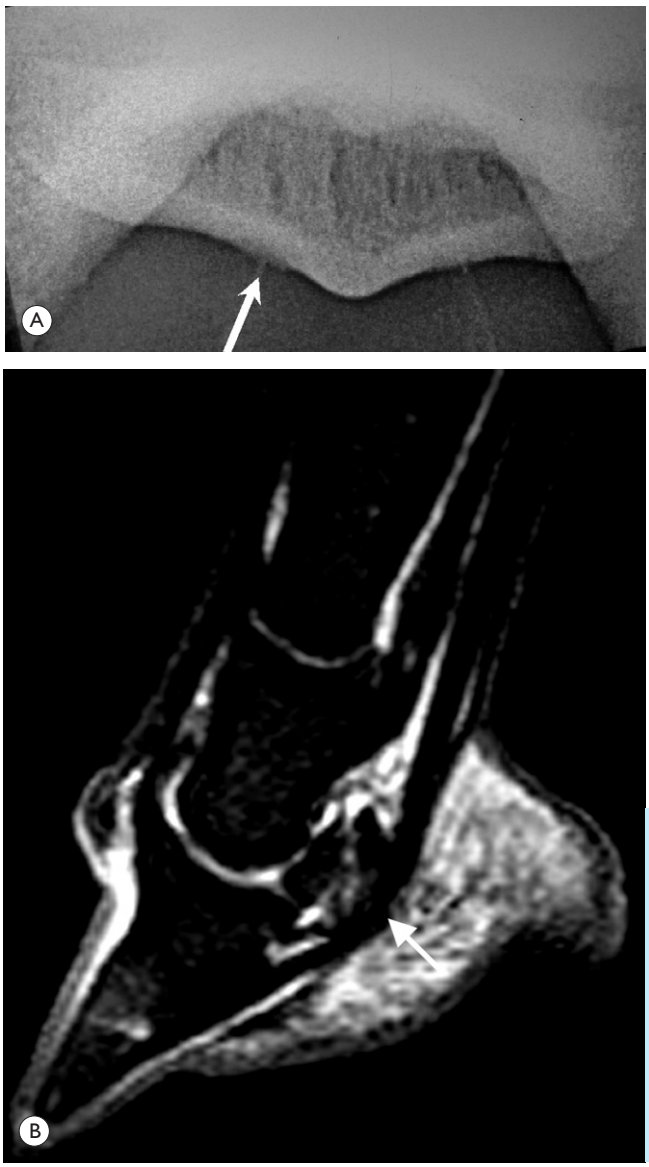


Fig. 10.50
Five-year-old Trackener male used for dressage presenting clinical, scintigraphic (same horse as Fig. 10.44), radiographic, ultrasonographic and MRI findings of podotrochlear syndrome (navicular disease). Transverse T1-weighted MRI scan of the right foot. There is a focal area with high signal in the palmar compact bone of the distal sesamoid (navicular) bone (arrow).



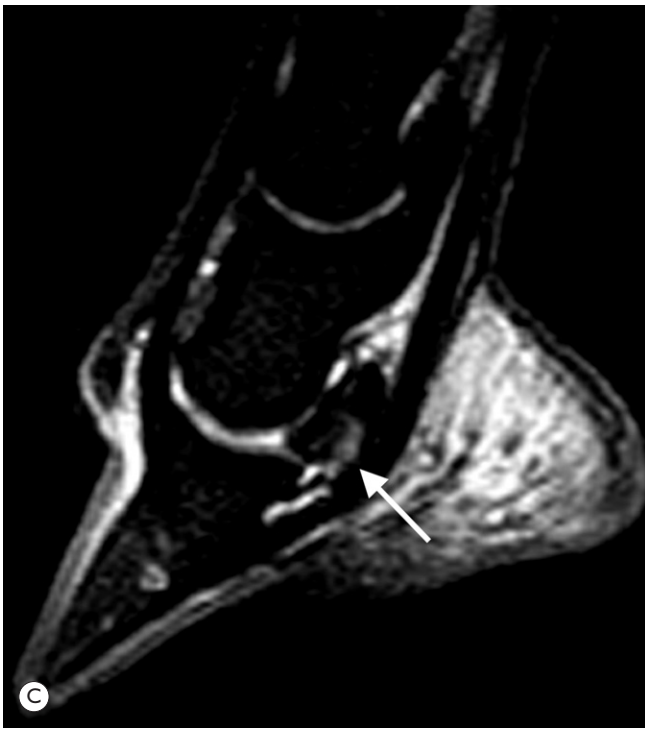


Fig. 10.51
Eight-year-old show jumper Selle-Français gelding presenting a chronic left front limb lameness. (A) Proximopalmar–distodorsal (skyline) projection of the distal sesamoid (navicular) bone (DSB). A discrete irregularity can be seen on the flexor surface of the DSB (arrow). (B) Sagittal T2-weighted MRI scan demonstrating an increased signal in the cancellous as well as palmar compact bone of the DSB (arrow). (C) Lateral parasagittal T2-weighted MRI scan demonstrating an increased signal in the cancellous as well as palmar compact bone of the DSB (arrow). These MRI findings are indicative of bone contusion in the palmar part of the DSB.

under development[49] and will probably allow MRI to be more available for horses in the future.

Images can be acquired in sagittal, transverse and frontal planes using different sequences. The most commonly used imaging sequences are T1-weighted spin echo and T2-weighted turbo spin echo. Inversion–recovery sequences designed to suppress the fat signal, therefore enhancing the fluid signal, are used for bone imaging. It is especially useful for evaluation of the subchondral bone.[50] Mixed T2-/T1-weighted 3D gradient echo sequences providing enhancement of fluid are particularly indicated for identification of articular cartilage lesion (arthrographic effect).

MRI is particularly sensitive for identification of bone lesions (Figs 10.49–10.52).[45] With T2-weighted and fat saturation sequences the high fluid signal can clearly be identified in contrast with the low signal in compact bone and fat (Figs 10.51, 10.52). This signal is produced by bone edema, inflammation, necrosis, fibrosis, and bone contusion (or bruise) with marrow edema and trabecular damage.[45] MRI is also very sensitive to changes in bone density, allowing diagnosis of sclerosis and osteolysis, as well as subchondral bone cysts, fracture lines, fatigue fractures and bone stress.[50] As for every cross-sectional imaging technique, MRI provides detailed information on alteration of bone surfaces for detection of periarticular osteophytes (Fig. 10.53) as well as enthesophytes at insertion sites.

In the diagnosis of joint diseases,[51] MRI has been demonstrated to provide information about the integrity and pathologic status of the articular cartilage in equine cadaver limbs[15,52] as well as in patients.[35,47,48] It is the only imaging technique that permits detection of early and limited cartilage degeneration.[53–55] MRI contrast arthrography with gadolinium diluted with sterile saline injected into the synovial cavity of joints has been used to improve visualization of articular cartilage. Dedicated sequences (for instance mixed T2-/T1-weighted 3D gradient echo sequence) are now available for direct and non-invasive imaging of this structure. MRI provides unique morphologic and biochemical

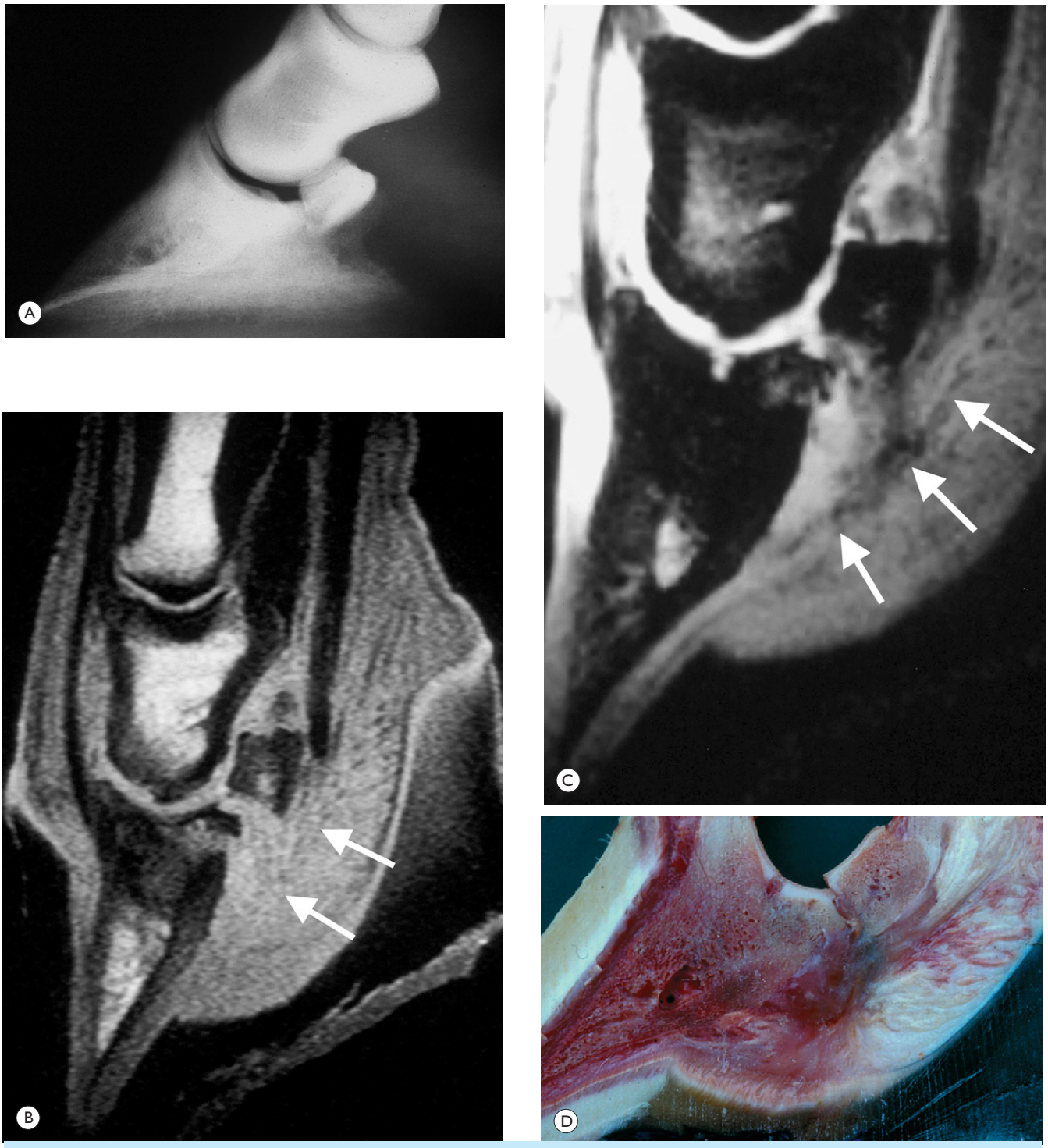


Fig. 10.52
Radiographic and ex vivo MRI examination of the foot of a 5-year-old Selle-Français male who had a deep puncture wound over the frog area of the left foot. (A) Lateromedial radiographic projection showing an osteolysis of the distal part of the distal sesamoid (navicular) bone (DSB) and sclerosis of the distal phalanx and rest of the DSB. (B) Sagittal T1-weighted MRI scan of the same foot showing abnormal hyposignal in the body of the DSB and distal phalanx compatible with bone sclerosis. Bone lysis is present at the distal aspect of the middle phalanx, DSB, and in the subchondral bone of the distal phalanx. The distal part of the deep digital flexor tendon (DDFT) is thickened and presents an abnormally intense signal (arrows). (C) Sagittal T2-weighted MRI scan of the same foot showing abnormal loss of signal in the distal phalanx, DSB and distal middle phalanx. Intense signal indicative of edema is present in the subchondral bone of both the middle and distal phalanx, as well as in the distal impar sesamoidean ligament (DISL) and DDFT. (D) Post-mortem specimen showing the subchondral bone lysis of the distal phalanx and the extensive scar tissue formation within the DISL and DDFT. The horse had septic arthritis of the DIP joint involving the DISL and a septic DDF tendinitis.

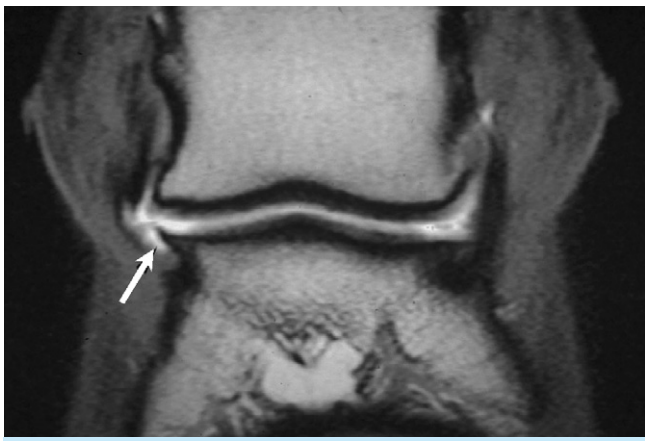
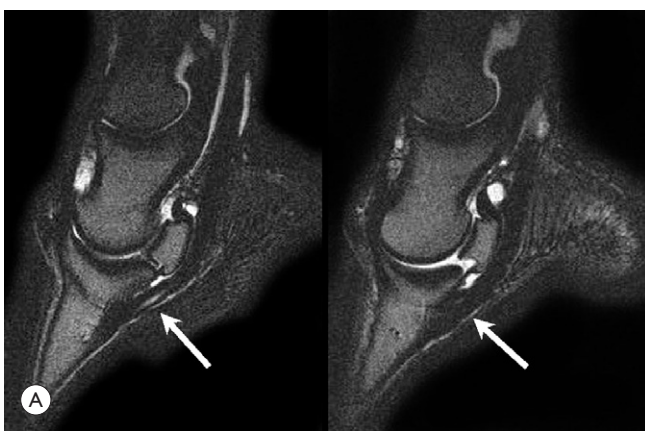


Fig. 10.53
Frontal T1-weighted MRI scan of the distal interphalangeal joint performed ex vivo on an isolated limb. A periarticular osteophyte (arrow) involving the medial margin of the distal phalanx can be seen in a site difficult to investigate with radiography and ultrasonography.



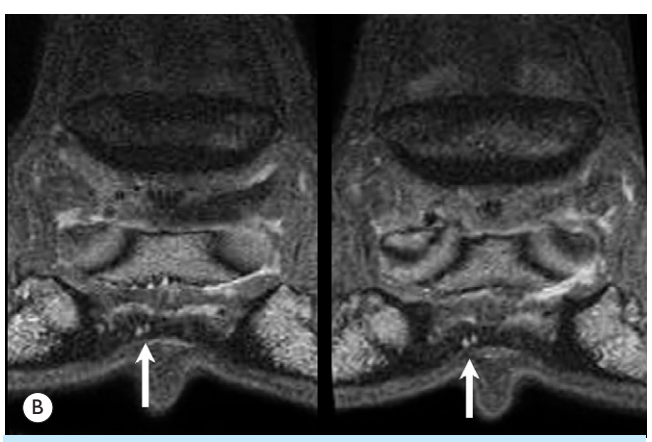
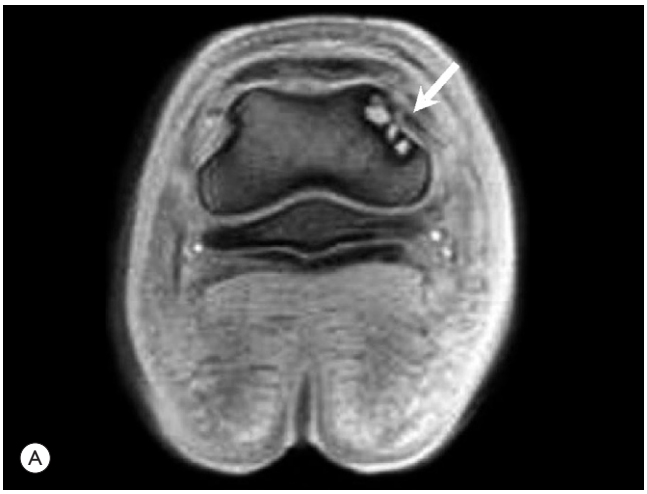


Fig. 10.54
MRI scans of the left foot of a 13-year-old Grand Prix show jumper, Selle-Français gelding with a chronic bilateral front limb lameness. (A) Sagittal and parasagittal T2-weighted MRI scans demonstrating a longitudinal hyposignal lesion (arrow) in the terminal part of the DDFT (left). The right image shows that the most distal part of the DDFT is thickened with an heterogeneous signal (arrow). These findings are indicative of distal DDF tendinitis. (B) Frontal mixed T2-/T1-weighted 3D gradient echo sequence scans of the same foot confirming the heterogenous signal of the distal part of the DDFT.



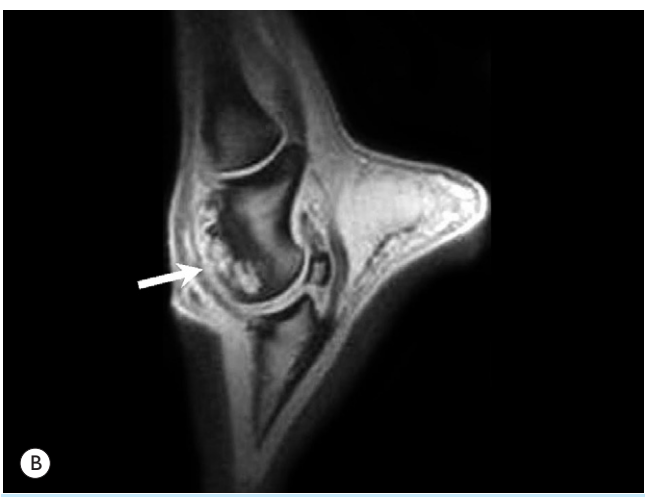


Fig. 10.55
Eight-year-old dressage, Selle-Français gelding presenting a chronic bilateral front limb lameness for 3 years. Transverse (A) and parasagittal (B) T1-weighted MRI scan of the right foot showing severe alteration of bone signal at the proximal attachment of the lateral collateral ligament. A diagnosis of chronic proximal collateral enthesopathy of the distal interphalangeal joint was made.

information on the articular cartilage. Its ability to acquire images in any plane considerably increases its sensitivity. MRI is also very sensitive to subchondral bone alterations such as contusion, bone stress, and sclerosis. With the use of fat suppression sequences, which eliminate the high fat signal within bone marrow, subchondral bone edema, an important feature of articular injuries, is better visualized.[50]

MRI is also very appropriate for the diagnosis of acute as well as chronic tendon (see Figs 10.52, 10.54) and ligament injuries providing an increased signal intensity on both T1- and T2-weighted sequences.[36,52,56] The capacity of the technique to detect edema as well as granulation or scar tissue and to document the lesion in three planes represents the main advantages of MRI compared to ultrasonography or CT scanning. Because of the sensitivity of MRI for bone, as well as tendon and ligament injuries, this technique has a high diagnostic value for enthesopathies, involving collateral ligaments (Figs 10.55, 10.56) tendons, or the interosseus

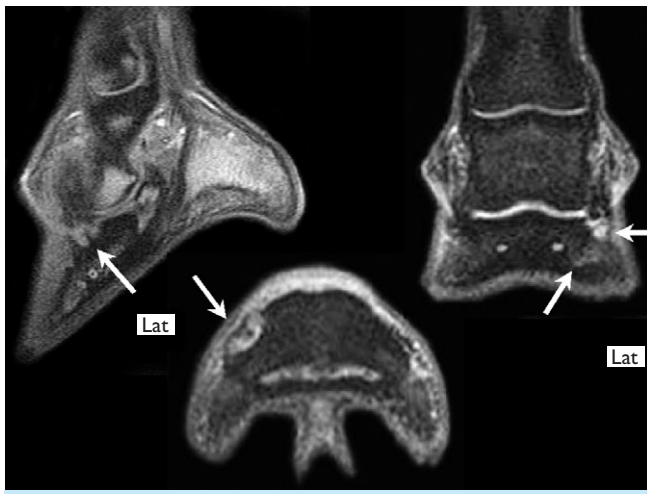


Fig. 10.56
Four-year-old Selle-Français female presenting a chronic left front limb lameness for 6 months. Parasagittal T1-weighted sequence (left), transverse inversion–recovery sequence (bottom) and frontal inversion–recovery sequence (right) MRI scans of the left foot showing an enthesophyte (arrow, left) and severe alteration of bone signal (arrow, right) at the distal attachment of the lateral collateral ligament. A diagnosis of chronic distal collateral enthesopathy of the distal interphalangeal joint was made.

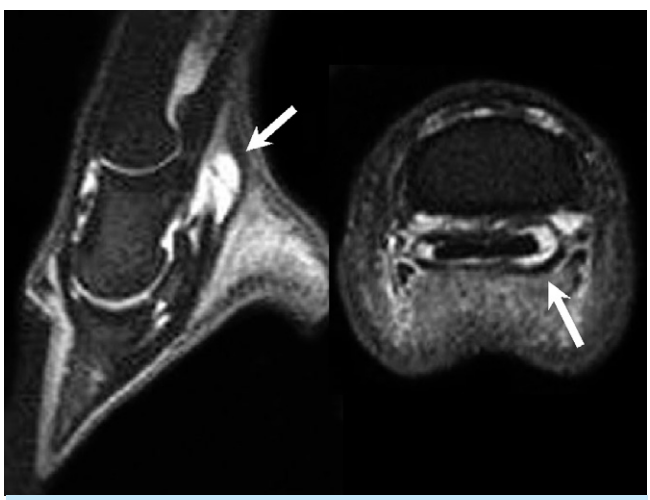


Fig. 10.57
Five-year-old Trackener male used for dressage presenting clinical, scintigraphic, radiographic, ultrasonographic and MRI findings of podotrochlear syndrome (navicular disease) in the right front limb (same horse as Figs 10.44 and 10.50). Sagittal and transverse T2-weighted sequence images showing an extensive fluid distension of the podotrochlear bursa. Intrasynovial analgesia of this bursa using 1.5 mL of local anesthetic solution resolved the lameness.

muscle. Moreover, fluid distension involving the synovial cavities (tendon sheaths, bursae, or joint cavities) is easily imaged especially in T2-weighted and mixed T2-/T1-weighted 3D gradient echo sequences (Fig. 10.57). Because of its cross-sectional characteristics, in axial regions, MRI can reveal the asymmetric appearance of structures

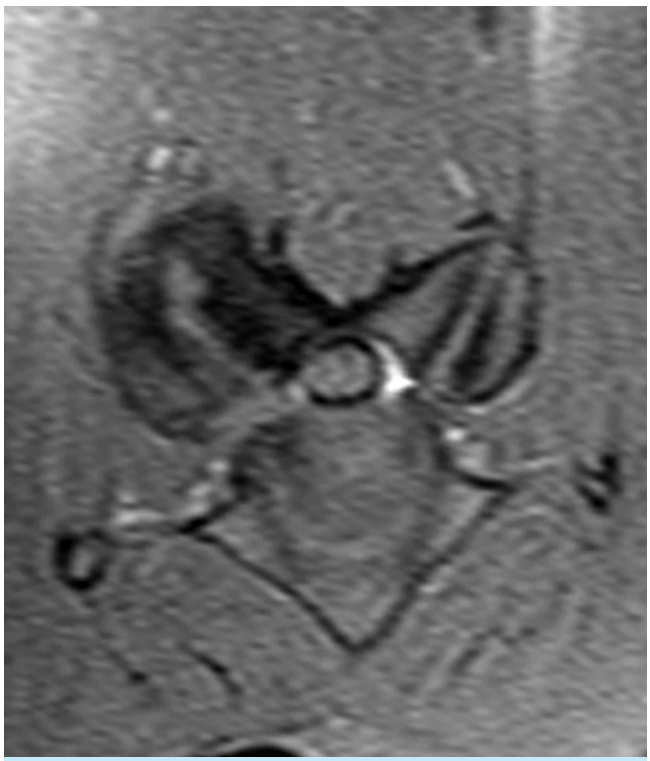


Fig. 10.58
Transverse T1-weighted MRI scan of the neck of a 6-month-old foal presenting a wobbler syndrome. There is marked asymmetry of the articular processes between the fifth and sixth cervical vertebrae. The hypertrophic articular processes present a loss of signal compatible with bone sclerosis. On the same side, there is marked dorsolateral stenosis of the vertebral canal inducing compression of the cervical spinal cord.

within the head or vertebrae that are difficult to demonstrate with radiography (Fig. 10.58).

This technique is indicated when the site of the lesion(s) is clearly identified and other imaging procedures do not provide a conclusive diagnosis. Unfortunately, as mentioned above, MRI is limited to anatomic regions that can be placed into the machine.

Providing specific information on both soft tissues and bone components, MRI is the most informative diagnostic imaging procedure available for all areas that are accessible with the device. In metacarpal (tarsal) areas and pastern, with the progressive improvement of ultrasound machines, ultrasonography challenges MRI for the diagnosis of tendon lesions (except insertion sites). Knowing the sensitivity of MRI to detect small bone, cartilaginous, tendon, and ligament lesions, we need to adapt our interpretation and, again, reconsider the clinical examination to establish the real clinical significance of any abnormal finding.

Conclusion

Diagnostic imaging of musculoskeletal conditions is a permanently evolving field; several imaging modalities are

now available for equine patients and therefore a rational utilization of each of them is essential. The use of different techniques for a better analysis of the same lesion increases the knowledge of the advantages and limitations of each of them and underlines the need for combining several procedures to reach a better diagnosis.

As radiography and ultrasonography present complementary advantages, they should be used in conjunction as basic imaging modalities in most clinical situations in field practice. With this combination, a re-evaluation of several 'well known' dogmatic pathologic entities and identification of many new clinical entities have already been made.

Apart from the diagnostic aspect, another development of imaging techniques is interventional imaging. Ultrasonography has now been incorporated in the treatment of several musculoskeletal conditions through ultrasonographic guided injections of synovial joints in the cervical and thoracolumbar spine or intrasynovial injections in joints, tendon sheaths, or bursae.

Unfortunately, at present, advanced technologies such as CT and MRI are available only in a limited number of equine referral centers. Nevertheless, they have already provided new data, allowing a better appraisal of the indications and limitations of radiography and ultrasonography. In the coming years, further technological progress in each modality will continue to provide better image quality. Development of 3D representation of lesions will improve in MRI, CT scanning, and ultrasonography. Communication between referral centers and equine practitioners will also be easier with computed or digital images. With this evolution, a better diagnosis and management of our patients will be possible, but we will have to avoid performing only an 'instrumental medicine', where images are manipulated and patients forgotten. In the teaching of new generations of practitioners, we have to keep an emphasis on the clinical examination, to make young colleagues think about the horse, not only discuss the images.

In the near future, another important aspect of diagnostic imaging in horses will be the need to establish the most adequate imaging protocols for specific clinical problems. In practice, the objective is to reach the diagnosis with the most appropriate technique(s), considering the ratio of information to cost as well as the impact of more information on the potential subsequent management of the condition. In the mean time, comparative or combined imaging for better documentation of musculoskeletal conditions is required to increase knowledge of pathologic processes and to establish the most effective diagnostic protocols.

Acknowledgments

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References

1. Becht JL, Park RD, Kraft SL, et al. Radiographic interpretation of normal skeletal variations and pseudolesions in the equine foot. Vet Clin North Am: Equine Pract 2001; 17:1–18.
2. Konde LJ. Aggressive versus non aggressive bone lesions. In Thrall DE, ed. Textbook of veterinary radiology, 3rd edn. Philadelphia: WB Saunders; 1998:37–44.
3. Butler J, Colles C, Dyson S, et al. Clinical radiology of the horse, 2nd edn. Oxford, Blackwell Scientific; 2000.
4. Dick KJ, Gunsser I. Atlas of diagnostic radiology of the horse (three parts). Schlütersche, Hannover; 1988.
5. Denoix J-M. Ultrasonographic examination in the diagnosis of joint disease. In: McIlwraith WC, Trotter GW, eds. Joint disease in the horse. Philadelphia: WB Saunders; 1996:165–202.
6. Roberts GD, Graham JP. Computed radiography. Vet Clin North Am: Equine Pract 2001; 17:47–62.
7. Reef VB. The musculoskeletal system. In: Atlas of equine ultrasonography. St. Louis: Mosby; 1998:1–108 and Philadelphia: WB Saunders; 1998:39–186.
8. Reimers JM. Musculoskeletal ultrasonography. In: Equine diagnostic ultrasound. St Louis: Mosby; 1998:1–108.
9. Reef VB. Superficial digital flexor tendon healing: ultrasonographic evaluation of therapies. Vet Clin North Am: Equine Pract 2001; 17:159–178.
10. Denoix J-M, Crevier N, Azevedo C. Ultrasound examination of the pastern in horses. Proceedings 37th Ann Convention Am Assoc Equine Pract 1991; 37:363–380.
11. Dyson SJ, Denoix J-M. Tendon, tendon sheath, and ligament injuries in the pastern. Vet Clin North Am: Equine Pract 1995; 11:217–233.
12. Denoix J-M. Diagnostic techniques for identification and documentation of tendon and ligament injuries. Vet Clin North Am: Equine Pract 1994; 10:365–407.
13. Denoix J-M, Busoni V. Ultrasonography of joints and synovia. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:643–654.
14. Denoix J-M. Ultrasound examination of joints and miscellaneous tendons. In: Rantanen NW, McKinnon AO, eds. Equine diagnostic ultrasound. Baltimore: Williams & Wilkins; 1998:475–514.
15. Denoix J-M. The equine distal limb: an atlas of clinical anatomy and comparative imaging. London: M Manson; 2000.
16. Denoix J-M, Busoni V, Olalla MJ. Ultrasonographic examination of the proximal scutum in the horse. Equine Vet J 1997; 29:136–141.
17. Denoix J-M, Jacot S, Perrot P et al. Ultrasonographic anatomy of the dorsal and abaxial aspect of the equine fetlock. Equine Vet J 1996; 28:54–62.
18. Busoni V, Denoix JM. Ultrasonography of the podotrochlear apparatus in the horse using a transcuneal approach: technique and reference images. Vet Radiol Ultrasound 2001; 42:534–540.
19. Denoix J-M. Ultrasonographic evaluation of back lesions. Vet Clin North Am: Equine Pract 1999; 15(1):131–159.
20. Turner TA. Diagnostic thermography. Vet Clin North Am: Equine Pract 2001; 17:95–113.
21. Ueltschi G. Bone and joint imaging with ^{99m}Tc labelled phosphates as a new diagnostic aid in veterinary orthopaedics. J Am Vet Radiol Soc 1997; 18:80–84.

22. Chambers MD, Martinelli MJ, Gordon JB, et al. Nuclear medicine for diagnosis of lameness in horses. J Am Vet Med Assoc 1995; 206:792–796.
23. Hoskinson JJ. Equine nuclear scintigraphy: indications, uses, and techniques. Vet Clin North Am: Equine Pract 2001; 17:63–74.
24. Trout DR, Hornoff WJ, O'Brien TR. Soft tissue and bone phase scintigraphy for diagnosis of navicular disease in horses. J Am Vet Med Assoc 1991; 198:73–77.
25. Dyson S, Lakhani K, Wood J. Factors influencing blood flow in the equine digit and their effect on uptake of 99m technetium methylene diphosphonate into bone. Equine Vet J 2001; 33:591–598.
26. Dyson S. Subjective and quantitative scintigraphic assessment of the equine foot and its relationship with foot pain. Equine Vet J 2002; 34:164–170.
27. Twardock AR. Equine bone scintigraphic uptake patterns related to age, breed, and occupation. Vet Clin North Am: Equine Pract 2001; 17:75–94.
28. Williams A, Evans R, Shirley PD. Imaging of sport injuries. London: Baillière Tindall; 1987.
29. Lloyd KC, Koblick P, Ragle C, et al. Incomplete palmar fracture of the proximal extremity of the third metacarpal bone in horses: ten cases (1981–1986). J Am Vet Med Assoc 1988; 192:798–803.
30. Edwards RB, Ducharme NG, Fubini SL, et al. Scintigraphy for diagnosis of avulsions of the origin of the suspensory ligament in horses: 51 cases (1980–1993). JAVMA 1995; 207:608–611.
31. Erichsen C, Berger M, Eksell P. The scintigraphic anatomy of the equine sacroiliac joint. Vet Radiol Ultrasound 2002; 43:287–292.
32. Morris E, Seeherman HJ, O'Callaghan MW, et al. Scintigraphic identification of skeletal muscle damage in horses 24 hours after strenous exercise. Equine Vet J 1991; 23:347–352.
33. André M, Resnick D. Computed tomography. In: Resnick D, ed. Bone and joint imaging, 2nd edn. Philadelphia: WB Saunders; 1996:70–83.
34. O'Callaghan M. Future diagnostic methods: a brief look at new technologies and their potential application to equine diagnosis. Vet Clin North Am, Equine Pract 1991; 2:467–479.
35. Tucker RL, Sande RD. Computed tomography and magnetic resonance imaging in equine musculoskeletal conditions. Vet Clin North Am: Equine Pract 2001; 17:145–157.
36. Kraft SL, Gavin P. Physical principles and technical considerations for equine computed tomography and magnetic resonance imaging. Vet Clin North Am: Equine Pract 2001; 17:115–130.
37. Martens P, Ihler C, Rennesund J. Detection of a radiographically occult fracture of the lateral palmar process of the distal phalanx in a horse using computed tomography. Vet Radiol Ultrasound 1999; 40:346–349.
38. Martens P, Asbjörn T, Jon T. Identification by computed tomography of a radiographically occult lesion of the distal phalanx in a standardbred racehorse. Equine Pract 2000; 22:12–15.
39. Widmer WR, Buckwalter KA, Fessler JF, et al. Use of radiography, computed tomography and magnetic resonance imaging for evaluation of navicular syndrome in the horse. Vet Radiol Ultrasound 2000; 41:108–116.
40. Hanson J, Seeherman H, O'Callaghan M. The role of computed tomography in evaluation of subchondral osseous lesions in seven horses with chronic synovitis. Equine Vet J 1996; 28:480–488.
41. Rose P, Seeherman H, O'Callaghan M. Computed tomographic evaluation of comminuted middle phalangeal fractures in the horse. Vet Radiol Ultrasound 1997; 38:424–429.
42. Sahel M, Ourrad E, Zouaoui A, et al. Angioscanner des anévrismes intracraniens en rendu volumique (volume rendering technique). J Radiol 2000; 81:127–132.
43. McEnery KW, Murphy WA. Magnetic resonance imaging. In: Resnick D, ed. Bone and joint imaging, 2nd edn. Philadelphia: WB Saunders; 1996:84–93.
44. Stoller DW. Magnetic resonance imaging in orthopaedics and sport medicine, 2nd edn. Philadelphia: Lippincott-Raven; 1997.
45. Eustace SJ. Magnetic resonance imaging of orthopedic trauma, 2nd edn. Philadelphia: Lippincott William & Wilkins; 1999.
46. Stark DD, Bradley WG. Musculoskeleton. Part III, volume II. In: Magnetic resonance imaging. St Louis: Mosby; 1999:673–1142.
47. Tapprest J, Audigié F, Radier C, et al. Examen d'imagerie par résonance magnétique du pied du cheval. Prat Vet Equine 2002; 34:97–101.
48. Dyson S, Murray R, Schramme M, et al. Magnetic resonance imaging of the equine foot: 15 horses. Equine Vet J 2003; 35:18–26.
49. Mair T. Magnetic resonance imaging of the distal limb in the standing horse. XV Tagung über Pferdekrankheiten, Essen 2003:78–79.
50. Tapprest J, Audigié F, Radier C et al. Magnetic resonance imaging for the diagnosis of stress fractures in a horse. Vet Radiol Ultrasound, in press.
51. Resnick D. Internal derangement of joints. In: Resnick D, ed. Bone and joint imaging, 2nd edn. Philadelphia: WB Saunders; 1996:819–883.
52. Denoix JM, Crevier N, Roger B, et al. Magnetic resonance imaging of the equine foot. Vet Radiol Ultrasound 1993; 34:405–411.
53. Kneeland BJ. MR imaging of articular cartilage and of cartilage degeneration. In: Stoller DW, ed. Magnetic resonance imaging in orthopaedics & sport medicine, 2nd edn. Philadelphia: Lippincott-Raven; 1997:83–91.
54. McCauley TR, Disler DG. MR imaging of articular cartilage. Radiology 1998; 209:629–640.
55. Sintzoff S, Sintzoff JR, Blum A, et al. Imagerie du cartilage: Etat actuel et perspectives. J Radiol 1999; 80:671–678.
56. Crass J, Geneovese R, Render J, et al. Magnetic resonance, ultrasound and histopathological correlation of acute and healing tendon injuries. Vet Radiol Ultrasound 1992; 33:206–216.

CHAPTER 11

Arthroscopic examination and surgery

John P. Walmsley

Introduction

Since the 1980s arthroscopy has become an important tool for the diagnosis and treatment of orthopedic disorders of many synovial spaces in the horse. It has several advantages: it is minimally invasive and, as a technique, has a low morbidity when compared to arthrotomy; it provides detailed information on arthroscopically accessible intrasynovial structures that cannot be obtained by radiography, ultrasonography or magnetic resonance imaging; it permits direct treatment of many injuries to these structures and concurrent removal of degradatory inflammatory enzymes by lavage. The main disadvantages are the necessity for general anesthesia, the expense of the equipment required for the procedure and the difficulty of the technique.

Indications

While there are many obvious and specific indications for arthroscopic surgery in the horse, there are several general points that may help decide if the procedure is indicated.

- The clinical investigation should have confirmed that the joint is the cause of lameness.
- The advantages to the patient of performing the procedure must outweigh the disadvantages.
- Where radiography and ultrasonography show no abnormalities and conservative treatment has failed, arthroscopy may be indicated as a diagnostic and potentially therapeutic option.
- Radiographic or ultrasonographic findings indicate that arthroscopy is the most appropriate course of action.
- Despite absence of radiographic or ultrasonographic findings, the joint injury is clinically so severe that arthroscopy is indicated as a primary course of action.

General points

Arthroscopic surgery should always be performed under strict aseptic conditions. Good-quality equipment is essential. A poor image or inadequate instrumentation can significantly compromise the surgery. Details of arthroscopic equipment are beyond the scope of this chapter but can be found in other texts.[1] The narrative in this chapter is based on the use of a 4 mm diameter telescope with a 25° lens angle. The surgeon should have a good anatomical knowledge and the necessary hand–eye co-ordination demanded by arthroscopy, best achieved by cadaver practice, before embarking on the clinical case. Fatigue affects the quality of surgery so it is important to ensure that the horse is positioned to enable the surgeon to operate comfortably.

Portals should be placed precisely to ensure that the surgical goals can be achieved as effectively as possible. Unless distension of the joint affects the landmarks, such as in the carpus, distension with sterile polyionic fluid prior to making the first incision is preferable. The skin incision should be wider than the incision into the joint capsule in order to reduce the possibility of subcutaneous extravasation of fluid during the surgery. The incision into the joint capsule for the introduction of the arthroscope sleeve and the conical obturator is made with a no. 11 scalpel blade. Because of the risk of damaging the articular cartilage, sharp trocars should never be used for this. The arthroscopic sleeve and obturator

are usually positioned at the site where the examination of the joint will begin before replacing the obturator with the telescope and attaching the light cable, camera and fluid system. When using an arthroscope it is very important to maintain the camera in the vertical plane so that the orientation of the image on the monitor is always the same as that in the joint. Oblique lenses widen the range of the telescope and increase triangulation.

The placement of the instrument portal is best determined by simulating the positioning of the instruments with a hypodermic needle. For ease of triangulation the instrument portal should be as far as possible both from the lesion to be operated and from the arthroscopic portal.

The treatment of lesions within the joint depends on the type of lesion. Bone fragments may require separation from the parent bone with an osteotome or dissection off their soft tissue attachments with a sharp instrument such as a meniscal knife or an O'Connor punch. It is wise never to free the fragment completely before removal in order to avoid it floating free into the joint. Ferris Smith rongeurs are ideal for removing fragments and several cup sizes are necessary ranging from 2 × 10 mm to 6 × 12 mm. When removing large fragments through the joint capsule, widening of the incision by sharp dissection may be necessary as the fragment is withdrawn. The debridement of soft tissue lesions such as infected synovial villi or torn ligamentous tissue can effectively be performed using a motorized synovial resector or a scissor-action punch instrument. Rongeurs tend to tear rather than cut soft tissue.

The correct treatment of articular cartilage lesions is still controversial: full-thickness defects should be curetted to healthy subchondral bone and micropicking of denuded bone is recommended by some.[2] Partial-thickness defects should be trimmed superficially, leaving intact tissue in situ but ensuring that all loose cartilage is removed. The use of radiofrequency instrumentation for debridement of soft tissue and articular cartilage lesions may have a place in equine arthroscopy but is still under evaluation.

Complications of arthroscopic surgery include infection, subcutaneous extravasation of fluid and instrument breakage. The most serious, postoperative infection, is rare but potentially catastrophic and emphasizes the importance of strict aseptic technique. Subcutaneous extravasation of fluid during surgery can hamper an arthroscopy by compressing the intra-articular space. Several technical points will help to avoid this: the skin incision should be large enough to allow excess fluid to escape through the skin incision rather than into the subcutaneous space; it should be kept in line with the incision into the joint capsule by avoiding too much flexion or extension of the joint once the portal has been made; and the flow of fluid should be maintained at the minimum necessary. A magnet for retrieval of a broken instrument should always be available. Old instruments and fine scalpel blades are the most susceptible to breakage. Scalpel blades can also be lost when creating portals for joints that are well covered with muscle, such as the shoulder joint or suprapatellar pouch of the femoropatellar joint. Using handles that are wider than the scalpel helps to prevent the hilt of the blade catching on tissue as the blade is withdrawn.

Synovial sepsis is an important indication for endoscopy of all the synovial spaces included below.

The carpus

Middle carpal joint

Positioning

Most surgeons prefer the horse in dorsal recumbency for easier access to both sides of the joint, but the surgery can be performed with the horse in lateral recumbency, preferably with the affected leg up. Active flexion and extension of the limb should be possible during surgery. The carpus should be flexed at 90°. The surgeon operates from the dorsal side and the arthroscopy equipment tower is placed behind the limb.

Arthroscopic approach

The standard arthroscope portal for the middle carpal (MC) joint lies on its dorsal surface in the center of the depression between the common digital extensor (CDE) tendon, the extensor carpi radialis (ECR) tendon and the middle and distal rows of carpal bones. The skin incision is made prior to distending the joint since the landmarks are more recognizable at this stage. The examination of the joint commences at the medial side of the joint. The instrument portal lies medial to the ECR tendon midway between the radial carpal (RC) and the third carpal (3C) bones. This is checked visually with a hypodermic needle to ensure that the portal is appropriately placed. The instrument and arthroscope portals can be exchanged if the lesion is on the lateral side of the joint.

Normal anatomy[3]

Viewing medially, the RC bone will be seen in the lower field and the 3C and second carpal (2C) bones in the upper field (Fig. 11.1). There is a synovial plica extending from the dorsomedial aspect of the RC bone medially and distally into the joint capsule. The dorsal surface of the RC bone can be examined followed by the palmar aspect of the joint, which contains a fossa in the palmar aspect of the 3C bone. The medial palmar intercarpal ligament (MPICL) lies within this

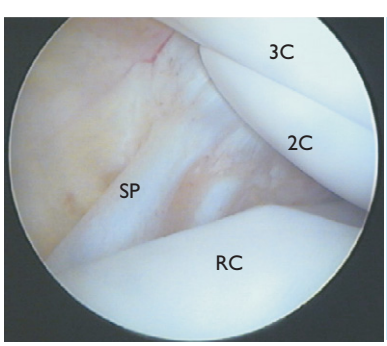

Fig. 11.1
Arthroscopic view of the medial aspect of the right middle carpal joint. 3C, third carpal bone; 2C, second carpal bone; RC, radial carpal bone; SP, synovial plica.

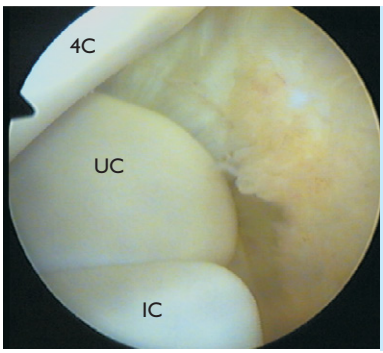

Fig. 11.2
Arthroscopic view of the lateral aspect of the right middle carpal joint. 4C, fourth carpal bone; UC, ulnar carpal bone; IC, intermediate carpal bone.

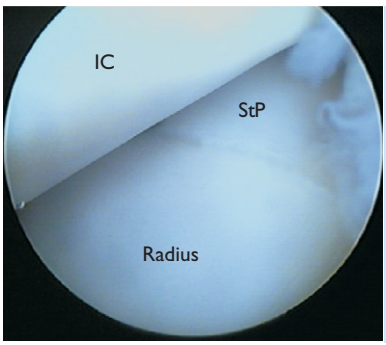

Fig. 11.4
Arthroscopic view of the lateral aspect of the right antebrachiocarpal joint. IC, intermediate carpal bone; StP, styloid process.

fossa and is a complex structure attached to the RC and 3C bones.[4] Increasing flexion of the joint improves the view of this structure. Examination of the dorsal aspect of the 3C bone is facilitated by extending the joint. The arthroscope can now be withdrawn to examine the prominent axial border of the RC bone, the intermediate carpal bone, the intermediate facet of the 3C bone and the axial part of the fourth carpal (4C) bone. Moving laterally, the ulnar carpal (UC) bone and 4C bone can be inspected (Fig. 11.2) and by rotating the arthroscope, the lateral palmar intercarpal ligament is seen lying between the 4C and the UC bones.

Antebrachiocarpal joint

Positioning

The general principles of positioning for the MC joint apply to the antebrachiocarpal (ABC) joint with the exception that the joint should be flexed at approximately 130°.

Arthroscopic approach

The incision for the arthroscope portal is made before distending the joint; both portals lie in the same relation to the ECR and CDE tendons and the center of the depression between the middle row of carpal bones and the radius. Inspection of the joint commences medially as for the MC joint. There is less room to maneuver within the ABC joint.

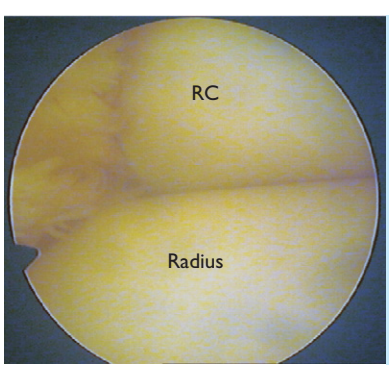

Fig. 11.3
Arthroscopic view of the medial aspect of the right antebrachiocarpal joint. RC, radial carpal bone.

Normal anatomy

The medial aspect of the distal radius and proximal RC bone is examined first (Fig. 11.3). The synovial villi can inhibit the visibility of the dorsal border of the radius but this can be counteracted by fluid distension and extension of the joint. As the arthroscope is withdrawn the junction between the IC and RC bones is seen opposite the midsagittal ridge of the radius. Moving laterally, the joint space becomes narrower and it can more easily be inspected with the arthroscope in the medial portal. In young horses the groove at the junction of the styloid process and the radius will be seen on the articular surface of the radius (Fig. 11.4). Looking distally and laterally, the axial part of the UC is visible.

Indications for arthroscopy of the carpus, specific techniques and results

Osteochondral chip fractures

These are most frequently seen in young race horses and are rare in competition and general riding horses. The reported order of incidence of the specific site of these injuries in the MC joint is the dorsodistal RC bone (Fig. 11.5), the dorsodistal IC bone and the dorsoproximal 3C bone.[5] In the ABC joint the reported order of incidence is the dorsoproximal IC bone, the dorsoproximal RC bone, the dorsodistal lateral radius and the dorsodistal medial radius.[5]

The arthroscope portal is best placed on the side of the joint away from the lesion. In both joints RC fragments are viewed from the lateral portal and IC fragments from the

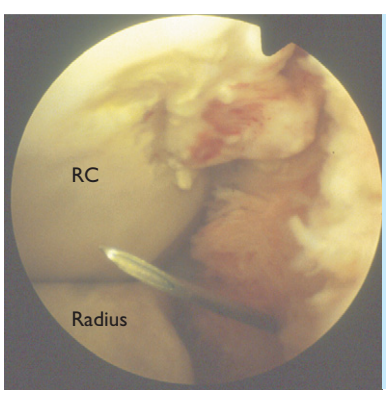

Fig. 11.5
Arthroscopic view of a fracture fragment of the left radiocarpal bone in the antebrachiocarpal joint showing a needle positioned at the site of the instrument portal.
RC, radial carpal bone.

medial portal. 3C fragments can be difficult to operate because they often lie under the ECR tendon and some extend beyond the attachment of the joint capsule. Decreasing the carpal flexion improves access to these lesions. In general some osteochondral chip fragments in the carpus may require loosening with an elevator but most can be removed directly with Ferris Smith rongeurs. Fragments with attachments to the joint capsule should be carefully dissected free before removal. Soft diseased bone in the fracture bed is curetted and the healthy articular cartilage on its borders is curetted to create a clean edge to the lesion.

The success rate of arthroscopic surgery for horses with osteochondral chip fractures in the carpus has been reported as 68% of horses returning to racing at their preinjury level.[5] The degree of articular damage was related to a worse prognosis. Another report on results of treatment in Standardbred horses showed similar findings, but the incidence of fracture sites was different. The most common sites were the dorsodistal RC bone and the dorsoproximal 3C bone in approximately equal numbers and very few ABC joint lesions were seen.[6]

Internal fixation of third carpal bone slab fractures

Frontal plane slab fractures of the 3C bone occur, in descending order of frequency, on the radial facet, on both the radial and intermediate facets and on the intermediate facet of the bone.[7] They can be repaired by internal fixation using arthroscopic and radiographic control.[8] Best results are obtained in the acute case. Comminuted or very thin slab fractures may be treated by fragment removal. For radial facet fractures the lateral arthroscope portal is used. The fracture is assessed arthroscopically, debrided and reduced. Reduction is assisted by flexion of the limb. Spinal needles (19 gauge, 9 cm) are inserted along the articular surface of the 3C bone at each edge of the fracture. An additional spinal needle is placed along the articular surface at the center of the fracture and a finer gauge needle is inserted into the carpometacarpal joint in the same plane as the center of the fracture. A needle that will mark the position of the screw is inserted and a radiograph is taken to confirm that this needle placement is correct (Fig. 11.6).

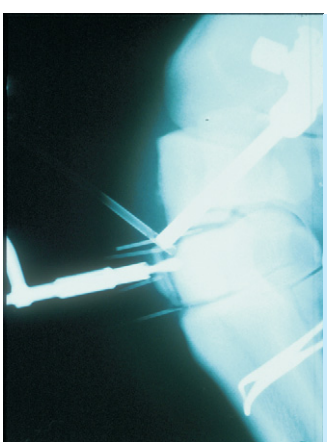

Fig. 11.6
Radiograph of slab fracture of the third carpal bone undergoing arthroscopically assisted internal fixation and demonstrating needle placement.

A stab incision is made at the site of the needle that marks the screw position and a 4.5 mm glide hole is drilled using the remaining needles as a guide for the drill angle. A further X-ray to check drill placement is taken. The 4.5 mm drill hole should be 14 mm to allow for the countersink instrument. Following placement of the 3.2 mm drill sleeve in the glide hole and drilling of the 3.2 mm pilot hole, the drill hole is countersunk, measured and tapped. An appropriate length 4.5 mm cortical ASIF (Association for the Study of Internal Fixation) cortical screw is inserted and the fracture line is examined arthroscopically to assess fracture reduction while the screw is tightened. Fractures across both the radial and intermediate facets usually require two screws. For small fracture fragments 3.5 mm cortical ASIF screws may be used.

The success of this surgery depends on many factors, including the quality of the reduction, the presence of degenerative joint disease, the age and gender of the horse and the duration of the injury.[9]

Chronic arthropathy and carpal lameness without radiographic signs

Arthroscopic investigation of horses with chronic carpal arthropathy can be useful to determine the extent of joint disease, lavage inflammatory debris from the joint and debride lesions where appropriate. In some cases this may at least temporarily extend the horse's working life and should improve prognostic accuracy. Arthroscopy is indicated for carpal lameness without radiographic signs that has not responded to conservative treatment.[10] In the young race horse tearing of the MPICL will sometimes be encountered and can be debrided using a punch or motorized resector.[11]

The fetlock

Dorsal fetlock

Positioning

Most surgeons prefer to operate the dorsal fetlock with the horse in dorsal recumbency and the fetlock extended. Operating from the dorsal aspect of the limb with the arthroscope monitor caudal to the limb allows easier interchange of portals and instrument manipulation. Extension of the joint relieves the pressure of the extensor tendon, which is especially important in the hind limb. Suspending hind limbs by the heel improves extension. Some surgeons prefer to position the horse in lateral recumbency.

Arthroscopic approach

Following distension there will be an outpouching of the joint either side of the extensor tendon. For surgeries involving the distal part of the joint, the arthroscope portal is made proximal to the center of either outpouching. If the portal is placed

too distally it is difficult to advance the arthroscope across the sagittal ridge. If the site of interest is in the proximal joint, the portal should be made at the center of the outpouching. The obturator and arthroscope sleeve should be passed across the joint before commencing the examination. The instrument portal is sited on the contralateral side of the joint.

Normal anatomy

If the arthroscope portal is lateral, the medial proximodorsal aspect of the first phalanx (P1) will be seen first. The synovial fronds of the joint capsule lie dorsal and the articular cartilage of the third metacarpal/metatarsal (MC3/MT3) condyles lie palmar/plantar in the field of view. Moving axially over the sagittal ridge, a similar view of lateral P1 is obtained. If the arthroscope is directed proximally the synovial pads proximodorsal in the joint both laterally and medially are examined.

Palmar/plantar fetlock

Positioning

There are advantages in positioning the horse either in dorsal or lateral recumbency for palmar/plantar fetlock arthroscopy and the choice depends on the surgery to be performed and the surgeon's preference. Dorsal recumbency is more satisfactory if both fetlocks require surgery or if there are both medial and lateral lesions in the affected joint. Where possible, the author prefers lateral recumbency. A tourniquet is necessary if the horse is in lateral recumbency, but it should not prevent the arthroscope being positioned parallel to the limb (Fig. 11.7). The limb must be supported so that it can readily be flexed and extended during surgery.

Arthroscopic approach

For most surgeries the arthroscope portal is placed in the most proximal outpouching of the palmar/plantar joint capsule and the obturator and arthroscope sleeve are passed to the distal, contralateral aspect of the joint. The site of the instrument portal will depend on the lesion involved.

Normal anatomy

The first view will be of the proximal sesamoid bone and the condyle of MC3/MT3 in the distal contralateral aspect of the joint. Looking distally, the palmar/plantar edge of P1 is usually screened by synovial villi, but can be seen when the joint is flexed. Proximally the apex of the proximal sesamoid is inspected before withdrawing the arthroscope to view the intersesamoidean ligament and the sagittal ridge of MC3/MT3, and finally the ipsilateral proximal sesamoid bone and MC3/MT3 condyle.

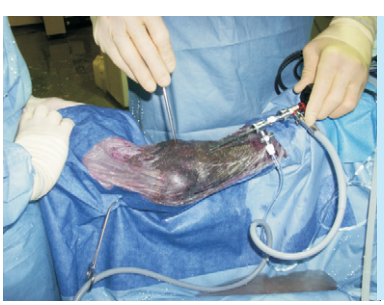

Fig. 11.7
Arthroscope and instrument portals for arthroscopic removal of palmar/plantar P1 osteochondral fragments. Note that the arthroscope and the camera are parallel to the limb.

Indications for arthroscopy of the fetlock, specific techniques and results

Osteochondral chip fractures in the dorsal joint

These occur in both racing and non-racing horses and sometimes they are incidental findings. They arise from the dorsal aspect of P1 in both fore- and hindlimbs and are more frequent in the medial aspect of the joint[12,13] (Fig. 11.8). The arthroscope portal is made on the dorsal aspect of the joint contralateral to the fragment and the instrument portal is ipsilateral. A careful examination of the joint is made to evaluate concurrent joint disease and to ensure that no fragments are hidden in the synovial villi. Wear lines and erosions of the articular cartilage in the condyle of MC3/MT3 are often associated with any osteochondral fragmentation in the fetlock[13] (Fig. 11.9). Most fragments are attached and should be dissected free, carefully avoiding complete separation to prevent them falling into the dependent part of the joint where they can be more difficult to retrieve. Small Ferris Smith rongeurs are suitable for grasping and removing the fragments. The site of the lesion on P1 requires debridement and usually consists of thickened irregular fibrous tissue covering softened bone.

In two studies of 336 and 461 horses respectively, return to use was reported in approximately 85% of horses following arthroscopic removal of fetlock fragments.[12,13] In one report 82% of horses achieved their original performance level,[12] while in the other this figure was 69% and the success rate declined by 10% if other fetlock lesions were present.

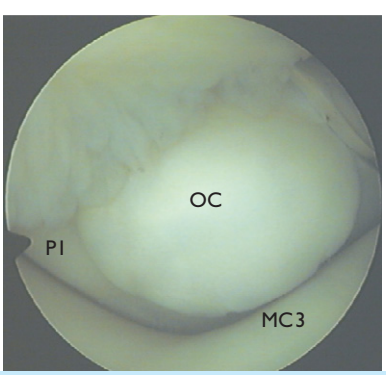

Fig. 11.8
Arthroscopic view of the dorsomedial aspect of the right fore fetlock showing an osteochondral fragment attached to the dorsoproximal aspect of the first phalanx. P1, first phalanx; MC3, medial distal condyle of the third metacarpal bone; OC, osteochondral fragment.

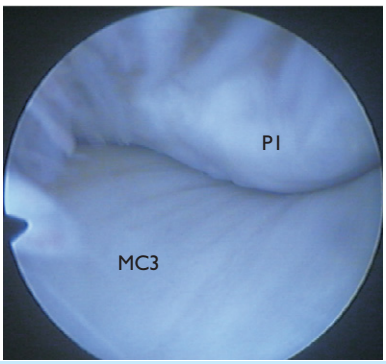

Fig. 11.9
Arthroscopic view of the dorsomedial aspect of the right fore fetlock showing wear lines on the articular cartilage of the distal third metacarpal bone (MC3). These fragments were associated with the presence of osteochondral fragmentation on the dorsal sagittal ridge. P1, first phalanx.

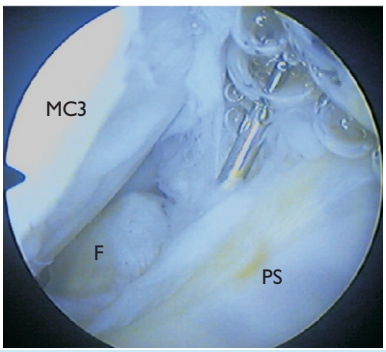

Fig. 11.10
Arthroscopic view of the palmaromedial distal aspect of the left fore fetlock showing a type I palmar P1 osteochondral fragment revealed by probing. MC3, medial distal condyle of the third metacarpal bone; F, fragment; PS, proximal sesamoid bone.

Osteochondritis dissecans lesions on the dorsal sagittal ridge of MC3/MT3

The approach for these lesions is similar to the approach for dorsal P1 fragments, with minor modifications. Triangulation is improved if the portals are made slightly further abaxially and distally to the standard portals.

Fibrotic proliferation of the synovial pad in the dorsoproximal aspect of the joint

This condition is also termed proliferative synovitis or villonodular synovitis. It is thought to be associated with chronic trauma in the metacarpophalangeal joint and is often associated with other traumatic lesions in the joint.[14] Partial or complete arthroscopic excision of one or both pads is accomplished using sharp dissection with a meniscal knife or a cutting instrument such as an O'Connor punch. An extra instrument portal sometimes facilitates the dissection. Debridement of underlying diseased bone is often necessary. A study of 63 horses with this condition reported that 43/50 horses treated arthroscopically and one out of eight horses treated medically returned to their previous level of racing.[14]

Type I palmar/plantar P1 osteochondral fragments[15]

These lesions occur in fore- and hindlimbs both medially and laterally but are more frequently seen in the medial aspect of hindlimbs.[16] They can be bilateral and can also be an incidental finding. This is one of the more difficult arthroscopic procedures.

The author prefers to place the horse in lateral recumbency with the lesion uppermost and approach this with both portals on the same side as the fragment (see Fig. 11.7). The arthroscope and camera must lie flush with the limb to permit a clear view of the distal ipsilateral part of the joint where the fragment often lies hidden by the synovial villi (Fig. 11.10). The instrument portal must be made distal enough for the instrument to pass distal to the MC3/MT3 condyle, giving direct access to the fragment. The fragment will often require extensive dissection from its attachments and this is more safely performed with a meniscal knife than a scalpel blade, which can easily be broken. A motorized synovial resector is useful for clearing away excessive synovial tissue. Dissection of the fragment with a radiofrequency probe is also effective but care should be taken to avoid charring tissue. Horses with fragments in both fetlocks or fragments in both medial and lateral aspects of the same joint are more easily operated in dorsal recumbency.

In a report on a series of 119 cases treated arthroscopically, 63% of 87 race horses and 100% of nine non-race horses returned to preoperative performance levels.[16] Concurrent joint disease worsened the prognosis.

Small articular basilar sesamoidean fracture fragments

These can be removed surgically using the same technique as for palmar/plantar P1 fragments. Dissection of the fragments off the attachments of the distal sesamoidean ligament is necessary and the prognosis for return to use is reasonable.[17]

Apical sesamoidean fracture fragments

Surgical removal is generally considered to be the most appropriate treatment for apical fractures involving up to one-third of the proximal sesamoid bone.[18] Arthroscopic removal is a relatively difficult procedure but does appear to have advantages over arthrotomy.[19] The author prefers an ipsilateral approach with the horse in lateral recumbency so that the lesion is uppermost, but some surgeons prefer to operate with the horse in dorsal recumbency and the arthroscope portal on the contralateral side of the joint to the lesion. When operating with the arthroscope ipsilaterally the arthroscopic portal must be as proximal as possible so that the whole apex of the bone is clearly visible (Fig. 11.11). The instrument portal is made in line with the fracture. The fragment is first dissected off the intersesamoidean ligament

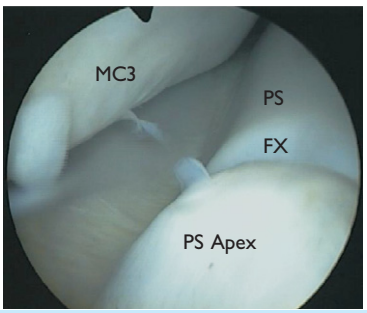

Fig. 11.11
Arthroscopic view of a fracture of the apex of the right fore lateral proximal sesamoid bone. PS, proximal sesamoid bone; MC3, median sagittal ridge of the distal third metacarpal bone; PS Apex, apex of proximal sesamoid bone; FX, fracture line in proximal sesamoid bone.

using a downcurved osteotome. A serrated meniscal knife is suitable for completion of the dissection of the fragment off the suspensory ligament (Fig. 11.12). The use of electrocautery for this dissection has also been reported.[20] Removal is completed with Ferris Smith rongeurs and may require enlargement of the portal for large fragments.

There are few reports of surgical excision of apical sesamoid fractures in a large number of horses. A retrospective study of 43 Standardbred race horses with apical sesamoid fractures showed a good prognosis following surgical removal, but the technique was not defined. Prognosis was not affected by the dimensions of the fracture nor by the degree of suspensory ligament damage.[21]

Articular abaxial sesamoidean fracture fragments

The approach for these lesions is similar to the approach for apical fracture fragments.[22] Sharp dissection of the fragment off the suspensory ligament can be performed entirely with a meniscal knife or similar instrument. Favorable results for return to racing were reported in a series of 47 horses. Non-race horses, horses with smaller fragments and horses with fragments that involved only the abaxial aspects of the bone had a better prognosis.[22]

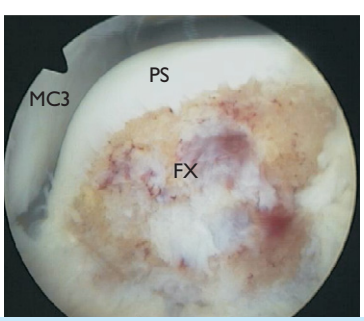

Fig. 11.12
Postoperative view of the apical sesamoid fracture in Fig. 11.11. MC3, median sagittal ridge of the distal third metacarpal bone; PS, proximal sesamoid bone; FX, fracture line in proximal sesamoid bone following removal of the apical fragment.

Chronic fetlock arthropathy and sepsis

Arthroscopy of the dorsal and palmar/plantar fetlock can be of value for joint disease that fails to respond to conservative treatment. Sepsis should be approached with appropriate medical therapy and through-and-through lavage can be achieved using dorsal and palmar/plantar portals.

The hock

Positioning

Most surgeons prefer to position the horse in dorsal recumbency and whether the arthroscopy is performed with the surgeon standing cranial to the limb and facing caudally or standing caudal to the limb and facing cranially is a matter of personal preference. The joint is placed in partial flexion in such a way that it can be flexed or extended during the surgery.

Dorsal tarsocrural joint

Arthroscopic approach

Once the saphenous vein has been identified, the standard arthroscopic portal is placed in the medial pouch of the tarsocrural joint just axial to the saphenous vein. Great care should be taken to avoid lacerating the vein. If the hock joint is sufficiently flexed the obturator and arthroscope sleeve can be advanced under the extensor tendons to the lateral reflection of the joint before inserting the arthroscope to commence the examination. Adjustments to this routine may be necessary for certain lesions.

Normal anatomy

The lateral reflection of the joint is first examined. Rotating the arthroscope proximally will bring the lateral malleolus into view. The lateral trochlear ridge (LTR) can be examined by withdrawing and rotating the arthroscope. As

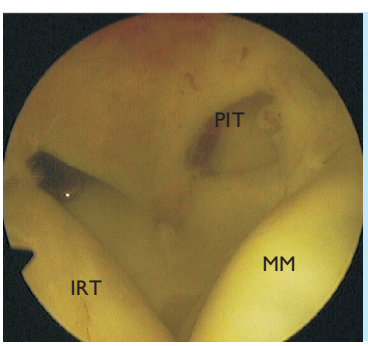

Fig. 11.13
Arthroscopic view of the mid tarsocrural joint showing the pouch over the proximal intertarsal joint (PIT), the intermediate ridge of the tibia (IRT) and the medial malleolus (MM).

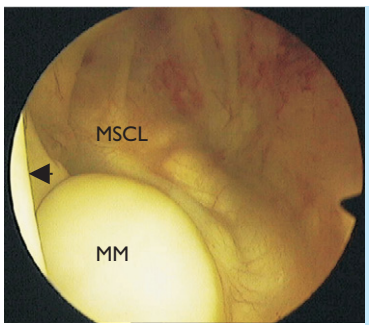

Fig. 11.14 Arthroscopic view of tarsocrural joint showing the medial malleolus (MM), the medial short collateral ligament (MSCL) and the edge of the medial trochlear ridge of the talus (arrow).

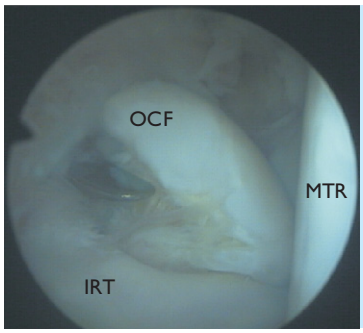

Fig. 11.15 Arthroscopic view of an OCD lesion on the intermediate ridge of the left tibia (IRT) being loosened with an elevator. OCF, osteochondral fragment; MTR, medial trochlear ridge of the talus.

the arthroscope is withdrawn further the intermediate ridge of the tibia, the axial aspect of the LTR and the proximal intertarsal joint come into view (Fig. 11.13) and finally the medial trochlear ridge (MTR), the medial malleolus and the medial short collateral ligament are visible when the arthroscope is withdrawn into the medial aspect of the joint (Fig. 11.14).

Plantar tarsocrural joint

Arthroscopic approach

The plantar aspect of the joint can be approached from the center of either the medial or the lateral outpouching of the joint.[23] With the joint flexed in a right angle the arthroscope sleeve and obturator can be passed across the joint before inserting the arthroscope.

Normal anatomy

From the plantaromedial portal the lateral malleolus is viewed by looking dorsally in the lateral reflection of the joint. With the arthroscope in the midjoint region the distal intermediate ridge of the tibia, the MTR and the LTR will lie dorsally and the synovial sheath of the deep digital flexor tendon will lie plantarly in the field of view. Withdrawing the arthroscope medially allows inspection of the MTR and the medial reflection of the joint but the medial malleolus is not visible. From the plantarolateral portal the same midjoint structures can be inspected and when examining the lateral reflection of the joint from the lateral side, the talocalcaneal ligament and the lateral malleolus are visible. Examination of the joint is facilitated by flexion and extension as required.

Indications for arthroscopy of the hock, specific techniques and results

Osteochondrosis dissecans (OCD)

The intermediate ridge of the tibia (IRT) in the dorsal tarsocrural joint is the most frequent site for OCD lesions in the hock.[24] Lesions are also encountered on the LTR, the medial malleolus and occasionally on the MTR.[24] OCD lesions in the hock may be an incidental radiographic finding and the decision to treat them surgically depends on there being evidence that they are causing clinical signs. When operating IRT lesions the instrument portal should be relatively dorsal in the lateral pouch and before making the incision the exact position of the portal can be confirmed using a 9 cm spinal needle to ensure that the whole lesion is accessible through the portal. Fragments often require loosening with an osteotome (Fig. 11.15) before being grasped with Ferris Smith rongeurs for removal. They should not be completely freed since they can be difficult to grasp when loose in the joint. The instrument portal may need to be enlarged for large fragments so it is preferable to remove smaller fragments first while joint distension is maintained. The lesion site is curetted smooth and all debris flushed from the joint at the end of surgery.

LTR lesions are more difficult to treat arthroscopically. Some surgeons prefer to place both the arthroscopic and instrument portals ipsilaterally since the distal part of the LTR is difficult to view from the medial position because of the extensor tendon. However, increasing joint flexion improves the view from the medial portal and this approach gives better triangulation. Medial malleolus lesions are best treated with both portals ipsilateral.

A 76.5% success rate for return to normal function has been reported for arthroscopic treatment of OCD lesions in the hock.[24] The size of IRT lesions did not affect outcome but accompanying degenerative joint disease worsened the prognosis. Resolution of synovial effusion was seen in approximately 80% of horses but was worse for medial malleolus and LTR lesions.

Intra-articular fractures

Some fractures in the hock that involve intra-articular fragmentation can be treated by arthroscopic removal of the fragments and debridement of the fracture bed. Care should be taken to ensure that the fractures do not extend into major supporting bones since there is a high chance of disintegration of the bone during anesthetic recovery. The approach depends on the site of the lesion but the standard portals are often appropriate. Some smaller lateral malleolus fractures can be removed arthroscopically. A dissecting instrument such as a meniscal knife is needed to resect the fractured fragment from its attachments.

Chronic arthropathy unresponsive to conservative treatment

Arthroscopic evaluation of the dorsal and plantar aspects of the tarsocrural joint can be useful diagnostically,

prognostically and for debridement of intra-articular lesions. Appropriate debridement of lesions and lavage of debris from the joint should improve the horse's comfort. Lesions in the short lateral collateral ligament will sometimes be evident arthroscopically and can also be debrided.

Septic joint disease

This indication is common to all the synovial spaces described in this section but it is especially common in the tarsocrural joint as a sequel to hock trauma. It requires aggressive treatment. Arthroscopic treatment often involves both dorsal and plantar pouches of the joint for investigation of the injury and for through-and-through lavage. Osteomyelitic lesions can develop particularly on the trochlear ridges and should be debrided by curettage to healthy tissue.

The stifle

Femoropatellar joint

Positioning

Most surgeons prefer operating this joint with the horse in dorsal recumbency. The limb must be in extension in order to allow the arthroscopic sleeve to pass easily under the patella into the suprapatellar pouch (Fig. 11.16). If the limb is positioned vertically the arthroscope can be held with the surgeon's arm passing caudally around the limb, which some find more comfortable, and this marginally increases the space beneath the joint capsule in the distal joint. The monitor is placed cranially and the surgeon faces forwards. The joint can also be operated with the limb extended more caudally so that the surgeon works with both hands on the cranial side of the limb.

Arthroscopic approach

For most procedures the arthroscopic portal is sited between the lateral and middle patellar ligaments midway between the patella and the tibial crest. In many horses a small blood vessel traverses just proximal to this site when the limb is vertical. Unless the joint is pathologically distended, at least 60 mL of fluid will be required for sufficient distension to lift the patella off the intertrochlear groove and permit the arthroscope sleeve and obturator to be passed into the suprapatellar pouch. If this is difficult, it may be facilitated by further distension of the joint.

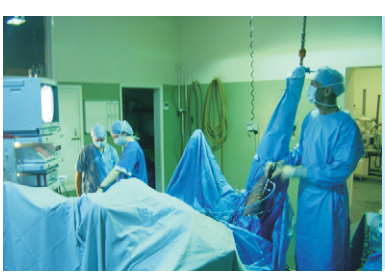

Fig. 11.16
Positioning for arthroscopy of the femoropatellar joint with the leg extended vertically.

Normal anatomy

The examination commences in the suprapatellar pouch where loose debris will accumulate. As the arthroscope is withdrawn, the base of the patella and proximal intertrochlear groove of the femur come into view. The articular surface of the patella and intertrochlear groove can be examined as the arthroscope is steadily withdrawn from beneath the patella. Once clear of the patella, its apex can be inspected followed by both medial and lateral trochlear ridges (MTR and LTR) to their most distal points where the plicae covering their communications with the medial and lateral femorotibial (MFT and LFT) joints are present in most horses.

Indications for arthroscopy of the femoropatellar joint, specific techniques and results

Osteochondrosis dissecans

In the femoropatellar joint (FP), OCD is most frequently encountered on the LTR (Fig. 11.17) and also occurs, though less commonly, on the patella, the intertrochlear groove (ITG) and MTR.[25] Both limbs are often affected. Before making the instrument portal a spinal needle is used to check that all the lesions can be reached at the correct angle, since a wrongly positioned portal may make it impossible to treat some of the

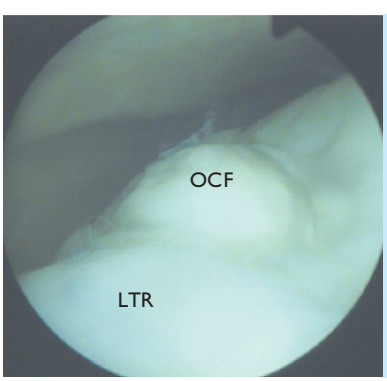

Fig. 11.17
OCD lesion containing attached osteochondral fragments on the lateral trochlear ridge of the right femur (LTR). OCF, osteochondral fragments.

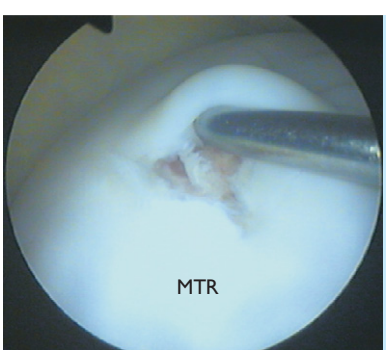

Fig. 11.18
OCD lesion on the medial trochlear ridge (MTR) of the left femur of a yearling Thoroughbred gelding. Probing has revealed poorly attached soft articular cartilage.

lesions. Most lesions can be reached from a lateral portal but an extra portal can be used if necessary. Osteochondral fragments may need partial loosening with an osteotome before removal with Ferris Smith rongeurs and following removal, the remainder of the lesion should be curetted to healthy subchondral bone. This can be achieved with both spoon and loop curettes, rongeurs and motorized equipment. Some lesions, particularly in foals and yearlings, appear as soft articular cartilage but when probed this peels off its attachment (Fig. 11.18). In older horses there may be associated degenerative change in the articular cartilage. Loose fibrillated cartilage can be trimmed with a synovial resector or a coblation wand. Many patellar, ITG and MTR lesions can be reached from the lateral instrument portal but if not, a more appropriate position is used.

The removal of debris and osteochondral fragments from the suprapatellar pouch is an inevitable part of arthroscopic surgery of OCD lesions in the FP joint. Long Ferris Smith rongeurs (shaft length 20 cm) are very useful for removing fragments and a long, wide-bore egress cannula in conjunction with high fluid flow rates and suction will effectively remove loose debris. Retrieval of fragments through a portal proximal to the patella into the suprapatellar pouch is also possible in the absence of long instruments, but it is difficult to maintain this portal because of the distance from the skin to the joint capsule. An alternative portal that is easier to manage can be made laterally between the proximal patella and the proximal edge of the LTR.

Occasionally very large fragments will be encountered and very large rongeurs are needed to remove them. Fixing the fragment with a spinal needle passed transcutaneously facilitates grasping it with the rongeurs. The instrument portal may need to be enlarged considerably when the fragment is extricated.

In one report 64% of 161 horses treated by arthroscopic surgery returned to athletic use.[25] Best results were seen in older horses and those with mild lesions. From a series of 57 horses operated at the author's practice, 83% returned to athletic use and the presence of associated degenerative change on the articular cartilage did not affect the prognosis (JP Walmsley and TJ Phillips, unpublished data, 2002).

Fractures of the patella

Fractures of the patella that can be treated by arthroscopic excision of the fracture fragment include medial sagittal, basilar and some apical fractures. These fractures can be evaluated from the standard arthroscopic portal, though some basilar fractures may be better assessed from a portal developed medially or laterally just proximal to the base of the patella. Medial sagittal fractures (Fig. 11.19) require dissection off their attachments to the parapatellar fibrocartilage of the medial patellar ligament, which can be difficult and extensive. Meniscal knives are useful instruments for this procedure. The prognosis for medial sagittal fractures treated by excision arthroscopically is reasonably good. In one case series of 12 horses 10 returned to full use.[26] Basilar fractures sometimes accompany other trauma in the joint. An appropriate instrument portal medial or lateral and proximal to the base of the patella will be necessary for removal of fragments. Some small fragments become embedded in the local soft tissue and may not cause lameness. Apical fracture fragments that can be removed arthroscopically are unusual but are approached as for fragmentation lesions.

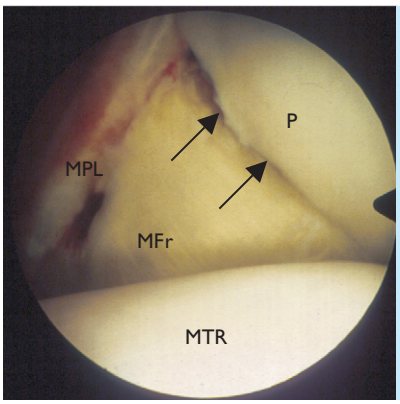

Fig. 11.19 Arthroscopic view of medial sagittal fracture of the left patella (P). MFr, medial fragment of the patella; MPL, medial patellar ligament; arrows, fracture line; MTR, medial trochlear ridge of the femur.

Fracture fragmentation of the trochlear ridges

These fragments are usually present as loose bodies that have fractured off a trochlear ridge in the FP joint. It can be difficult to ascertain the source of the fracture. Following examination of the joint to assess the injury, the fragments are located and removed with rongeurs. They will usually fall into the suprapatellar space but they may be attached to the joint capsule and difficult to find. Any remaining lesions in the joint are debrided appropriately. Depending on the effect of any concurrent injuries, there is a good chance of return to athletic use following treatment.[27,28]

Fragmentation of the patella

This condition is usually a sequel to medial patellar desmotomy and requires arthroscopic debridement when it causes lameness.[29] It may develop without causing lameness. The fragments usually lie in the synovium just distal to the apex of the patella and the synovial villi may not be immediately visible. The arthroscopic portal can be placed slightly more distal than the standard site and the instrument portal is placed on the lateral side of the joint since the diseased patellar tissue mostly lies on the lateral side of the apex. The fragments are removed with rongeurs and the patellar lesion is curetted to healthy bone. The prognosis is favorable.[29]

Femorotibial joints

Positioning

If all accessible parts of the FT joints are to be examined, placing the horse in dorsal recumbency is preferred with the tibia horizontal and a hock angle of 90°. It is important to be

able to flex and extend the limb during surgery. The cranial and caudal compartments of the joints can be arthroscoped with the horse in this position though some surgeons partially extend the joint when examining the caudal compartments.[30] The surgeon operates facing cranially with the monitor placed cranial on the opposite side of the horse.

Arthroscopic approach, cranial compartments

Three approaches to the cranial compartments of the FT joints have been described.

Cranial approach[31] The arthroscopic portal for the medial femorotibial joint (MFT) is made 2 cm proximal to the tibial crest between the middle and medial patellar ligaments. The joint can be distended with 50 mL of fluid using a spinal needle inserted medial to this site over the medial femoral condyle (MFC), which is a useful, easily palpable landmark. The instrument portal is at the site of the spinal needle, which if left in place can be manipulated to confirm that all the appropriate structures will be accessible through the portal. Its position can be readjusted if necessary. The lateral femorotibial joint (LFT) is approached from the MFT by first replacing the telescope with the conical obturator in the arthroscope sleeve and then passing it through the median septum and under the tendon of origin of the long digital extensor tendon (LDE) into the lateral aspect of the joint. This has to be done by feel and if positioning is correct the instrument should pass relatively easily across the LFT after the median septum has been penetrated. The LFT instrument portal lies about 6 cm lateral to the arthroscopic portal. Because of the distance between the joint capsule and the skin, the portal should be carefully sited with a spinal needle before making the incision. When creating portals in the FT joints, advancing the scalpel until it is visible within the joint facilitates the subsequent passage of instruments. Care must be taken not to catch the hilt of the scalpel in subcutaneous tissue so that it is pulled off the handle whilst being retrieved.

Lateral approach[32] Used mainly for surgical treatment of subchondral bone cysts in the MFC, this portal lies between the lateral patellar ligament and the tendon of origin of the LDE, 2 cm proximal to the tibial plateau. The arthroscopic obturator and sleeve are inserted parallel to the tibial plateau and passed through the LFT into the MFT. This is facilitated by palpating the MFC and aiming across the joint at it. The instrument portal is positioned over the lesion.

Approach from the FP joint This approach follows examination of the FP joint and the limb is maintained in extension (KJ Boening, personal communication, 1992). It is more easily performed with a longer arthroscope. The slit-like communication with the MFT is viewed and dissected open with arthroscopic scissors. A window is then created in the septum between the FP and FT joints. This approach provides a good view of the axial parts of the FT joints but poor access to their lateral and medial aspects.

Normal anatomy

From the cranial approach the surgeon's landmark is the medial intercondylar eminence of the tibia (MICET). The median septum occupies the axial field of view and partially covers the cranial cruciate ligament (CrCL), which can be palpated with the arthroscopic probe beneath its fascia. In the caudal aspect of the MFT the caudal cruciate ligament (CaCL) is seen extending from the roof of the intercondylar notch of the femur distally towards its caudal tibial insertion. Moving medially, the cranial aspect of the articular surface of the MFC can be viewed. The cranial pole of the medial meniscus (MM) lies between the MFC and the tibial plateau, and the cranial ligament of the medial meniscus (CrLMM) extends from the MM to the cranial border of the MICET (Fig. 11.20). When examining the LFT by the cranial approach, the popliteal tendon in the most lateral aspect of the LFT joint will be the first structure viewed. As the arthroscope is withdrawn it will slip out from underneath the LDE, which can then be followed proximally to its origin in the lateral femoral condyle (LFC). In the more axial part of the joint the lateral

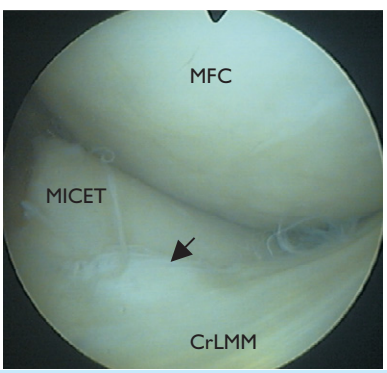

Fig. 11.20
Arthroscopic view of the right medial femoral condyle (MFC), the medial intercondylar eminence of the tibia (MICET) and the cranial ligament of the medial meniscus (CrLMM). There is fibrillation of the axial border of the ligament (arrow).

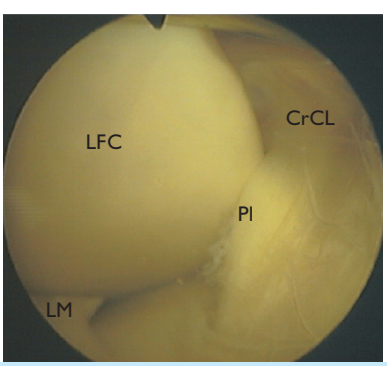

Fig. 11.21
Arthroscopic view of the right lateral femoral condyle (LFC), the cranial pole of the lateral meniscus and its cranial ligament (LM). The cranial cruciate ligament lies under the median septum in the right of the picture with the plica-like branch (PI) coursing towards the tibial plateau.

meniscus (LM) and its cranial ligament have a similar configuration to their medial counterparts. Axial to this the CrCL is almost completely covered by the median septum and a small plica-like branch of the ligament is present at about the level of the articulation of the LFC and tibial plateau (Fig. 11.21).

Arthroscopic approach to the caudal compartment of the medial femorotibial joint

The author prefers to position the stifle in flexion for this procedure, though some authors suggest positioning in partial flexion[30] and others in extension.[33] Distension of the caudal MFT is achieved through a 9 cm spinal needle placed just proximal and caudal to the caudal most palpable point of the medial tibial condyle. The arthroscopic portal is placed about 2 cm caudal to this and the sleeve and blunt obturator aimed towards the caudal articulation of the femur and tibia. The joint capsule lies approximately 3 cm deep to the skin. Sharp trocars should only be used for penetration of either caudal FT joint with great caution because of the risk of penetrating the popliteal artery, which lies between the two caudal compartments of the FT joints. The instrument portal is placed according to the position indicated by spinal needle guidance.

Normal anatomy

The relatively large sac of the caudal MFT is easily inspected. The caudal articular surface of the femur can be followed to its articulation with the medial meniscus on the tibial condyle. In the axial aspect of this articulation the caudal ligament of the medial meniscus can usually be seen and caudal to this the outline of the CaCL is detectable in most horses where it lies deep to the synovial membrane as it courses from its distal attachment to its femoral insertion proximomedially between the femoral condyles (Fig. 11.22).

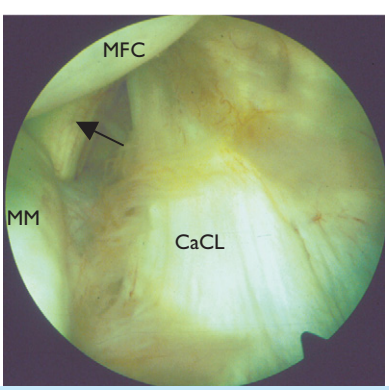

Fig. 11.22
Arthroscopic view of the left caudal compartment of the medial femorotibial joint, showing the caudal cruciate ligament (CaCL) under the synovial capsule and the caudal ligament of the medial meniscus (arrow). MFC, medial femoral condyle of the femur; MM, medial meniscus.

Arthroscopic approach to the caudal compartment of the lateral femorotibial joint

Arthroscopy of this joint is easier with the stifle partially flexed.[30,33,34] The joint is divided by the popliteal tendon. Distension is best achieved through a spinal needle inserted caudal to the lateral collateral ligament and just proximal to the level of the tibial plateau. The arthroscope portal for the joint proximal to the popliteal tendon is situated 2.5 cm proximal to the tibial plateau and 3 cm caudal to the collateral ligament. The distal part of the joint is entered through a portal which lies at the level of the tibial plateau and 1.5 cm caudal to the lateral collateral ligament. The common peroneal nerve lies approximately 7 cm caudal to the lateral collateral ligament, so all portals should be sited cranial to this. The instrument portal is placed according to the position indicated by spinal needle guidance.

Normal anatomy

Proximal to the popliteal tendon, apart from the tendon itself, the caudal part of the lateral femoral condyle is the main structure identified. Through the distal portal the LFC and caudal lateral meniscus are visible.

Indications for arthroscopy of the femorotibial joints, specific techniques and results

Stifle lameness unresponsive to conservative treatment

Diagnostic and therapeutic arthroscopy of the FT joints of horses whose lameness is alleviated by intra-articular analgesia and which does not respond to conservative treatment is one of the most frequent indications for arthroscopy of the FT joints (240 in a series of 403 stifle arthroscopies performed at the author's hospital).[35] Lesions most likely to be encountered are articular cartilage injuries, meniscal tears and cruciate ligament lesions. Multiple lesions are common which emphasizes the importance of a careful examination of the whole joint.

Articular cartilage lesions vary from severe, extensive, full-thickness lesions to mild fibrillation of the surface of the cartilage. Treatment involves debridement of loose material, but only full-thickness defects should be curetted to subchondral bone. Large areas of denuded bone may benefit from micropicking.[2] With careful management and in the absence of other injuries, the prognosis for primary articular cartilage lesions is reasonable. In one study six out of seven focal lesions returned to racing though five horses with larger lesions remained lame.[36] In the author's practice, 44 horses with cartilage lesions out of 61 followed up returned to full use but there was no differentiation between size of lesions in the study.

Meniscal and meniscal ligament tears are more common in the medial meniscus.[37] Loose tissue should be resected

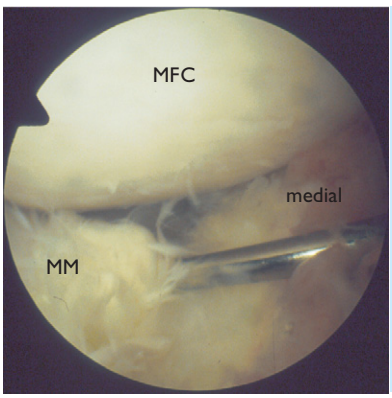

Fig. 11.23 Arthroscopic view of a torn right medial meniscus (MM) with associated articular cartilage lesions on the medial femoral condyle (MFC).

wherever possible although in more severe lesions some of the damaged tissue will be inaccessible beneath the femoral condyle. The prognosis is statistically related to severity of injury and it is worse if there are concurrent cartilage lesions[37] (Fig. 11.23). Of 80 horses which were diagnosed with meniscal tears by arthroscopy at the author's hospital, 33 out of 70 horses followed up returned to full use.[37]

Cruciate ligament injuries are more difficult to assess because of the covering of synovium and median septum. This can be removed with a synovial resector to improve the visualization of the ligament but care should be taken to avoid hemorrhage. Light debridement of loose tissue is all that can be achieved with mild to moderate lesions and over 50% can be expected to return to use. Severe lesions, which are sometimes accompanied by avulsion fractures, require more drastic debridement and have a poorer prognosis.

Subchondral bone cysts and osseous cyst-like lesions

Subchondral bone cysts (SBC) in the distal MFC and more rarely in the proximal tibia can be treated surgically. Surgical treatment is generally considered to be indicated for articular lesions and those that have not responded to conservative treatment.[38–40] Small articular defects on the MFC can be worsened by aggressive debridement. The use of the lateral arthroscopic portal permits better triangulation with the standard instrument portal, which is sited over the lesion, but the cranial arthroscope portal can also be used. The articular defect may be quite small (Fig. 11.24) but a probe can easily be pushed through into the subchondral lesion if the cyst communicates with the joint. All the contents of the cyst should be removed. Hooked curettes can be useful for curetting the sides of the lesion. Postoperatively intralesional treatment with corticosteroids has been advocated to suppress inflammatory mediators which are thought to contribute to the development of the cyst.[41] Forage of the subchondral bone can provoke worsening of the lesion[38] and one study showed that a cancellous bone graft in the lesion did not improve the outcome.[42] Over 70% success has been reported in young horses[38,40] but the author has noted that worse results might be expected in horses over 3 years old though this has not been analyzed statistically.

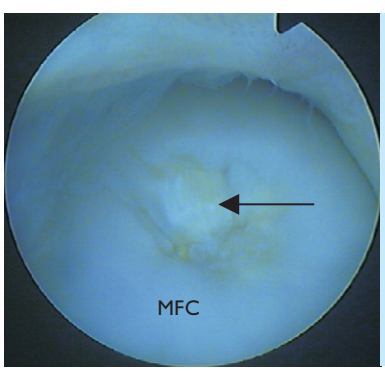

Fig. 11.24 Arthroscopic view of articular cartilage lesion (arrow) associated with a subchondral bone cyst in the medial femoral condyle (MFC).

Most tibial SBCs can be approached from the cranial arthroscopic and instrument portals though some may lie beneath the cranial meniscal ligament and if very abaxial, may not be accessible.[43] Osseous cyst-like lesions in the caudal femoral condyles may be candidates for surgery if there is no response to conservative treatment; they are approached through the standard portals, the proximal lateral one being the more appropriate for LFC lesions.[33]

Fracture fragmentation of the femoral condyles

Small fracture fragments may occur in any compartment of the FT joints. They frequently accompany other joint injuries and a thorough examination of the whole joint is indicated. Fragments may require dissection from their soft tissue attachments. The prognosis depends on the extent of damage in the whole joint.

Fracture of the intercondylar eminence of the tibia

These fractures are not always associated with CrCL injuries and each should be assessed objectively. Some fragments can be removed by dissection off the fracture bed,[44] while internal fixation under arthroscopic control may be more appropriate if removal involves extensive soft tissue dissection.[45] Occasionally long-standing fractures will have healed by fibrous union and may be better left in situ. As for all traumatic FT injuries, other joint lesions are often present and a careful evaluation of the whole joint is essential. It is often the associated injuries that determine the prognosis.

Distal interphalangeal joint

Positioning

With the horse in dorsal recumbency and the foot fixed to a crossbar so that the distal interphalangeal (DIP) joint is in extension, good access to the dorsal aspect of the joint is obtained for both arthroscopic and instrument portals. By flexing the joint, this position is also appropriate for arthroscopy of the palmar/plantar aspect of the joint. If the

horse is placed in lateral recumbency it is more difficult to enter the joint from the lower side, but some surgeons prefer this approach as the lateral pouch is larger.

Arthroscopic approach

Dorsal joint Both the arthroscope and instrument portals for the dorsal aspect of the DIP joint are situated 2 cm abaxial to the midline and approximately 2 cm proximal to the coronary band.[46]

Palmar/plantar joint This is entered medially or laterally just proximal to the collateral cartilage, palmar/plantar to the second phalanx and dorsal to the deep digital flexor tendon.[47] The lateral pouch is larger.[47]

Normal anatomy

Dorsal joint The extensor process of the third phalanx lies in the immediate field of view, though it is often partially covered with synovium. The most proximal dorsal surface of the articular cartilage of the second phalanx can be inspected and proximal to this is the dorsal, proximal reflection of the joint.

Palmar/plantar joint The palmaro/plantaroproximal articular surface of the second phalanx and proximal border of the navicular bone are readily seen and distension of the joint increases the area of observable articular cartilage (Fig. 11.25). Underlying the joint capsule the collateral sesamoidean ligament of the navicular bone can be viewed inserting on the proximal border of the navicular bone.

Indications for arthroscopy of the distal interphalangeal joint, specific techniques and results

Fracture fragmentation of the extensor process of the third phalanx and the distal second phalanx

Smaller fracture fragments are readily removed arthroscopically using the standard portals. It may be necessary to clear away synovium that sometimes obscures the fracture with a motorized synovial resector before loosening the fragment with an elevator and removing it with small rongeurs (Fig. 11.26). Larger fragments can be split with an osteotome or burred down to a manageable size with a motorized arthroburr; the latter is usually easier and less traumatic. Arthroscopy can also be used to assist internal fixation of very large fragments. The prognosis is generally good if there is minimal concurrent degenerative joint disease. In a series of 16 horses with fracture fragments of the extensor process treated by arthroscopic excision, 14 horses became sound.[46]

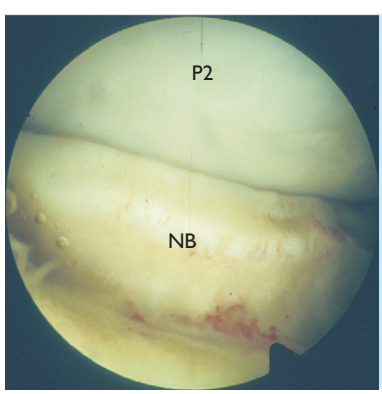

Fig. 11.25 Arthroscopic view of the palmar aspect of the left distal interphalangeal joint showing the proximal border of the navicular bone (NB) and the palmar articular surface of the second phalanx (P2).

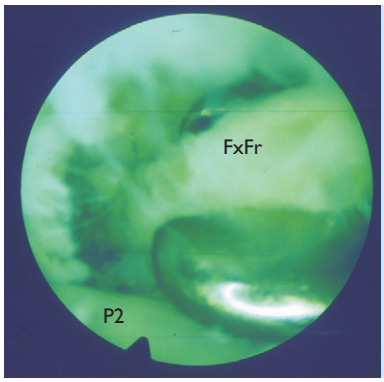

Fig. 11.26 Arthroscopic view of removal of a type IV fracture of the third phalanx with Ferris Smith rongeurs. FxFr, fracture fragment; P2, second phalanx.

Articular fracture fragments off the distal dorsal articular border of the second phalanx can sometimes be accessed and removed arthroscopically using a standard arthroscope portal and an instrument portal located over the fragment.[48] Some dissection is required to free the fragment.

Assessment of joint disease

Arthroscopic evaluation and debridement of degenerative joint disease can be of value.[49] From a series of 36 horses treated arthroscopically for chronic DIP joint disease at the author's hospital, 18 horses were followed up and eight of these returned to work for 1 year or more, though the prognosis for long-term soundness was poor.

The shoulder

Positioning

The shoulder joint is most easily examined with the horse in lateral recumbency, having the affected leg uppermost and slightly adducted.

Arthroscopic approach

Two arthroscopic approaches have been described. The arthroscope portal for the cranial approach, which the author prefers, is sited between the cranial and caudal eminences of the greater tubercle of the humerus.[50] An 18 gauge, 9 cm spinal needle is used to distend the joint with 60 mL of fluid. The arthroscope sleeve with conical obturator is passed into the joint and then advanced caudally under the infraspinatus tendon in the lateral aspect of the joint before

inserting the arthroscope. The arthroscope portal for the caudal approach is sited 1 cm caudal to the infraspinatus tendon[51] just proximal to the level of the humeral head. In order to widen the joint space curved, blunt-tipped forceps are passed into the cranial portal so that the tip of the forceps can be placed in the glenoid notch and used to lever open the joint.[51]

The instrument portal site depends upon the lesion to be operated and is usually more caudal. It should be carefully sited using a spinal needle. Some lesions are difficult to reach and almost impossible if the portal is incorrectly positioned. The portal should be accurately incised into the joint to create a smooth path for instruments since the skin is several centimeters from the joint capsule and extracapsular extravasation of fluid is almost inevitable during surgery. Adduction and traction of the limb provide more space between the articular surfaces.

Normal anatomy

The lateral rim of the glenoid is visible for its full length. The humeral head and articular surface of the glenoid can be examined but the caudomedial surfaces are difficult to see without extra joint separation or a 70° arthroscope lens. The cranial rim of the glenoid is clearly visible and the glenoid notch lies medially and caudally to this. Synovial bands lie in the caudolateral and craniomedial joint capsule and there is a single synovial band medial to the glenoid notch. The glenohumeral ligament may be seen under the joint capsule just caudal to the glenoid notch.

Indications for arthroscopy of the shoulder, specific techniques and results

Osteochondrosis dissecans

Lesions may involve the glenoid cavity, the humeral head or both of these and vary from deep areas of severe erosion to articular fissures only detectable on probing (Fig. 11.27). Medial lesions can be difficult to operate and it is almost impossible to perform a complete debridement of large caudomedial lesions. A right-angled curette is useful. Because of the development of extracapsular fluid, surgery should be performed as efficiently as possible. Bertone et al[52] reported a return to full athletic function in five out of 11 horses with shoulder OCD following arthroscopic surgery and a similar success rate of 45% from 49 horses operated was reported by McIlwraith.[53]

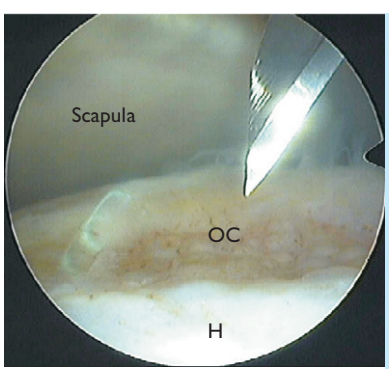

Fig. 11.27 Arthroscopic view of an OCD lesion (OC) on the lateral left humeral head (H). The scalpel is incising the instrument portal. The lateral margin of the scapula is in the top of the picture.

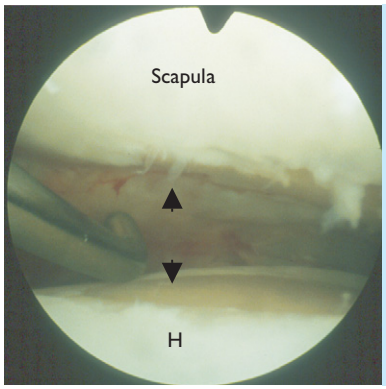

Fig. 11.28 Arthroscopic view of left midcranial shoulder showing full-thickness cartilage lesions (arrows) in the articular cartilage of the humeral head (H) and the scapula.

Articular cartilage lesions

Arthroscopy of the shoulder can be a worthwhile treatment for shoulder lameness, with or without abnormal radiographic signs, that has not responded to conservative treatment. Lesions include cartilage fissures, full-thickness cartilage defects, fibrillation of the cartilage surface, and humeral and glenoid subchondral cysts (Fig. 11.28). The lesions are debrided to healthy tissue and the joint lavaged. Twelve of 15 horses treated arthroscopically for these lesions returned to their previous use,[54] but in a series of 11 cases at the author's hospital only three out of eight followed up returned to full use. Scapulohumeral osteoarthritis in miniature horses has not responded well to arthroscopic treatment.[55]

The elbow

Positioning

Arthroscopy of the elbow is most easily performed with the horse in lateral recumbency. The affected leg is placed uppermost when operating from the lateral side and placed lowermost when operating the medial side. Flexion and extension of the joint should be possible during surgery.

Arthroscopic approach

For all approaches the joint can be distended with 100–200 mL of fluid using a 9 cm spinal needle inserted parallel to the joint surface caudal or cranial to the lateral collateral ligament.

Craniolateral approach The arthroscope portal is placed 2 cm proximal to the radial head and at the cranial border of the lateral condyle of the humerus.[56,57] The arthroscope

sleeve and conical obturator are passed to the medial side of the joint before inserting the arthroscope into the sleeve to commence the examination. The instrument portal is usually made slightly more cranial and medial to the arthroscope portal.

Proximocaudal approach When the joint is distended the synovial pouch in the olecranon fossa is palpable and a portal is created in the distal part of the outpouching.[56]

Caudomedial approach This is sited 2 cm distal to the radiohumeral articulation between the flexor carpi radialis and flexor carpi ulnaris muscles.[57] The instrument portal is placed caudal to and at the level of the joint articulation. The ulnar nerve lies caudal and the median nerve lies cranial to these muscles so these portals must be positioned accurately. This approach is a more hazardous access to the caudal joint than the proximocaudal approach but it allows a better view of the caudal, medial, humeral condyle.

Normal anatomy

Cranially both condyles of the humerus and the cranial proximal rim of the radius are visible. A synovial fossa usually divides the humeral condyles and there are synovial bands extending from the radius to the humerus in the midjoint region (Fig. 11.29). From the proximocaudal approach the lateral humeral condyle and part of the medial condyle can be seen together with the lateral aspect of the anconeus and caudal radius. The caudomedial approach provides a good view of the medial humeral condyle. The trochlear notch of the ulna can be followed caudad and more caudad still, in the caudoproximal sac, it is possible to see the medial epicondyle of the humerus, the deep digital flexor tendon and the cranial border of the ulna.[57]

Indications for arthroscopy of the elbow, specific techniques and results

In the author's hospital the main indication for arthroscopy of the elbow is sepsis. The craniolateral and proximocaudal portals can be used to obtain through-and-through lavage. Less commonly, the joint has been examined to evaluate chronic trauma, and potentially arthroscopy could be used for treatment of OCD lesions and subchondral bone cysts in the humerus if the lesions are accessible.

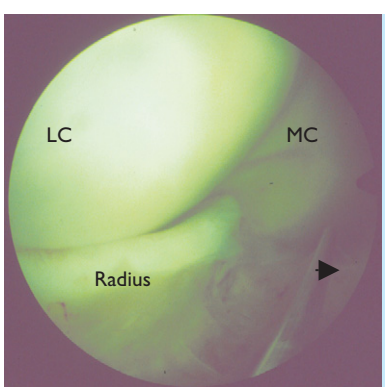

Fig. 11.29 Arthroscopic view of the right elbow from the craniolateral approach. The lateral (LC) and medial (MC) humeral condyles are visible and a probe is placed on the cranial synovial bands (arrow).

Endoscopy of the navicular bursa

Positioning

The horse is positioned in lateral recumbency with the affected leg uppermost and supported in the proximal metacarpal/metatarsal region. The foot is free so that it can be manipulated. A tourniquet is applied.

Endoscopic approach

The portal for the arthroscope is situated immediately proximal to the collateral cartilage on the abaxial border of the deep digital flexor tendon (DDFT) and axial to the palmar/plantar digital neurovascular bundle.[58,59] The author prefers to distend the bursa using a 9 cm spinal needle prior to introducing the arthroscope sleeve with the conical obturator. The sleeve and obturator are passed distally along the dorsal surface of the DDFT and into the bursa. If they are directed too dorsally or if the foot is overflexed the distal interphalangeal joint may be entered. When operating penetrating wounds the penetration track can usually be used as the instrument portal (Fig. 11.30). If not, an equivalent portal to the arthroscope portal on the contralateral side is used.

Normal anatomy

The impar ligament, most of the palmar/plantar surface of the navicular bone and opposing DDFT can be examined. Some flexion of the foot is required to examine the more distal part of the bursa. Abaxially the collateral ligament of the navicular bone is visible under the lining of the bursa. Because of the angle of entry into the bursa, the ipsilateral side is more difficult to examine.

Indications for endoscopy of the navicular bursa, specific techniques and results

Penetration of the navicular bursa

The penetration track can usually be used as the instrument portal for this procedure (Fig. 11.31). The lesions are debrided with hand tools and motorized equipment which is

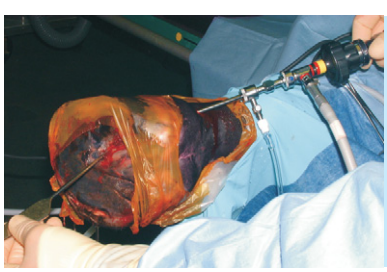

Fig. 11.30 Endoscopy of the navicular bursa using the penetration in the frog as the instrument portal.

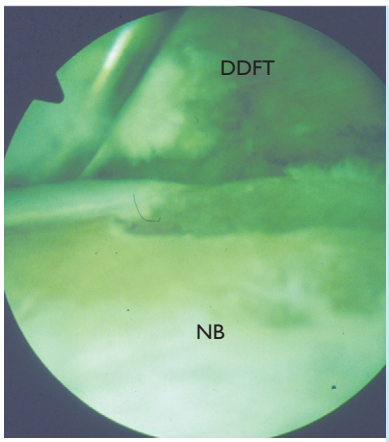

Fig. 11.31
Endoscopic view of the left fore navicular bursa which had sustained a penetrating wound 7 days previously. There is extensive cartilage loss on the navicular bone (NB) and a deep erosion in the bone. A probe has been passed into the bursa through the penetration in the deep digital flexor tendon (DDFT).

particularly useful for debriding the edges of the DDFT. In closed cases a contralateral portal to the arthroscope portal is used. An efficient lavage system is essential to achieve the pressure and quantity of fluid required for effective bursal lavage. Early reports on the use of bursoscopy for the treatment of navicular bursa penetrations show improved results compared with the open 'streetnail' procedure.[58,60]

Investigation for abnormalities in the navicular bursa

This has been postulated as a more sensitive method of identifying disease in the navicular bursa,[59] but at present there are no published reports on the value of the procedure.

Tenoscopy of the palmar/plantar digital sheath

Positioning

The digital sheath can be operated from its medial or its lateral side. The horse is placed in lateral recumbency with a tourniquet on the affected limb above the hock/carpus so that it does not obstruct the use of instruments parallel to the limb. The limb can be supported at the foot or above the fetlock.

Tenoscopic approach

Distension of the sheath can be effected with approximately 30 mL fluid either into the small outpouching of the digital sheath distal to the proximal digital annular ligament or into the sheath at the site of the arthroscope portal.[61] This lies between the proximal digital annular ligament and the annular ligament of the fetlock 1 cm distal to the base of the sesamoid bone and halfway between the ergot and the neurovascular bundle. An incision is made into the sheath and the arthroscope sleeve and a conical obturator passed obliquely into the sheath towards the contralateral side and lateral to the flexor tendons (Fig. 11.32). If the sleeve does not pass easily it should be redirected since the flexor tendons can readily be damaged by excessive pressure with the arthroscope sleeve and obturator. The digital sheath can also be entered proximally on the abaxial border of the superficial digital flexor tendon (SDFT).

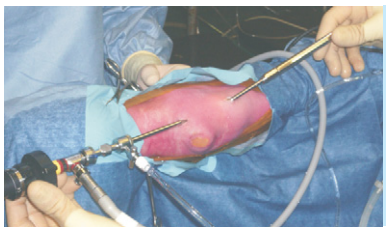

Fig. 11.32
Tenoscopic annular ligament desmotomy using a meniscal knife.

Normal anatomy

Examination of the proximal part of the sheath can be hampered by the bulb of the heel obstructing manipulation of the arthroscope, but this can be partially alleviated by flexing the foot. On insertion of the arthroscope into the sleeve, its position will be either between the DDFT and SDFT, superficial to the SDFT or dorsal to the DDFT. Superficially an important landmark is the manica flexoria coursing around the DDFT. The attachment of the SDFT to the synovial capsule prevents examination of the contralateral surface palmar/plantar to the SDFT. The best access to the proximal reflection of the sheath is obtained by passing the arthroscope between the DDFT and the SDFT or dorsal to the DDFT. Directing the arthroscope into the distal sheath reveals the division of the SDFT overlying the DDFT. The straight sesamoidean ligament can be identified beneath the synovial lining dorsal to the DDFT. The branches of the SDFT can be followed to their insertion either side of the DDFT. The distal attachments of the digital sheath to the DDFT are visible by passing the arthroscope more distally.

Indications for tenoscopy of the palmar/plantar digital sheath, specific techniques and results

Annular ligament desmitis

This procedure can be performed using a proprietary slotted cannula and angle tip knife system (Smith and Nephew Dyonics Inc, Andover, Massachusetts)[62] but the author prefers to use a meniscal knife to cut the annular ligament under tenoscopic control (see Fig. 11.32). The arthroscope is passed proximally and superficially so that the manica flexoria is identified, confirming that the arthroscope lies between the SDFT and the annular ligament. An instrument portal is made proximal to the annular ligament and ipsilateral to the arthroscope following careful positioning with a hypodermic needle so that the portal can be viewed tenoscopically. The meniscal knife is passed through the portal to

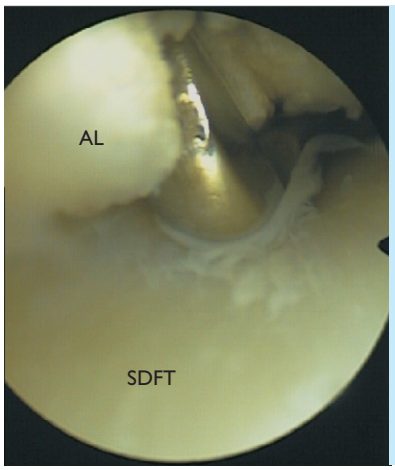

Fig. 11.33 Tenoscopic view of meniscal knife sectioning annular ligament (AL). SDFT, superficial digital flexor tendon.

the distal end of the annular ligament in order to cut the ligament by withdrawing the knife under tenoscopic control (Fig. 11.33). Confirmation that the distal end has been adequately released can be achieved by reversing the portals. Anecdotally there seems to be a better cosmetic result and very low incidence of incisional problems in comparison with open surgery. A comparison of the results of 56 desmotomies performed by open surgery and 45 desmotomies performed tenoscopically has been made at the author's hospital. Follow-up information was obtained on 32 and 28 horses respectively and of these, 63% treated by open surgery and 82% treated tenoscopically returned to work (Walmsley and Phillips, unpublished data, 2002).

Treatment of synovial masses, adhesions and manica flexoria injuries

These conditions often accompany annular ligament desmitis and have been named 'complex digital sheath tenosynovitis'[63] (Fig. 11.34). The lesions can be operated through the same portals used for annular ligament release. A motorized synovial resector may facilitate the resection of lesions and the debriding of the surface of the flexor tendons.[63] It is preferable to perform annular ligament desmotomy after debriding the lesions. Tenoscopic treatment for this condition has been reported for 25 horses, 75% of which returned to athletic use.[63]

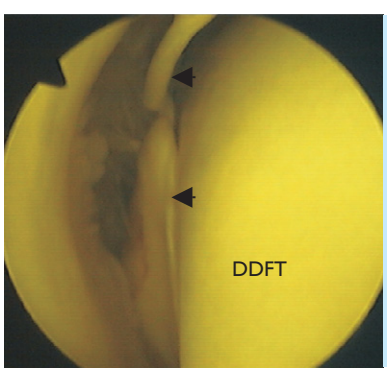

Fig. 11.34 Tenoscopic view of torn manica flexoria (arrows). DDFT, deep digital flexor tendon.

Tenoscopy of the carpal sheath

Positioning

For this procedure the horse can be positioned either in lateral recumbency, with the affected leg uppermost, or in dorsal recumbency. The carpus should be slightly flexed. A tourniquet is useful when using lateral recumbency.

Tenoscopic approach

The sheath is distended with 60–120 mL of fluid using an 18 gauge, 5 cm needle inserted at an angle of 60° distally between the ulnaris lateralis and lateral digital extensor tendons, 1.5 cm proximal to the distal radial physis.[64] The proximal arthroscope portal is sited 3 cm proximal to the radial physis and 2.5 cm caudal to the radius.[64] The distal portal can be made distal to the accessory carpal bone in the outpouching of the distended sheath.[65]

Normal anatomy[64–66]

Proximally the DDFT lies in the caudal aspect of the sheath and is joined by the radial head of the deep digital flexor muscle which courses from the cranioproximal aspect of the sheath. The accessory ligament (AL) of the SDFT, with its fibers running perpendicular to the radius, can be seen medial to the radius just caudal to the DDFT. The distal radial physis can be detected distal to the arthroscope portal and from here the DDFT can be followed medial to the accessory carpal bone to the distal end of the carpal sheath. The lateral border of the SDFT is found palmar to the DDFT and proximal to the antebrachiocarpal joint but the arthroscope cannot be passed medially between them because of an intertendinous ligament joining their medial borders.

Indications for tenoscopy of the carpal sheath, specific techniques and results

Osteochondroma of the distal radius

These lesions are viewed from a proximal portal. The osteochondroma can be separated with an osteotome and removed with large rongeurs.[67,68] The radius is then smoothed with a curette or burr and excessive fibrillation in the sheath removed with a synovial resector. Good results have been achieved in the few reported cases.[67,68]

Desmotomy of the accessory ligament of the superficial digital flexor tendon (AL-SDFT)

The use of this technique in experimental horses has been reported.[69] The arthroscopic portal lies 2–3 cm proximal to the distal radial physis in order to observe the proximal part of the

AL-SDFT underneath the radial head of the DDFT, and the limb is flexed to a right angle after distension of the sheath and insertion of the arthroscope. Using a meniscal knife, the ligament is sectioned under the DDFT as close as possible to its caudal edge where it joins the SDFT. The incision must be extended through the proximal end of the sheath in order to reach the proximal limit of the ligament and care must be taken to avoid the perforating vessel. Maintenance of sheath distension is important.

Other indications

These include tenosynovitis of the carpal sheath and any inflammatory condition of the sheath.

Tenoscopy of the tarsal sheath

Positioning

The horse can be placed in dorsal or lateral recumbency unless access to the lateral side of the proximal pouch is required.

Tenoscopic approach

Best access into both the proximal and the distal tarsal sheath is obtained through an arthroscopic portal sited on the medial aspect of sustentaculum tali (ST).[70] The incision is made through the retinaculum and the arthroscope sleeve and obturator are passed into the sheath proximally or laterally from this site since it is at the point where the DDFT changes direction within the sheath.[70] Portals into the proximal or distal pouches can be made at their most prominent points.

Normal anatomy[70]

The lateral deep digital flexor tendon (LDDFT) occupies the full length of the sheath. It is attached to the sheath by a mesotendon on its medial aspect. The proximal pouch is spacious. In the tarsal groove there is much less room but the arthroscope can still be directed either side of the LDDFT. The fibrocartilage covering the ST can be seen medial and dorsal to the LDDFT. In the distal pouch there is a clear demarcation between the fibrocartilaginous groove of the tarsal canal and the insertion of the accessory ligament of the DDFT. Dorsomedially there is a synovial fold attached to the LDDFT.

Indications for tenoscopy of the tarsal sheath, specific techniques and results

Sustentaculum tali injuries

Fractures or bony proliferations or other lesions of the medial border of the ST can be treated tenoscopically[70] (Fig. 11.35). Lesions extending beyond the medial plantar edge may require open surgery. In order to gain access to the lesion, the arthroscope portal described above can be used as an instrument portal and the arthroscope placed medially in the proximal pouch.

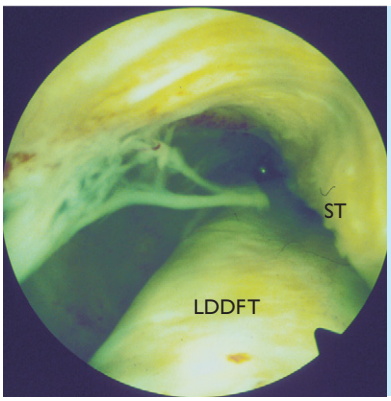

Fig. 11.35 Tenoscopic view of an infected right tarsal sheath from a proximal portal. LDDFT, lateral deep digital flexor tendon; ST, sustentaculum tali.

Chronic traumatic tenosynovitis, adhesions, nodular hypertrophic villi

Any chronic condition of the tarsal sheath that has not responded to conservative treatment may benefit from tenoscopy. Portal positions will depend on the lesions and radiographic and ultrasonographic preoperative assessment can be useful when determining the best portal sites.

Endoscopy of the intertubercular bursa of the humerus

Positioning

The horse should be placed in lateral recumbency with the affected leg uppermost. It is useful to be able to extend the limb cranially and abduct the limb during endoscopy.

Endoscopic approach

The bursa is distended with 100 mL of fluid through a 9 cm, 18 gauge spinal needle. The distal arthroscope portal is sited 2–3 cm proximal to the deltoid tuberosity on the dorsolateral aspect of the humerus.[71] The arthroscope sleeve and obturator are advanced proximomedially through the brachiocephalicus and caudal to the biceps brachii muscles into the bursa on the dorsal surface of the humerus. The proximal portal can be sited endoscopically using needle placement to position the portal, which is 2–3 cm proximal to the greater humeral tubercle and lateral to the biceps brachii tendon.[71] Either portal can be used as an instrument portal.

Normal anatomy

From the distal portal the distal medial and lateral aspects of the humeral tubercles and the intertubercular grooves can be

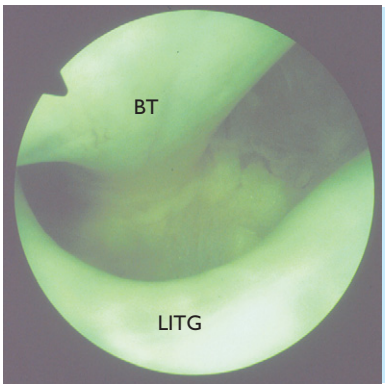

Fig. 11.36 Endoscopic view of left bicipital bursa from the distal portal. The lateral lobe of the tendon of the biceps brachii (BT) lies above the lateral intertubercular groove (LITG).

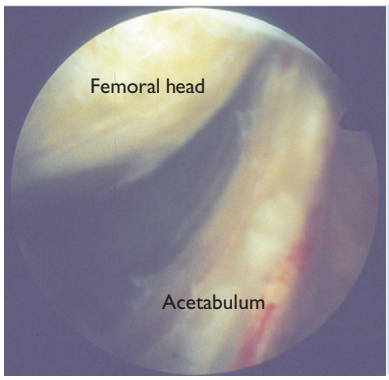

Fig. 11.37 Arthroscopic view of right coxofemoral joint. There is extensive cartilage loss on the femoral head and acetabulum.

seen caudal to the biceps brachii. The two diverging lobes of the biceps brachii lie in the intertubercular grooves. The proximal recess is viewed by passing the arthroscope proximally along the lateral aspect of the biceps brachii (Fig. 11.36). The proximal recess can also be examined from the proximal portal. The medial intertubercular groove is inaccessible to instruments from these portals.

Indications for endoscopy of the intertubercular bursa, specific techniques and results

Traumatic bursitis

In the author's experience sepsis of the bursa is the most frequent indication for endoscopy and this has also been reported,[72] but chronic aseptic bursitis is an occasional indication for endoscopy. Lesions involving the medial aspect of the bursa are difficult to access and may not be treatable endoscopically.

Joints seldom approached arthroscopically

Proximal interphalangeal joint

Arthroscopy of this joint is occasionally indicated for removal of bone fragments[73] or treatment of sepsis. There is very little room to maneuver in this joint. The horse can be placed in dorsal or lateral recumbency. Following distension of the joint, the arthroscopic portal is made medial or lateral to the extensor tendon at the distal edge of the distended joint capsule. The position of the instrument portal can be decided by needle placement over the lesion.

Coxofemoral joint

Arthroscopy can be useful diagnostically and therapeutically in horses with traumatic injuries, osteochondrosis and sepsis in the coxofemoral joint[74,75] (Fig. 11.37). For horses whose bodyweight is greater than 300 kg all instrumentation must be 25 cm long.[74]

With the horse in lateral recumbency the joint is distended and the arthroscope portal made over the notch between the cranial and caudal prominences of the greater trochanter of the femur. The arthroscope sleeve with its obturator is advanced along the femoral neck into the joint. The margins of the acetabulum and femurs can be examined but axial traction on the limb is necessary to view the central part of the joint and the round ligament. The medial joint is difficult to examine, particularly in adults. A 70° arthroscope improves the examination of the caudomedial and craniomedial aspects of the femoral head.[74] The instrument portal is made 4–6 cm cranial to the arthroscope portal and checked by needle placement.

Temporomandibular joint

This joint is divided into a smaller ventral compartment (discomandibular joint) and a larger dorsal compartment (discotemporal joint) by an intra-articular disc. Disorders of the joint include degenerative joint disease, tearing of the articular disc and sepsis.[76] Ultrasonography can be used to identify the joint space between the lateral eminences of the temporal bone and the mandibular condyle,[76] as well as identifying the overlying parotid salivary gland and facial vessels. When the joint has been distended with 5 mL of fluid, the discotemporal joint is entered caudodorsally at the center of the outpouching.[76,77] A standard 4 mm arthroscope can be used but there is very little room to maneuver it. The discomandibular joint is a smaller joint and can only be entered rostrolaterally.[76] The facial vessels lie close to the site of access. Only the lateral part of either joint can be examined.

References

1. McIlwraith CW. Diagnostic and surgical arthroscopy in the horse, 2nd edn. Philadelphia, PA: Lea and Febiger; 1990:5–19.

2. Frisbie DD, Trotter GW, Powers BE, et al. Arthroscopic subchondral bone plate microfracture technique augments healing of large osteochondral defects in the radial carpal bone and medial femoral condyle of horses. Vet Surg 1999; 28:242–255.
3. Martin GS, McIlwraith CW. Arthroscopic anatomy of the intercarpal and radiocarpal joints of the horse. Equine Vet J 1985; 17(5):373–376.
4. Whitton RC, McCarthy PH, Rose RJ. The intercarpal ligaments of the equine midcarpal joint, Part 1: The anatomy of the palmar and dorsomedial intercarpal ligaments of the midcarpal joint. Vet Surg 1997; 26:359–366.
5. McIlwraith CW, Yovich JV, Martin GS. Arthroscopic surgery for the treatment of osteochondral chip fractures in the equine carpus. J Am Vet Med Assoc 1987; 191(5):531–540.
6. Lucas JM, Ross MW, Richardson DW. Post operative performance of racing Standardbreds treated arthroscopically for carpal chip fractures: 176 cases (1986–1993). Equine Vet J 1999; 31(1):48–52.
7. Schneider RK, Bramlage LR, Gabel AA, et al. Incidence, location and classification of 371 third carpal bone fractures in 313 horses. Equine Vet J 1988; 6(suppl):33–42.
8. Richardson DW. Technique for arthroscopic repair of third carpal bone slab fractures in horses. J Am Vet Med Assoc 1986; 188(3):288–291.
9. Stephens PR, Richardson DW, Spencer PA. Slab fractures of the third carpal bone in Standardbreds and Thoroughbreds: 155 cases (1977–1984). J Am Vet Med Assoc 1988; 193(3):353–358.
10. Moore RM, Schneider RK. Arthroscopic findings in the carpal joints of lame horses without radiographically visible abnormalities: 41 cases (1986–1991). J Am Vet Med Assoc 1995; 206(11):1741–1746.
11. McIlwraith CW. Tearing of the medial palmar intercarpal ligament in the equine midcarpal joint. Equine Vet J 1992; 24(5):367–371.
12. Colón JL, Bramlage LR, Hance SR, et al. Qualitative and quantitative documentation of the racing performance of 471 Thoroughbred racehorses after arthroscopic removal of dorsoproximal first phalanx osteochondral fractures (1986–1995). Equine Vet J 2000; 32(6):475–481.
13. Kawcak CE, McIlwraith CW. Proximodorsal first phalanx osteochondral chip fragmentation in 336 horses. Equine Vet J 1994; 26(5):392–396.
14. Dabareiner RM, White NA, Sullins KE. Metacarpophalangeal joint synovial pad fibrotic proliferation in 63 horses. Vet Surg 1996; 25:199–206.
15. Foerner JJ, Barclay WP, Phillips TN, et al. Osteochondral fragments of the palmar/plantar aspect of the fetlock joint. Proceedings of the 33rd Annual Meeting of the American Association of Equine Practitioners, 1987; 739–744.
16. Fortier LA, Foerner JJ, Nixon AJ. Arthroscopic removal of axial osteochondral fragments of the plantar/palmar proximal aspect of the proximal phalanx in horses: 119 cases (1988–1992). J Am Vet Med Assoc 1995; 206(1):71–74.
17. Southwood LL, McIlwraith CW. Arthroscopic removal of fracture fragments involving a portion of the base of the proximal sesamoid bone in horses: 26 cases (1984–1997). J Am Vet Med Assoc 2000; 217(2):236–240.
18. Spurlock GH, Gabel AA. Apical fractures of the proximal sesamoid bones in 109 Standardbred horses. J Am Vet Med Assoc 1983; 183:76–79.
19. Lepage OM, Marcoux M. Type I sesamoid fracture (apical) treated by arthrotomy or arthroscopy. Report of 17 surgical cases over a 2-year period. Fifth Annual Meeting of European College of Veterinary Surgeons, 1996; 110–111.
20. Bouré L, Marcoux M, Laverty S, et al. Use of electrocautery probes in arthroscopic removal of apical sesamoid fracture fragments in 18 Standardbred horses. Vet Surg 1999; 28:226–232.
21. Woodie JB, Ruggles AJ, Bertone AL, et al. Apical fracture of the proximal sesamoid bone in Standardbred horses: 43 cases (1990–1996). J Am Vet Med Assoc 1999; 214(11):1653–1656.
22. Southwood LL, Trotter GW, McIlwraith CW. Arthroscopic removal of abaxial fracture fragments of the proximal sesamoid bones in horses: 47 cases (1989–1997). J Am Vet Med Assoc 1998; 213(7):1016–1021.
23. Zamos DT, Honnas CM, Hoffman AG. Arthroscopic approach and intra-articular anatomy of the plantar pouch of the equine tarsocrural joint. Vet Surg 1994; 23:161–166.
24. McIlwraith CW, Foerner JJ, Davis DM. Osteochondritis dissecans of the tarsocrural joint: results of treatment with arthroscopic surgery. Equine Vet J 1991; 23(3):155–162.
25. Foland JW, McIlwraith CW, Trotter GW. Arthroscopic surgery for osteochondritis dissecans of the femoropatellar joint of the horse. Equine Vet J 1992; 24:419–423.
26. Dyson SJ, Wright I, Kold S, Vatistas N. Clinical and radiographic features, treatment and outcome in 15 horses with fracture of the medial aspect of the patella. Equine Vet J 1992; 24:264–268.
27. Dyson SJ. Stifle trauma in the event horse. Equine Vet Educ 1994; 6:234–240.
28. Montesso F, Wright IM. Removal of chip fractures of the femoral trochlear ridges of three horses. Vet Rec 1995; 137:94–96.
29. McIlwraith CW. Osteochondral fragmentation of the distal aspect of the patella in horses. Equine Vet J 1990; 22:157–163.
30. Trumble TN, Stick JA, Arnoczy SP, Rosenstein D. Consideration of anatomic and radiographic features of the caudal pouches of the femorotibial joints of horses for the purpose of arthroscopy. Am J Vet Res 1994; 55:1682–1689.
31. Moustafa MAI, Boero MJ, Baker GJ. Arthroscopic examination of the femorotibial joints of horses. Vet Surg 1987; 16(5):352–357.
32. Lewis RL. A retrospective study of diagnostic and surgical arthroscopy of the equine femorotibial joint. Proc Am Assoc Equine Pract 1987; 23:887–893.
33. Hance R, Schneider RK, Embertson RM, et al. Lesions of the caudal aspect of the femoral condyles in foals: 20 cases (1980–1990). J Am Vet Med Assoc 1993; 202:637–646.
34. Stick JA, Borg LA, Nickels FA, Peloso JG, Perau DL. Arthroscopic removal of an osteochondral fragment from the caudal pouch of the lateral femorotibial joint in a colt. J Am Vet Med Assoc 1992; 200(11):1695–1697.
35. Walmsley JP. Outcome of arthroscopic surgery in stifle lameness. Fortieth Annual Congress, British Equine Veterinary Association, Harrogate, September 12–15 2001:113.
36. Schneider RK, Jenson P, Moore RM. Evaluation of cartilage lesions on the medial femoral condyle as a cause of lameness in horses: 11 cases 1988–1994. J Am Vet Med Assoc 1997; 210:1649–1652.
37. Walmsley JP, Phillips TJ, Townsend HGG. Meniscal tears in horses: an evaluation of clinical signs and arthroscopic treatment of 80 cases. Equine Vet J 2003;35:402–406.
38. Howard RD, McIlwraith CW, Trotter GW. Arthroscopic surgery for subchondral cystic lesions of the medial femoral condyle in horses; 41 cases (1988–1991). J Am Vet Med Assoc 1995; 206:842–850.

39. Bramlage LR. Osteochondrosis related bone cysts. Proceedings of the 36th Annual Meeting of the American Association of Equine Practitioners, 1993; 83–85.
40. Greet T. The management of subchondral cysts associated with the medial femoral condyle by arthroscopic surgery in horses. Proceedings of the 7th Annual Scientific Meeting, European College of Veterinary Surgeons, 1998; 191–192.
41. von Rechenberg B, McIlwraith CW, Luetenegger C, et al. Fibrous tissue of subchondral bone cyst lesions (SCL) in horses produce inflammatory mediators and neutral metalloproteinases and cause bone resorption in vitro. Vet Surg 1998; 27: 520.
42. Jackson WA, Stick JA, Arnoczky SP, Nickels FA. The effect of compacted cancellous bone grafting on the healing of subchondral bone defects of the medial femoral condyle in horses. Vet Surg 2000; 29:8–16.
43. Textor JA, Nixon AJ, Lumsden J, Ducharme NG. Subchondral cystic lesions of the proximal extremity of the tibia in horses: 12 cases (1983–2000). J Am Vet Med Assoc 2001; 218:408–413.
44. Wisner AB. Surgical removal of an avulsion fracture of the stifle joint. Equine Vet Med Surg 1979; 3:337–339.
45. Walmsley JP. Fracture of the intercondylar eminence of the tibia treated by arthroscopic internal fixation. Equine Vet J 1997; 29:148–150.
46. Boening KJ, von Saldern F, Leendertse IP, et al. Diagnostische und operative Arthroskopie am Hufgelenk des. Pferdeheilkunde 1988; 4(4):155–160.
47. Vacek JR, Welch RD, Honnas CM. Arthroscopic approach and intra-articular anatomy of the palmaroproximal or plantaroproximal aspect of distal interphalangeal joints. Vet Surg 1992; 21(4):257–260.
48. Vail TB, McIlwraith CW. Arthroscopic removal of an osteochondral fragment from the middle phalanx of a horse. Vet Surg 1992; 21(4):269–272.
49. Walmsley JP. The coffin and pastern joints. Proceedings of the 21st Bain-Fallon Memorial Lectures, Perth, 1999; 124–129.
50. Bertone AL, McIlwraith CW. Arthroscopic surgical approaches and intraarticular anatomy of the equine shoulder joint. Vet Surg 1987; 16(4):312–317.
51. Nixon AJ. Diagnostic and surgical arthroscopy of the equine shoulder joint. Vet Surg 1987; 16(1):44–52.
52. Bertone AL, McIlwraith CW, Powers BE, et al. Arthroscopic surgery for the treatment of osteochondrosis in the equine shoulder joint. Vet Surg 1987; 16(4):303–311.
53. McIlwraith CW. Clinical aspects of osteochondrosis dissecans. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadephia, PA: Saunders; 380–382.
54. Doyle PS, White NA. Diagnostic findings and prognosis following arthroscopic treatment of subtle osteochondral lesions in the shoulder joint of horses: 15 cases (1996–1999). J Am Vet Med Assoc 2000; 217(12):1878–1882.
55. Clegg PD, Dyson SJ, Summerhays GES, et al. Scapulohumeral osteoarthritis in 20 Shetland ponies, miniature horses and falabella ponies. Vet Rec 2001; 148:175–179.
56. McIlwraith CW. Other uses of arthroscopy in the horse. In: McIlwraith CW. Diagnostic and surgical arthroscopy in the horse, 2nd edn. Philadelphia: Lea and Febiger; 1990; 220–221.
57. Nixon AJ. Arthroscopic approaches and intraarticular anatomy of the equine elbow. Vet Surg 1990; 19(2):93–101.
58. Wright IM, Phillips TJ, Walmsley JP. Endoscopy of the navicular bursa: a new technique for the treatment of contaminated and septic bursae. Equine Vet J 1999; 31(1):5–11.
59. Cruz AM, Pharr JW, Bailey JV, et al. Podotrochlear bursa endoscopy in the horse: a cadaver study. Vet Surg 2001; 30:539–545.
60. Walmsley JP. Penetrating wounds to the sole, navicular bursa and DIP joint. Proceedings of the 21st Bain-Fallon Memorial Lectures, Perth, 1999; 110–123.
61. Nixon AJ. Endoscopy of the digital flexor tendon sheath in horses. Vet Surg 1990; 19(4):266–271.
62. Nixon AJ, Sams AE, Ducharme NG. Endoscopically assisted annular ligament release in horses. Vet Surg 1993; 22(6):501–507.
63. Fortier LA, Nixon AJ, Ducharme NG, et al. Tenoscopic examination and proximal annular ligament desmotomy for treatment of equine 'complex' digital sheath tenosynovitis. Vet Surg 1999; 28:429–435.
64. Southwood LL, Stashak TS, Kainer RA. Tenoscopic anatomy of the equine carpal flexor synovial sheath. Vet Surg 1998; 27:150–157.
65. Cauvin ERJ, Munroe GA, Boyd JS. Endoscopic examination of the carpal flexor tendon sheath in horses. Equine Vet J 1997; 29(6):459–466.
66. Cauvin ERJ, Munroe GA, Boswell J, et al. Gross and ultrasonographic anatomy of the carpal flexor tendon sheath in horses. Vet Rec 1997; 141:489–495.
67. Ter Braake F, Rijkenhuizen ABM. Endoscopic removal of osteochondroma at the caudodistal aspect of the radius; an evaluation in 4 cases. Equine Vet Educ 2001; 13(2):90–93.
68. Squire RRE, Adams SB, Widmer WR, Coatney RW, Habig C. Arthroscopic removal of a palmar radial osteochondroma causing carpal canal syndrome in a horse. J Am Vet Med Assoc 1992; 201:1166–1168.
69. Southwood LL, Stashak TS, Kainer RA, et al. Desmotomy of the accessory ligament of the superficial digital flexor tendon in the horse with use of a tenoscopic approach to the carpal sheath. Vet Surg 1999; 28:99–105.
70. Cauvin ERJ, Tapprest J, Munroe GA, et al. Endoscopic examination of the tarsal sheath of the lateral digital flexor tendon in horses. Equine Vet J 1999; 31(3):219–227.
71. Adams MN, Turner TA. Endoscopy of the intertubercular bursa in horses. J Am Vet Med Assoc 1999; 214(2):1584–1585.
72. Tudor RA, Bowman KF, Redding WR, et al. Endoscopic treatment of suspected infectious intertubercular bursitis in a horse. J Am Vet Med Assoc 1998; 213(11):221–225.
73. Schneider RK, Ragle CA, Carter BG, et al. Arthroscopic removal of osteochondral fragments from the proximal interphalangeal joint of the pelvic limbs in three horses. J Am Vet Med Assoc 1994; 205(1):79–82.
74. Nixon AJ. Diagnostic and operative arthroscopy of the coxofemoral joint in horses. Vet Surg 1994; 23:377–385.
75. Honnas CM, Zamos DT, Ford TS. Arthroscopy of the coxofemoral joint of foals. Vet Surg 1993; 22(2):115–121.
76. Weller R, Maierl J, Bowen IM, May SA, Liebech H-G. The arthroscopic approach and intra-articular anatomy of the equine temporomandibular joint. Equine Vet J 2002; 34(4):421–424.
77. May KA, Moll HD, Howard RD, et al. Arthroscopic anatomy of the equine temporomandibular joint. Vet Surg 2001; 30:564–571.

CHAPTER 12

Biomechanics of locomotion in the athletic horse

Eric Barrey

Introduction

The horse is a superathlete which often suffers from injuries of its locomotor apparatus because of human management errors (nutrition, training, shoeing, breeding), bad environmental conditions (tracks, weather) and/or an unfavorable constitution (limb conformation, genetics). In stables specializing in gallop racing, about 53–68% of the wastage in race horses is due to lamenesses.[1,2] This economical disaster justifies the great effort now being put into equine locomotion research, including clinical applications and techniques for preventing lameness. Currently, economic constraints also favor the development of early performance evaluation in order to improve the training and selection of young horses.

This chapter presents a review on equine locomotion and the applications of gait analysis. Current knowledge concerning the equine locomotion variables in various sporting disciplines and the influence of training are discussed. Finally, a survey of the practical applications of equine gait analysis will be presented.

Locomotion analysis

The body of the horse is composed of a set of rigid segments articulated one to another. Consequently, the body of the horse follows exactly the same mechanical laws as a series of

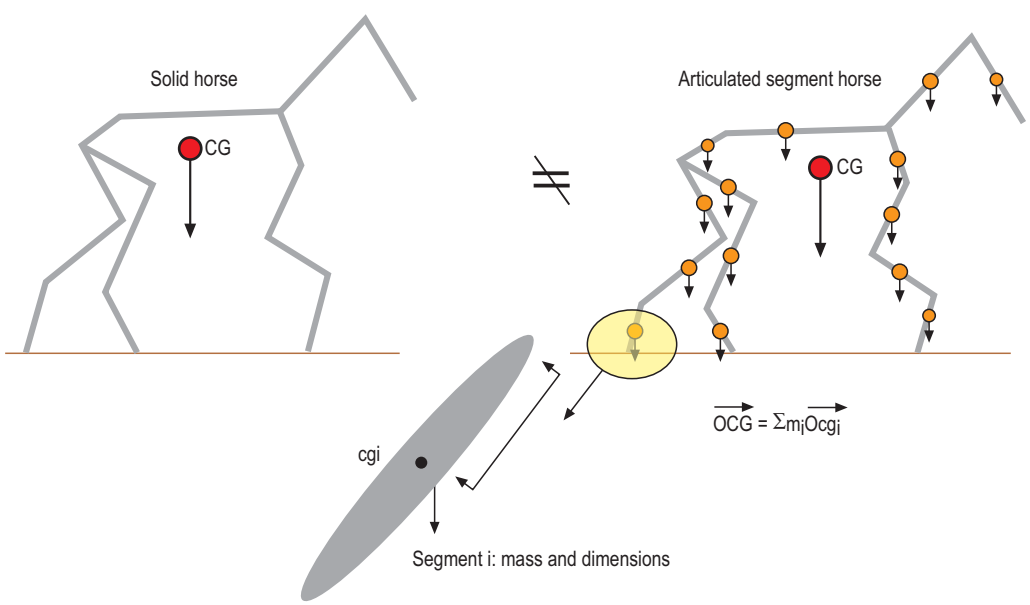

Fig. 12.1
A horse mechanical model composed of articulated body segments. It is very different from a mechanical model with only one solid segment. For each segment (i) of the body, the center of gravity (cg_i) and the moment of inertia can be calculated. The location of the general center of gravity (CG) of the horse can be calculated by considering the mass and the co-ordinates of each center of gravity segment. Reproduced from Barrey E. Methods, applications and limitations of gait analysis in horses. The Veterinary Journal 1999; 157:7–22.

Box 12.1 Advantages and limits of the methods

Kinetics	Kinematics
Explain cause of motion	Describe the motion
Forces, kinetic moments, accelerations, work, energy	Trajectories, angles, velocities, accelerations
Transducers → signals	Images → co-ordinates
Rapid analysis	Time consuming
Synthetic information	Details of the movements
Physical sensitivity	Visual

inanimate objects (Fig. 12.1). However, these laws need to be applied carefully because the mechanical equations which determine the motions of a set of articulated body segments are much more complicated than those that determine the motion of a single inanimate object like a bullet. There are two complementary methods for studying the body in motion: kinetics and kinematics (Box 12.1).

- *Kinetics or dynamics* studies the cause of the motion, which can be explained by the force applied to the body, its mass distribution and its dimensions. Kinetics is concerned with forces, energy and work which are also related to kinematic variables such as acceleration and velocity. Acceleration can be directly measured by specific sensors. However, acceleration is defined as an instantaneous change of velocity (i.e. the derivative of the velocity against time). Consequently, it can be deduced from velocity data obtained in kinematics by displacement measurements.
- *Kinematics* studies the changes in the position of the body segments in space during a specified time. The motions are described quantitatively by linear and angular variables which relate time, displacement, velocity and acceleration. No reference is made in kinematics to the cause of motion. The kinematic approach is more commonly employed, probably because it is easier to measure and visualize some displacements or velocities than to measure and imagine some forces, moments or accelerations applied to the body.

Kinematic analysis

The use of chronophotography was first developed by Muybridge and Marey for animal locomotion analysis. Currently new technology, using high-speed cameras (16 mm, 500 images/s), is used for example to film the locomotion of Standardbred horses from a camera car under track conditions.[3] Markers are used which are composed of small white spots or half spheres glued onto the skin over standard anatomical locations (Fig. 12.2A).[4,5] They are intended to indicate the approximate instantaneous center of rotation of the joint.[6,7] However, the skin displacements over the skeleton during locomotion generate some artifacts, especially in the proximal joints.[8,9]

The processing of the film for collecting the joint marker co-ordinates is undertaken using a computer. This is a relatively time-consuming task but many time and linear characteristics of the strides can be obtained for describing individual gait variations. With the improvement of the video camera sensors (CCD) many professional high-speed video cameras (100–2000 images/s) and home video cameras (PAL or NTSC Standard: 25–30 images/s or 50–60 frames/s) can be employed for locomotion analysis. The video signal can be treated by a video interface in order to digitize the images which are then analyzed by the appropriate software to collect semiautomatically or automatically the marker co-ordinates in space and time.[10] A more sophisticated motion analysis system uses active markers which consist of photodiodes (modified Cartesian Optoelectronic Dynamic Anthropometer; CODA-3). The advantage of this system is its good resolution (0.2–2.6 mm) in three dimensions, high recording frequency (300 Hz) and the automatic tracking possibilities of the active markers.[11] The main disadvantage is that the subject needs to be equipped with many photodiodes connected to wires.

Most equine locomotion studies show two-dimensional motion analysis but some systems with four or more video cameras make it possible to reconstruct the motion in three dimensions and to analyze the limb motions of both sides.[12,13] One limit of these sophisticated gait analysis systems is the restricted field of view. This is only about 5 meters which corresponds to several walking strides or one trotting stride. In order to analyze sporting exercise in a wider field (up to 30 m), a camera panning technique has been developed and used to study gait parameters in dressage and jumping horses.[10,14,15] This technique can be used for the kinematic analysis of athletic locomotion under real exercise conditions (Fig. 12.2B).

After filming, the operator needs to track manually, semiautomatically or automatically, the co-ordinates of the markers on each image of the film. In most of the systems, the tracking phase is a long task because there are many images to analyze and as the markers are not always easy to detect automatically, manual supervision is required. Nowadays, the use of specific algorithms such as direct linear transform (DLT) is an efficent way to automatically determine the trajectory of the markers. This makes it possible to use these systems for practical applications such as lameness quantification or athletic gait evaluation.

After collecting the co-ordinates of the markers, the linear and angular velocities can be obtained by computing the first derivative of the trajectories and angles with respect to time. If the filming image frequency is high, the second-order derivative of a trajectory or angular variation with respect to time, using appropriate smoothing and filtering techniques, provides linear and angular acceleration data. The advantage of kinematics methods is that you can obtain all the kinematic parameters (displacement, velocity, linear acceleration, angle of rotation, angular velocity and angular acceleration) of the identified segments. If the center of gravity and the moment of inertia of each segment can be determined by measuring their mass distribution and dimensions, it is possible to calculate the kinetic parameters (forces and kinetic moment), which determine the motion of each segment, from the kinematic data. Finally, the kinetic energy can be estimated for each segment and for the whole body in motion. Several methods have been described to estimate the location of center of gravity and the moment of inertia of each segment (Fig. 12.2C).[15–17]

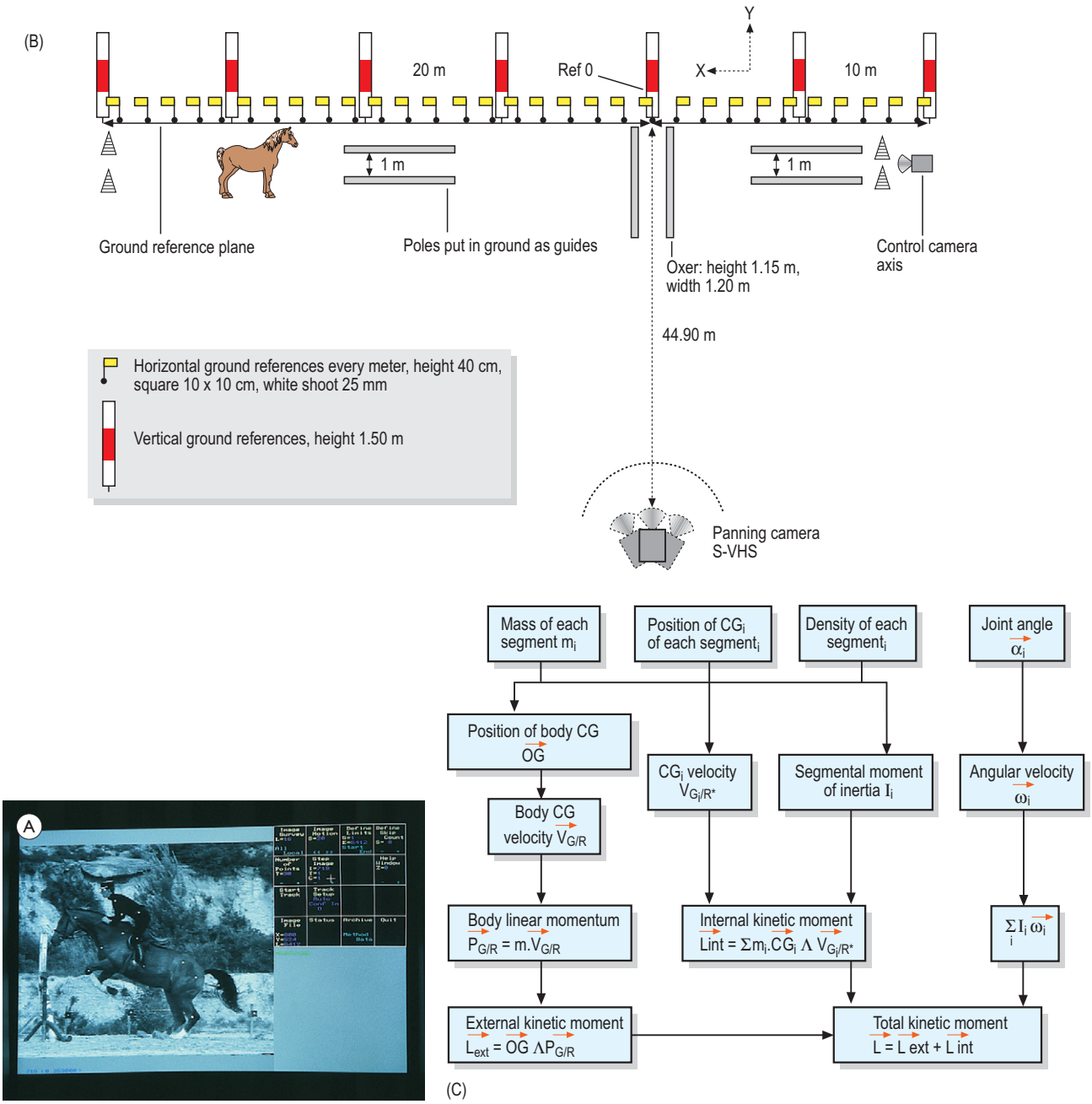

Fig. 12.2
Example of two-dimensional kinematic study of jumping horse. (A) One image extracted from the video film shows the horse and rider equipped with white anatomic markers. These markers are used to identify the location of each joint on each image. (B) Film recording procedure for a panning camera system to film and analyze the motion of a large field (30 m) as in jumping exercise. A set of ground reference planes was placed parallel and behind the horse trajectory. (C) Data analysis procedure to compute the center of gravity (CG) and total kinetic moment (L). After tracking the markers of each joint, the co-ordinates data were used to calculate the center of gravity (CG_i) of each segment, the velocity (Vg_i), the moment of inertia (I_i), the angles (α_i), the angular velocity (ω_i) and the external and internal kinetic moment. (Fig. 12.2B, C reproduced from Galloux and Barry[15] with permission.)

Kinetic analysis

Another approach to the study of the biomechanics of locomotion is to measure either the external forces applied to the body or the accelerations of the center of gravity of the body segments. Marey (1873) was the first author to use a pressure sensor attached to the ground surface of a horse shoe and accelerometers attached to the limbs to measure the hoof–ground contact durations at the various gaits.[18] All the sensors measured forces using pneumatic principles. The variations in pressure generated by the various transducers were recorded by tracing curves with a portable pneumotachograph.

Ground reaction forces

Modern sensor technology is much impoved and is capable of making accurate measurements over a large range of conditions. However, the measurement principles have remained identical. The external forces are measured using electronic force sensors which record the ground reaction forces when the hooves are in contact with the ground. The sensors can be installed either on the ground in a force plate device or in a shoe attached to the hoof. The force plates can provide the force amplitude and orientation (vector co-ordinates in three dimensions; Fig. 12.3), the co-ordinates of the point of application of the force and the moment value at this point.[19–23]

The accuracy of this type of device is usually good but the sensitive surface is rather small (about 0.5 m^2) and a visual control of the hoof trajectory is required.

In human biomechanics, the treadmill has been used to measure vertical ground reaction forces in standardized exercise conditions. In equine biomechanics, vertical ground reaction forces are measured for all four limbs simultaneously with the treadmill integrated force measuring system.[24] It is used for lameness evaluation in standardized conditions of speed, hardness of the ground and environment.[25]

In order to measure the ground reaction forces during various exercises, several authors have developed hoof force shoes including one or several force sensors (Fig. 12.4).[18,26–30]

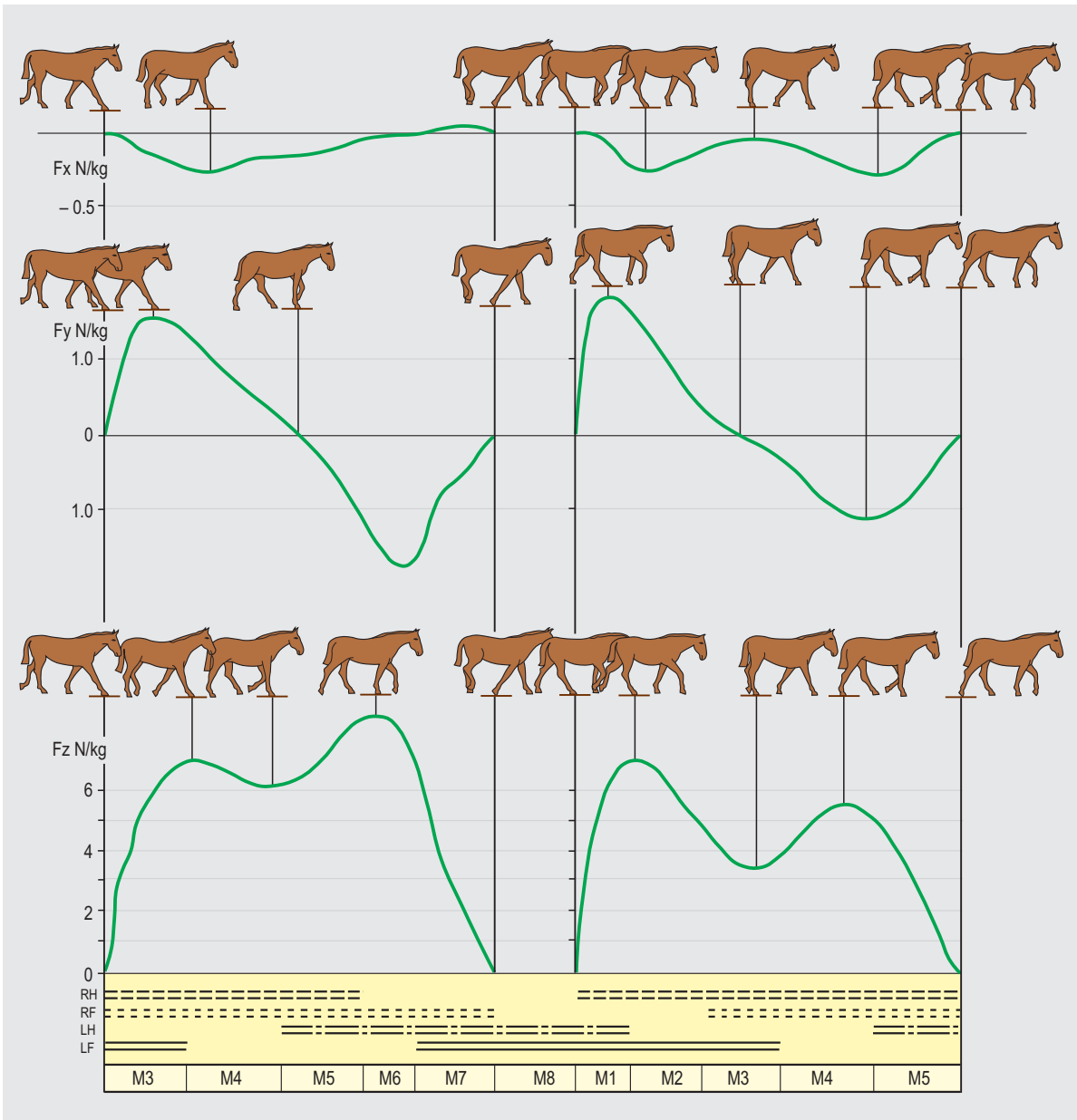

Fig. 12.3
Limb positioning at the time of characteristic ground reaction force amplitudes of the right fore and hindlimbs of a clinically sound Dutch Warmblood horse at normal walk. The phases of the concurrently loaded limbs are presented in a bar diagram. (Reproduced from Merkens[23] with permission.)

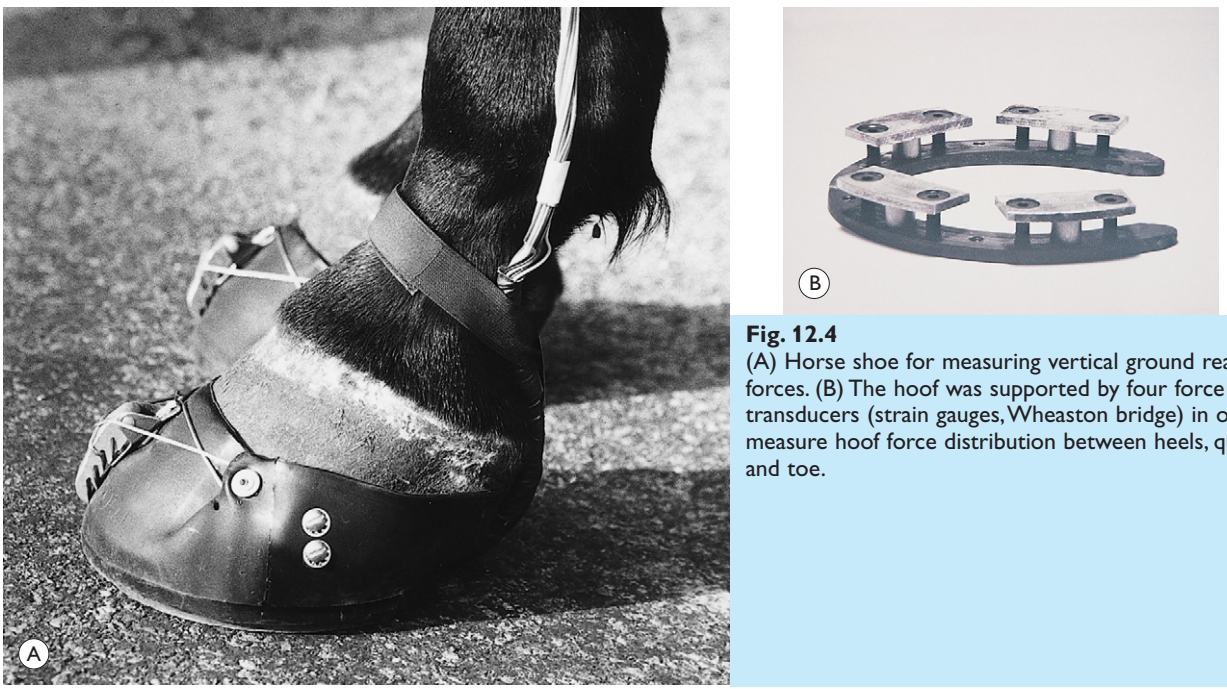

Fig. 12.4
(A) Horse shoe for measuring vertical ground reaction forces. (B) The hoof was supported by four force transducers (strain gauges, Wheaston bridge) in order to measure hoof force distribution between heels, quarters and toe.

Depending on their design, these devices can give between one and three components of the ground reaction forces and the point of application. They are generally less accurate than the force plate and their main disadvantage is the additional weight and thickness of the special shoe. Recently, another indirect ambulatory technique of ground reaction force evaluation was proposed using strain gauges glued onto the hoof wall. After the training of the appropriate artificial neural networks, the ground reaction forces can be estimated from the hoof wall deformations.[31]

Acceleration analysis

Acceleration analysis is a kinetic method which measures instantaneous change of velocity which is produced by applying a force on a solid during the same duration. Acceleration measurements are performed using small sensors (accelerometers) which should be firmly attached to the body segment under study. These sensors are made of a small suspended mass giving a signal which is proportional to the acceleration. A sudden change in velocity can give a high acceleration or deceleration (decrease of acceleration) even if the displacement is small. The acceleration vector is proportional to the resultant force applied to the body's center of gravity and its measurement provides a convenient way to study the kinetics of a body in motion.

In order to analyze horse locomotion, the accelerometer should be placed as near as possible to the body center of gravity. The caudal part of the sternum between the right and left pectoralis ascendens muscles at the level of the girth

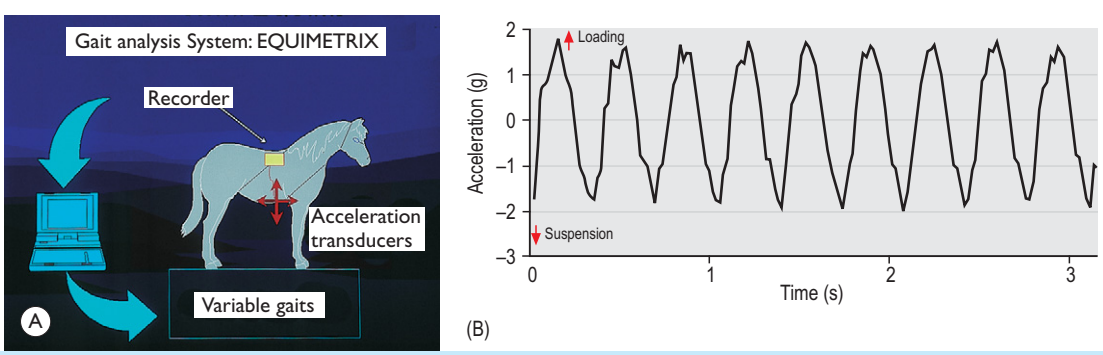

Fig. 12.5
Accelerometric Equimetrix gait analysis system. (A) Two- or three-dimensional accelerometers are fixed on the sternum by an elastic belt or the girth of the saddle. The accelerations are recorded continuously during the exercise. Then data analysis calculates gait characteristics such as stride frequency, vertical and longitudinal activity, regularity and other gait variables specific to the exercise. (B) Example of the vertical acceleration recorded at the trot. The peaks correspond to the maximum loading of the diagonal. The valleys correspond to the suspension phases.

provides a good compromise between transducer stability and closeness to the horse's center of gravity (about 65 cm dorsocaudally at the gallop). The acceleration signal is transmitted to a PC or recorded with a small data logger placed in the saddle pad (Fig. 12.5A). The first application of this gait analysis system (Equimetrix TM) was used for harnessed trotters evaluation.[32] The acceleration signal, such as dorsoventral acceleration of the trot (Fig. 12.5B), could be treated by signal analysis procedures in order to extract the dynamic and temporal stride variables. Calculating the double integral of the linear acceleration makes it possible to find kinematic variables (linear or angular displacement) such as the instantaneous displacement of the saddle in space.[33] Several examples of gait variables calculated from acceleration data will be presented in the following paragraphs.

Acceleration measurements could also be employed for analyzing the energy characteristics of shocks and vibrations which are transient in the hoof.[34–36] An accelerometer could be fixed on the hoof wall in order to measure the maximal deceleration of the hoof impact on the ground and the vibration frequency (Fig. 12.6). The influence of horse shoes and ground surface characteristics could be studied using this method.

The main advantage of using an accelerometric transducer is the simplicity of the measuring technique. It can easily be used under field conditions. The main limitation is that the measurements are given with respect to a set of body axes and consequently it is not easy to calculate the acceleration, velocity or displacement values with respect to a set of ground axes.

Fig. 12.6
Accelerometer fixed on the hoof to study the shocks and vibrations of the hoof after impact on the ground. The influence of the ground surface and the shoe on the shock damping was studied using this transducer.

Conditions of gait measurements: treadmill exercise versus ground exercise

Under laboratory conditions it is possible to study the locomotion of horses running on an experimental track or on a treadmill. The latter provides an excellent means of controlling the regularity of the gaits because the velocity and slope of the treadmill belt are entirely fixed by the operator. In order to analyze the gait of a horse without stress, some preexperimental exercise sessions are required to accustom it to this unusual exercise condition.[37] The horse adapts rapidly at the trot and stride measurements can be undertaken beginning at the third session. For the walk, many stride parameters are not stable even after the ninth training session. Within a session, a minimum of 5 min of walking or trotting is required to reach a steady state of locomotion.

Many fundamental locomotion studies have been performed on commercially available high-speed treadmills, since the development of the first installation of this type of machine at the Swedish University of Agricultural Science in Uppsala.[38] At the beginning of human treadmill use, it was suggested that locomotion on a treadmill would be exactly the same as on the ground.[39] This hypothesis did not take into account the fact that the human body is not a rigid body system but an articulated set of segments. In horses, it was

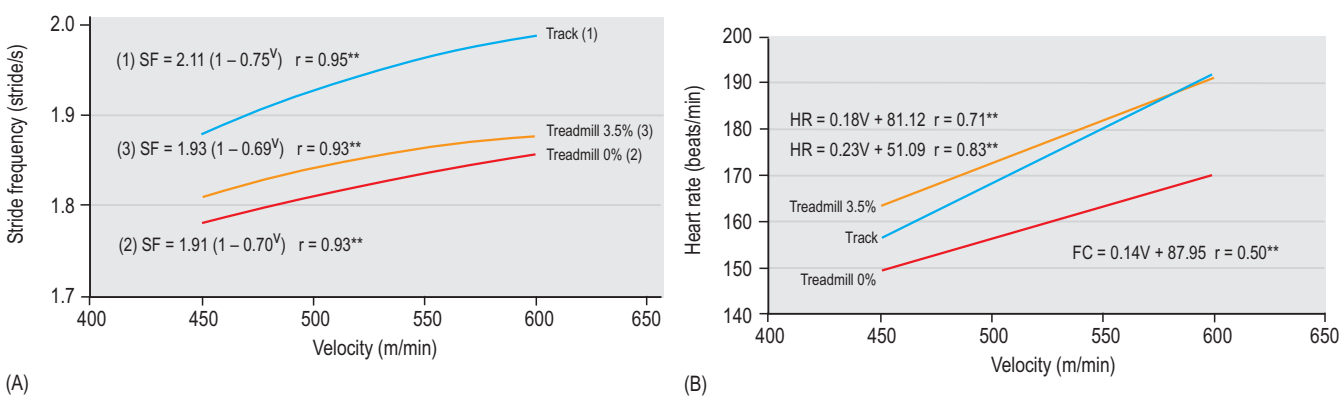

Fig. 12.7
Comparison of the stride frequency (A) and heart rate (B) of horses galloping on track, flat treadmill and 3.5% inclined treadmill. At the same velocity, the stride frequency is lower on the treadmill (i.e. stride length longer) than on the track. The heart rate response is the same on track and 3.5% inclined treadmill. (Reproduced from Barrey et al. Equine Athlete 1993; 6:14–19, with permission.)

demonstrated experimentally that the stride parameters are modified in flat and inclined exercise at trot and canter.[23] At the same speed, the stride frequency was lower on the treadmill and the stride length was longer than in overground conditions (Fig. 12.7A). The exercise on a flat treadmill generated a lower cardiac and blood lactate response than exercise on the track at the same velocities.[23,40] In Trotters tested under two training tracks and treadmill conditions, there were no significant differences in locomotor and physiological variables between tracks but the treadmill had the same influence as in saddle horses.[41] In order to reproduce approximately the same energetic exercise on a treadmill, it was found that a treadmill incline of 3.5% gives the same heart rate response as in overground conditions (Fig. 12.7B).

The mechanical reasons for these differences are still not entirely understood but some explanations have been suggested by the experimental and theoretical results. The treadmill belt is driven by the motor and it helps the horse's limbs to move backwards (Fig. 12.8). The speed of the treadmill belt fluctuates in relationship to the hoof impact on the belt.[31] The total kinetic energy of human runners filmed at the same speed on flat track and treadmill was calculated using the kinematic data (all the body segments taken into account). It was found that the total kinetic energy was reduced by a factor of 10 on the treadmill compared with on the track.[42] This difference was mainly explained by a reduction of the kinetic energy of each limb and arm segment, which moved with a lower amplitude around the total body center of gravity on the treadmill as compared with track conditions. However, these results cannot be extrapolated to the horse because the measurements and calculations do not relate to quadrupedal locomotion.

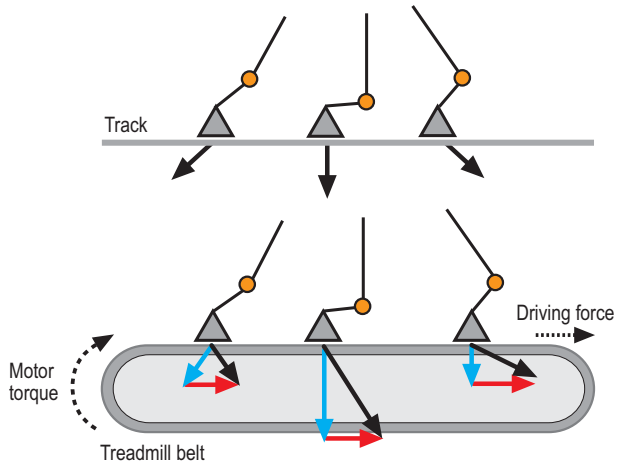

Fig. 12.8
Schematic diagram of hoof force differences in overground and treadmill locomotion. The additional force of the treadmill motor acts on the hoof which could explain the decrease of work and increase of stride length observed in treadmill exercise. (Reproduced from Barrey et al. Equine Athlete 1993; 6:14–19, with permission.)

At a slow trot, a 6% inclination of the treadmill tends to increase the stride duration and significantly increases the stance duration of the forelimbs and hindlimbs.[43] Kinematic analysis has confirmed that the hindlimbs generated higher propulsion work on the inclined, rather than flat, treadmill. The inclination of the treadmill did not change the stride length nor did it change the stance, swing and stride duration in a cantering Thoroughbred.[44]

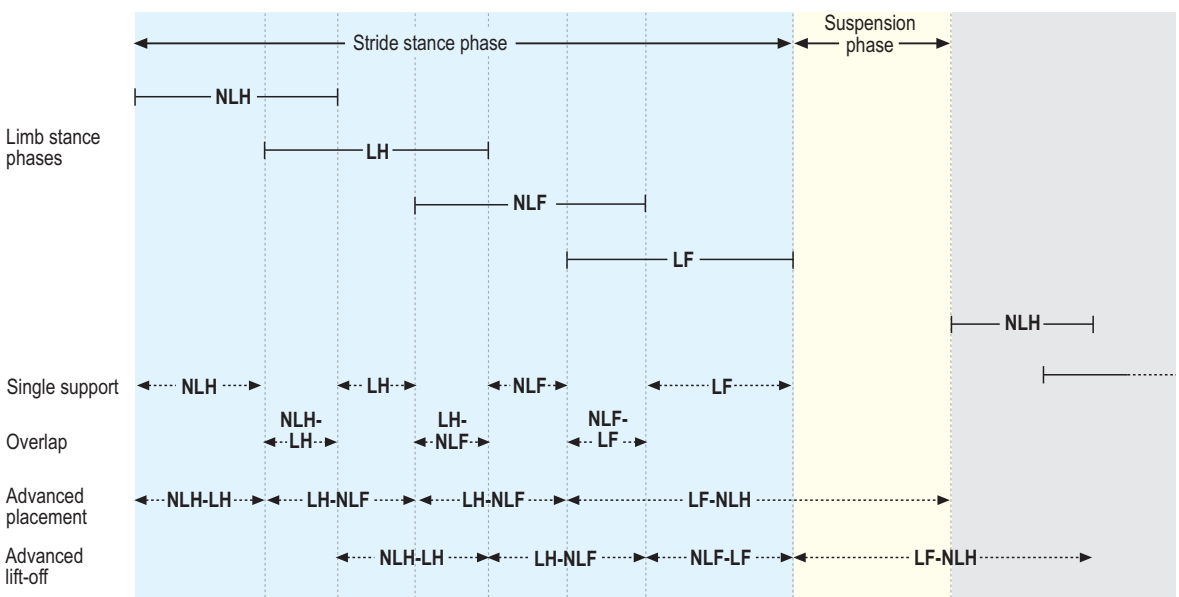

Fig. 12.9
Example of temporal stride variables at the gallop. Bars indicate the stance phase of the limbs. NLH, non-lead hindlimb; LH, lead hindlimb; NLF, non-lead forelimb; LF, lead forelimb. (Reproduced from Clayton[49] with permission.)

Response to exercise: velocity-related changes in gaits and stride characteristics

Gait terminology and definitions of stride characteristics

Gait variety and complexity have always created difficulties because of the need for adequate terminology to describe the locomotor phenomenon. Some efforts have been made to define a standard terminology for describing equine locomotion.[45–47] A *gait* can be defined as a complex and strictly coordinated rhythmic and automatic movement of the limbs and the entire body of the animal which results in the production of progressive movements. A two-, three- or four-beat gait corresponds to the number of hoof impacts that can be heard during a stride of trot, canter and gallop, respectively. The sounds are related to the footfall sequence of the gait but small asynchrony cannot be detected audibly. To describe the footfall sequence of each gait, it is useful to name the four limbs: right forelimb (RF), left forelimb (LF), right hindlimb (RH) and left hindlimb (LH). Many methods have been proposed to describe more precisely in time and space the limb movements: drawings, chronophotographies, stick bar (Fig. 12.9), phase and pie diagrams.[18,48–50]

The stride is defined as a full cycle of limb motion. Since the pattern is repeated, the beginning of the stride can be at any point in the pattern and the end of that stride at the same place in the beginning of the next pattern. A complete limb cycle includes a stance phase when the limb is in contact with the ground, a swing phase when the limb is not in contact with the ground and a suspension phase when none of the hooves is in contact with the ground. The stride duration is composed of the stride stance phase (total duration of ground contact) plus the suspension phase. It is also equal to the sum of the stance and swing phase duration of one limb. The stride frequency corresponds to the number of strides performed per unit of time. The stride frequency is equal to the inverse of stride duration and it is usually expressed in stride/s or in hertz (Hz).

During a unipodal stance phase, only one limb is in contact with the ground, as in the gallop. One forelimb and hindlimb can be synchronized in two different ways.

1. During a diagonal stance phase, for example at the trot, a hindlimb and the contralateral forelimb are in contact with the ground at the same time. The left diagonal is composed of the left forelimb and right hindlimb; the right diagonal is composed of the right forelimb and left hindlimb.
2. During a lateral stance phase, for example at the pace, the hindlimb and forelimb of the same side are in contact with the ground at the same time.

When the forelimbs and hindlimbs hit the ground non-synchronously during a lateral or diagonal stance phase, the time elapsed between the hindlimb and forelimb contact is called the advanced placement. It is positive if the hindlimb hits the ground first. Similarly, the advanced lift-off can be measured between the hooves lifting off.

The stride length corresponds to the distance between two successive hoof placements of the same limb. The over-reach or overtrack is defined as the distance between the hindlimb imprint and the ipsilateral forelimb imprint. It can be positive or negative if the imprint of the hindlimb is in front of the forelimb imprint (positive) or behind it (negative).

The number of lines defined by the successive hoof imprints on the ground defines the number of tracks. This qualitative information characterizes the transverse motion of the gait. If the horse locomotion is slow and straight, there should be two tracks because the forefeet are exactly in the same line as the ipsilateral hindfeet. In some dressage exercises, such as 'shoulder in', 'haunches in', 'quarters-in', 'quarters-out' or 'half pass', the horse can use two, three or four tracks. During the examination of a hindlimb lameness, three or four tracks can be observed and usually the lame hindlimb follows one of the median tracks. The fast trot of a harness trotter usually shows four tracks with the two hindlimbs most abaxial.

Variety of gaits

The main characteristics of the equine gaits are described in Table 12.1. Within each gait there exist continuous variations from slow speed with a collected gait to higher speed with an extended gait. Two types of gait can be distinguished by the symmetry of the limb movement sequence with respect to time and the median plane of the horse:

- *symmetric gaits*: walk, trot, toelt (paso) and pace
- *asymmetric gaits*: canter, transverse and rotary gallop.

Several methods have been proposed to classify the gaits acording to their temporal characteristics. The continuum of symmetric gaits was described by a diagram proposed by Hildebrand.[51] The stance duration of the hindlimb was plotted against the lateral advanced placement. On the *x* axis, the stance duration of the hindlimb indicates if the gait is walked (no suspension phase) or run (two suspension phases). On the *y* axis, the lateral advanced placement quantifies the asynchrony or the phase lag of the lateral forelimbs and hindlimbs. The two-beat gaits are up and down the diagram and the four-beat gaits are in the middle part of the diagram. Another diagram has been proposed for illustrating the diagonal gaits by plotting the hind stance phase duration against the diagonal advanced placement.[52]

Another method, based on a series of coupled oscillators, has been proposed to describe and simulate both symmetric and asymmetric gaits. This model also has the advantage of describing the gait transitions and unique gaits like 'aubin' and 'traquenard'. The model uses four coupled oscillators which simulate the cyclical patterns of the four limb

Table 12.1 Gait characteristics

Classification	Gait	Gait variations	Footfall sequence	Rhythm (beat/stride)	Type of symmetry	Speed (m/s)	Stride length (m)	Stride frequency (stride/s)	Limb stance phase (s or % stride)	Suspension phase (s or % stride)
Symmetric gaits	Walk	Collected, medium, extended	RH,RF,LH,LF	4	Right/left bipedal	1.2–1.8	1.5–1.9	0.8–1.1	65–75%	0
	Toelt = Paso		RH,RF,LH,LF	4	Right/left lateral	3.4–5.3	1.7–2.3	2.23–2.36	40–55%	0
	Trot	Piaffe, passage, collected, medium, extended, flying trot	RH-LF, Susp., LH-RF, Susp.	2	Right/left diagonal	2.8–14.2	1.8–5.9	0.9–2.52	26–53%	0–9%
	Pace		RH-RF, Susp., LH-LF, Susp.	2	Right/left lateral	9.1–16.0	4.5–6.3	1.8–2.4	0.130–0.138 s	0.081–0.094 s
Asymmetric gaits	Canter	Collected, medium, extended, disunited	Trail.H,Lead.H-Trail.F,Lead.F, Susp.	3	Asymmetry with a phase lag between limb pairs	2.9–9	1.9–4.6	1.6–2.0	0.28–0.30 s	0–0.013 s
	Gallop	Transverse, rotary	Transverse: Trail.H,Lead.H, Trail.F,Lead.F, Susp.	4	Asymmetry with a phase lag between limb pairs	9–20	4.5–7.2	2.27–2.92	0.085–0.09 s	0.063–0.114 s 16–28%

movements. By using five methods of coupling the oscillators, it was possible to generate all types of equine gaits. This type of functional model can be useful to understand the locomotor control which includes rhythmic pattern generators.

Symmetric gaits

Walk The walk is a four-beat gait with a large overlap time between stance phases of the limbs. This is the slowest equine gait but probably one of the more complex because of overlap and lag phase variability. During lameness examination, the variability of stride regularity and symmetry measured at the walk was higher than at the trot.[53] In dressage horses, the speed of the walk increases from the collected walk (1.37 m/s) to the extended walk (1.82 m/s) and simultaneously there is a small increase in stride frequency.[54] The change in speed was primarily the result of lengthening of the stride by increasing the overtracking distance. Even in horses trained for dressage, the regular four-beat rhythm of the footfall was observed in only one of the six horses measured.

Toelt Icelandic and Paso Fino exhibit a four-beat symmetric lateral gait (Fig. 12.6). This gait can be called 'toelt', 'paso', 'rack', 'fox-trot' or 'slow gait'. The toelt is comfortable for the rider because the amplitude of the dorsoventral displacement is lower than at the trot. The speed ranges between 1.7 and 2.3 m/s and the natural gait transition for toelter is walk–toelt–canter.

Trot The slow trot is a two-beat symmetric diagonal gait. Among the normal variations of the trot of saddle horses, the speed of the gait increases from collected to extended trot. Passage and piaffe are two dressage exercises derived from collected trot. However, their temporal variables are different as was shown in the dressage finals at the Olympic Games in Barcelona.[52] The stride duration is longer (i.e. slower stride frequency) for piaffe (1.08 s) and passage (1.09 s) than for collected trot (0.84 s). For most of the other temporal variables, collected trot and passage were very similar except for the suspension phase which was shorter in passage. A positive diagonal advanced placement measured at the collected trot was observed in the elite dressage horses.[52,55] This means that the hindlimb hits the ground about 20–30 ms before the diagonal forelimb.

In harness trotters, the trot is so extended that it can reach a maximum speed of 14.2 m/s with a maximum stride frequency of 2.52 strides/s and a maximum stride length of 5.92 m.[56] The diagonal sequence is usually affected and this particular gait is named the flying trot. It is a four-beat gait because there is an asynchrony of the impact and/or lift-off of the diagonal.[57] In most cases the hindlimb touches the ground first (a positive advanced placement). The dissociation at lift-off is greater than at impact.

Various trot irregularities can occur during a harness race and the horse can be disqualified by the gait judges: at the aubin, the forelimbs gallop and the hindlimbs trot while at the traquenard, the forelimbs trot and the hindlimbs gallop. A trotter is also disqualified if it breaks into a pace or gallop.

With increasing speed the stride length increases linearly but the interference between the hindlimb and the lateral forelimb becomes a limiting factor. A large over-reach of the hindlimbs can be performed only if the hindlimbs follow two lateral tracks (track abaxial to the forelimbs) during the swing phase.

Pace This lateral symmetric gait is used in harness racing mainly in North America and Australia. The maximum speed can be faster than at the flying trot. It is also a four-beat gait at high speeds with dissociation of lateral symmetry at impact and lift-off. The hindlimb hits the ground before the ipsilateral forelimb. This lateral advanced placement of the hindlimb is about 26–30 ms. In comparison with the flying trot there is less problem with limb interference because the lateral sequence avoids any contact between the ipsilateral limbs. Consequently, there are fewer co-ordination difficulties and it is easier for the horse to increase stride length. These differences may explain the faster speed records obtained by pacers (9.4–16.0 m/s) than by trotters (11.8–14.2 m/s).

Asymmetric gaits: canter and gallop

Canter and gallop refer to the same gait at increasing speed: the canter is a three-beat gait at slow speed and the gallop is a four-beat gait at a higher speed. At the canter, the diagonal stance phase is synchronized while at the gallop the footfalls of the diagonal limbs are dissociated. The first hindlimb hits the ground before the diagonal forelimb at the gallop. The gallop is the fastest equine gait and is used by racing horses such as Thoroughbreds and Quarter Horses.

These two gaits are composed of asymmetric movements of the hindlimbs and forelimbs. Because of this asymmetry, each limb is referred to differently: the lead limb is the last one of the limb pairs to leave the ground. The contralateral limb is called the non-lead limb or trailing limb. Consequently, there are two possible symmetric footfall sequences: right lead canter and left lead canter, and similarly, right lead gallop and left lead gallop. In free conditions the horse prefers to canter or gallop on the right lead to go into a right curve. If it is cantering on the right lead before going into a left curve, the horse will probably change the lead limb to maintain balance in the curve.

The lead change is the transition between right lead canter and the left lead canter footfall sequence. It is commonly accomplished by initially having the horse change the order of hindlimb placements and then the forelimb placements. However, in dressage the rider can elicit the canter lead change during the suspension phase. Racing horses change leads eight or more times per mile to avoid excessive muscular fatigue due to asymmetric work of the limbs and also to minimize the centrifugal forces as they accommodate to the curve.[58]

At the gallop, there are two types of footfall sequences called the transverse gallop and the rotary gallop. The transverse gallop is more frequently used by the horse than the rotary gallop but the latter may be used briefly under some circumstances, for example after a lead change or when muscular fatigue occurs during a racing gallop. A disunited canter occurs with the same footfall sequence as a rotary gallop except that the stance phase of the diagonal is synchronized. It can be observed for a few strides after a bad lead change in dressage or following a jump.

The jump is a unique gallop stride where the airborne phase is a long dissociation of the diagonal. The footfalls of the jump stride are: trail-H, lead-H at take-off and trail-F, lead-F at landing. At take-off, the hindlimb stance phase is more synchronized than in a normal gallop stride to provide a powerful push-off. The footfalls of the forelimbs at landing are not synchronized.[59] A lead change can take place during the airborne phase and in this case the change of forelimb placement order takes place before those of the hindlimbs. A disunited canter can be observed after the jump if the lead change of the hindlimbs does not occur immediately after the landing phase.

Gait transitions

To increase its velocity, the horse can switch gait from walk to trot and from trot to canter and then extend the canter to gallop. Each gait can also be extended by changing the spatial and temporal characteristics of the stride. From a dynamic point of view, a gait transition can be characterized by a gait change with non-stationary motions of the limbs. Periodicity and rhythm of the limb motions change suddenly. Gait transition is one of the most difficult basic exercises in dressage where specific co-ordination should be learned during training exercise.

There is little information about gait transitions in the scientific literature. The footfall sequence of various gait transitions has been described by Marey and Lenoble du Teil.[18,50] One kinematic study described four types of footfall sequences observed in dressage horses during the walk–trot transition.[60] One accelerometric study described the instantaneous changes of stride frequency and dorsoventral activity during all types of transitions recorded in competitions.[61]

From an energetic point of view, it appears that each equid has a preferred speed for the trot to gallop transition and this particular speed is related to an optimal metabolic cost of running.[62] However, another experiment demonstrated that the trot–gallop transition is triggered when the peak of ground reaction force reaches a critical level of about 1–1.25 times the bodyweight (Fig. 12.10).[63] Carrying additional weight reduced the speed of trot–gallop transition.

Velocity-related changes in stride characteristics

For increasing the speed at a particular gait, the amplitude of the steps becomes larger and the duration of the limb cycle is reduced in order to repeat the limb movements more frequently. Stride frequency (SF) and stride length (SL) are the two main components of gait speed. The mean speed (V) can be estimated by the product of stride frequency by stride length: $V = SF \times SL$. The velocity-related changes in stride parameters have been studied in many horse breeds and disciplines. Stride length increases linearly with the speed of the gait. Stride frequency increases non-linearly and more slowly.[5,64,65] For a quick increase of running velocity such as that occurring at the start

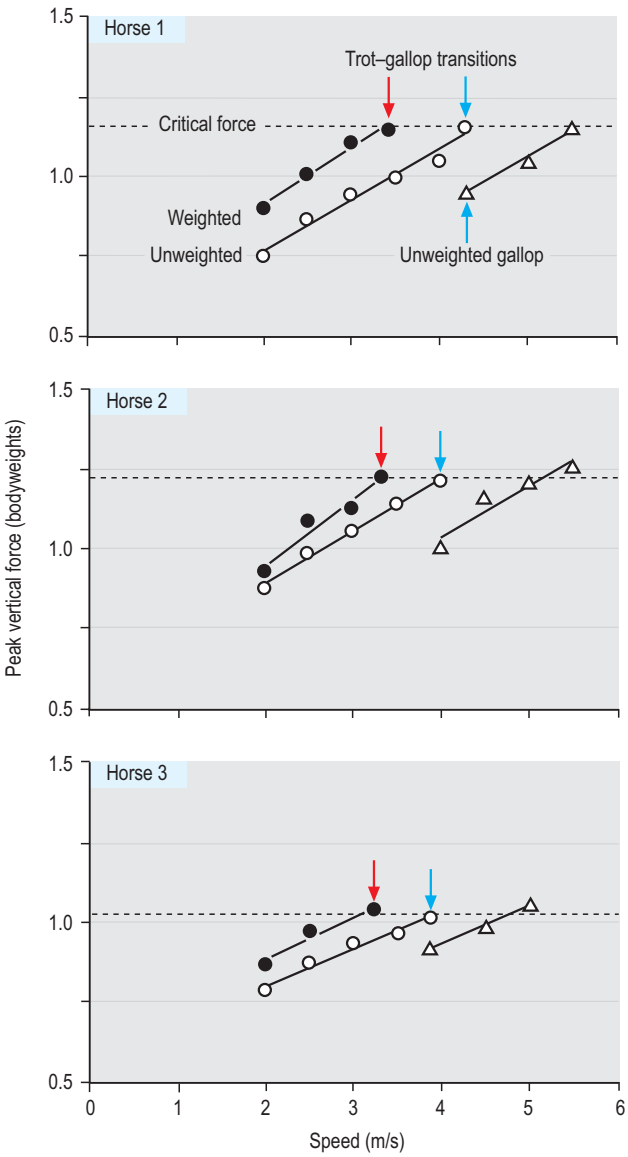

Fig. 12.10
Gait transition determinism. When the horses carried weights, they switched to a gallop at a lower speed but essentially the same critical level of forces as when they did not carry weights. By switching to a gallop, the peak ground reaction force was reduced by an average of 14%. The open circles and triangles denote unweighted trotting and galloping, respectively, and the closed circles denote weighted trotting. The plotted values are the average of the peak forces under each of the four limbs. The lines are linear least squares regressions. (Reproduced from Farley and Taylor[63] with permission.)

of a gallop race, stride frequency reaches its maximum value first to produce the acceleration, while the maximum stride length slowly reaches its maximum value.[66]

In Thoroughbred race horses, the fatigue effect on stride characteristics increases the overlap time between the lead hindlimb and the non-lead forelimb, the stride duration and the suspension phase duration.[67] The compliance of the track surface also can influence the stride parameters when the horse is trotting or galloping at high speed. At the gallop, stride duration tends to be reduced on a harder track surface.[38] There is a slight increase in stride duration on wood-fiber tracks in comparison with turf tracks at the same speed. When the rider stimulated the horse with a stick, a reduction in stride length and an increase in stride frequency corresponding to a reduction of the forelimb stance phase duration were observed. However, velocity was not significantly influenced.[68]

Most of the kinetic and temporal stride variables were influenced by the velocity of the gallop. Stride frequency, stride length and diagonal dissociation increased linearly with velocity. Velocity was mainly increased by the increase in stride length and secondly by stride frequency. Increase in stride length is mainly explained by the lengthening of the diagonal and airborne phases of the stride.[65] The overlap duration of the diagonal decreased linearly to about 50 ms as the galloping speed increases.[58,69] In order to increase gallop stride length, the movements of the hindlimbs and forelimbs are dissociated and length between the footfalls of the diagonal increases. The time elapsed between forelimb midstance phases and between hindlimb midstance phases is kept constant and independent from velocity.[65]

Respiratory coupling at trot, canter and gallop

Some relationships have been established between stride parameters and other physiological variables. At the canter and gallop, the respiratory and limb cycle are synchronized. Inspiration starts from the beginning of the suspension phase and ends at the beginning of the non-lead forelimb stance phase. Expiration then occurs during the stance phase of the non-lead and lead forelimbs (Fig. 12.11).[70] Expiration is facilitated by compression of the rib cage during weight bearing of the forelimbs. This functional coupling might be a limiting factor for ventilation at maximal exercise intensity. At the walk, trot and pace there is not a consistent coupling of locomotion and the respiratory cycle. At a trot, the ratio between locomotor and respiratory frequency ranged between 1 and 3 with respect to the speed, the duration of exercise and the breed.[71,72] The same type of low-level coupling was observed at a pace where the ratio between stride and respiratory frequency was 1–1.5.[73]

Muscle fiber characteristics and locomotion

The relationship between stride parameters and muscle fiber composition was studied in Standardbreds at high speed.[74] The stride length and frequency were extrapolated at a speed of V200 or V = 9 m/s. The stride length is positively correlated with the percentages of type I fiber (aerobic slow twitch) and type IIA (aero-anaerobic fast twitch) and negatively correlated with the percentages of fiber type IIB (anaerobic fast twitch). The stride frequency was positively correlated with only the percentage of type IIA fiber. However, in another study the opposite result was found: a negative correlation between the

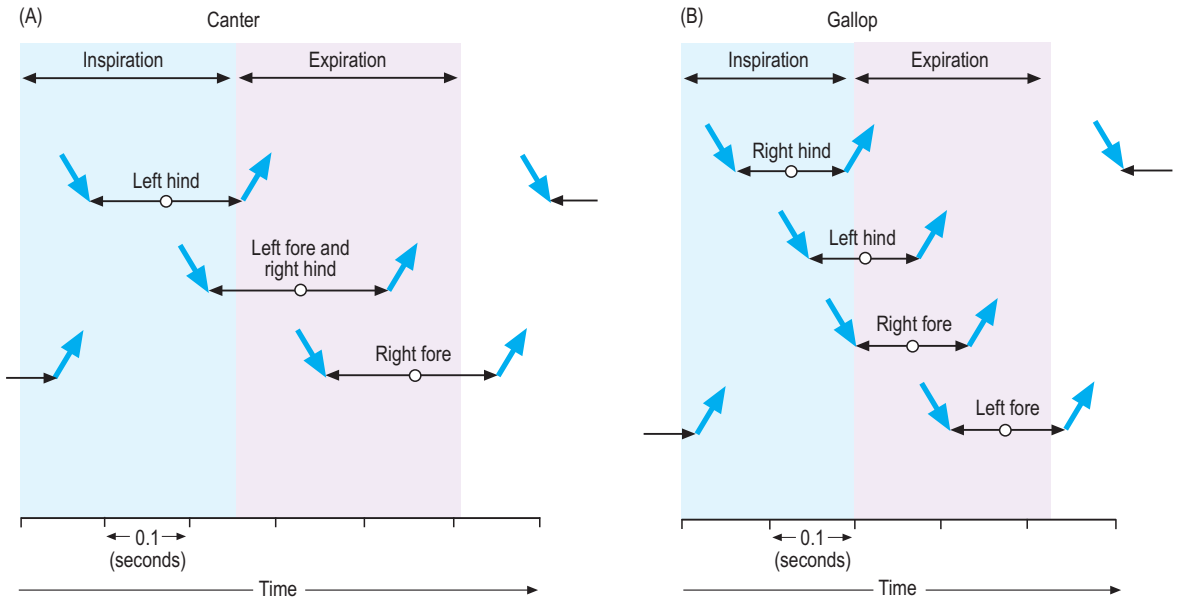

Fig. 12.11
Schematic diagram showing the relationship between the timing of the events of the respiratory cycle and the timing of the events in the cycle of limb movement when a normal horse is cantering (A) or galloping (B), leading with the right forelimb. The distances between arrowheads represent the periods of ground contact of the feet. (Reproduced from Attenburrow[70] with permission.)

stance duration of young Trotters and the percentage of type IIB fibers.[75] For race Trotters the force–velocity relationship for skeletal muscles implied in limb protraction and retraction might be an important limiting factor of maximal stride frequency.[58] In Andalusian horses, there is no significant correlation between the stance duration and the fiber type percentages. However, the diameter of fibers was negatively correlated with stance duration.[76] The propulsive force during the stance phase might be higher with larger fibers, especially of type I.

During a treadmill exercise test, blood lactate concentration and heart rate at high speed seem to be more correlated to stride length than to stride frequency.[74,77] This finding confirms that the high speed which elicited a cardiac and metabolic response is primarily explained by an increase in stride length. Furthermore, the velocity relating to change of stride frequency is not linear and consequently decreases the coefficient of correlation. In ponies tested on the track, stride frequency was more correlated to blood lactate concentration and heart rate than to stride length, which is more limited in this animal.[40]

Response to training: influence of age and training on locomotor variables

Gait development in foals and yearlings

Gait patterns are influenced by the age of the horse, but little is known about gait development. The relationship between conformation and stride variables in foals aged 6–8 months has been reported. Speed increases were achieved by longer stride length in heavier foals and higher stride frequency in taller foals.[5] The elbow, carpal and fetlock joint angle flexions were the most significant differences between the foals.[78] The stride and stance duration increased with age but the swing duration and pro-retraction angle were consistent. The joint angle patterns recorded at 4 and 26 months were nearly similar. The good correlations of some of the kinematic parameters measured in foals and adults make it possible to predict the gait quality of adult horses.[79]

Training effects

According to several studies, some of the gait characteristics can also be modified after a training period. However, little is known about the training effect, because few data from longitudinal studies are available. In one study, after 70 days of dressage and jumping training, the stance duration of the hindlimb decreased, its flexion increased and its maximal protraction occurred earlier. In addition, the protraction and retraction range of the forelimb decreased and the stride duration was unchanged. After the same period, the horses which had been left in pasture showed other locomotion modifications. They had a longer swing and stride duration and the range of the forelimb movement was larger.[80]

In race horses, the training influence has been investigated in Standardbreds and Thoroughbreds. After 3 years of training, the following changes in the trotting strides were observed: the stride length, the stride duration and swing phase increased.[57] Another study on Standardbreds trained on a treadmill did not show any change in temporal or linear stride variables after 5 months of training. In gallop racing, a stride duration and stride length increase was found.[67] After 8 weeks of a high-intensity training regime on a treadmill,

Table 12.2 Changes in trot variables with the stage of training in dressage horses

	4 years	5 years	6 years	7 years and older
Stride frequency (stride/s)	1.34 a	1.32 a	1.26 b	1.27 b
Stride regularity (/200)	186 a	185 a	185 a	179 b
Dorsoventral activity (g^2/Hz or W/kg)	7.8	8.3	8.7	10.4
Longitudinal activity (g^2/Hz or W/kg)	1.14	1.62	1.55	2.1
Propulsion acceleration vector (g)	2.3	2.2	1.4	3
Dorsoventral displacement (m)	0.11 a	0.13 b	0.13 b	0.13 b

Means followed by different letters are significantly different at $P<0.05$.

the stance phase duration of the Thoroughbred gallop stride was reduced by 8–20%.[81]

Dressage horses should be trained to improve their coordination, their suppleness and their gait collection. Collection of the gait means that the forward movement becomes more upward movement and the stride frequency slows down. A group of dressage horses were tested from 4 to 7 years of age to determine the training-related changes in locomotion variables. The changes of the trot were more pronounced than the changes in the walk and gallop (Table 12.2). At the trot, the stride frequency decreases between 5 and 6 years old. During the same time walk and gallop stride frequency remains the same. At the trot dorsoventral displacement increases after the first year of training. The increase of dorsoventral activity with age corresponded to an increase of muscular power and an increase of the dorsoventral displacement with collected gaits. Stride regularity and symmetry increase in early training and then decrease after 6 years of age.

Applications of equine gait analysis

Gait tests for breeding

Early jumping evaluation

Free jumping tests are often used in the performance evaluation of 3-year-old horses. These tests are useful for selection of stallions and mares for breeding, and to select potential performance horses. Gallop, take-off, jump path and landing characteristics were measured during a free jumping test using the Equimetrix system. Heritabilities of these jump measurements were calculated in French saddle horses to determine the use of breeding criteria (Table 12.3). The heritabilities of jumping characteristics are moderate to high and can be used effectively in selection of bloodlines for breeding.

Table 12.3 Heritabilities (h^2 and standard errors) of the variables measured during a free jumping test in French saddle horses

Gait variables	h^2 (SE) for walk
Approach strides	
Stride frequency	0.32 (0.19)
Dorsoventral activity	0.50 (0.13)
Longitudinal activity	0.46 (0.20)
Take-off stride	
Sum of the accelerations produced by the forelimbs and hindlimbs	0.47 (0.14)
Power of the take-off exercise	0.40 (0.09)
Take-off impulse duration	0.26 (0.13)
Jump	
Jump duration	0.47 (0.12)
Height of the sternum	0.21 (0.16)
Landing	
Forelimbs deceleration	0.64 (0.13)
Power of the landing exercise	0.64 (0.15)
Speed at landing	0.35 (0.20)

h^2 Heritability
SE Standard error of heritability

Basic gait characteristics of young dressage horses

Gait and conformation test information is useful in making breeding plans and to more accurately identify young horses with good dressage potential. Gait characteristics may be measured early in a horse's saddle training. Walk and trot may be measured earlier in hand. Several studies were conducted in France and Germany to measure gait and conformation variables in 3-year-old horses presented in a performance test.[82,83] The relationships between these measurements and the judges' scores were analyzed. The locomotor profile of future dressage horses should have the following gait characteristics.

- *Walk*: large vertical limb displacement and propulsion activity, high regularity
- *Trot*: slow cadence, large vertical displacement, high regularity, large propulsion activity
- *Gallop*: three-beat gallop with high regularity, slow cadence and good propulsion activity

Horses having these basic gait characteristics obtain better scores in performance tests and they have better perfomance during the first year of dressage competition.

The 3-year-old German horses evaluated had gait characteristics more advantageously adapted for dressage competition. The results obtained in the best German horses tested could be considered as a reference standard for dressage breeding. Purebred Spanish horses should be considered as a reference standard for collected gaits used in farm work and classical dressage. Specific conformation and gait characteristics in German breeds may explain their higher level of success in dressage competition.[84] For dressage performance the trot characteristics and its variations are very important

Table 12.4 Comparison of the trot characteristics measured by the Equimetrix system in three groups of breeds used for dressage: German horses (Hannoverian, Westphalian, Oldenburger), purebred Spanish horses and French saddle horses

Trot characteristics	GER	SF	PRE
Speed (m/s)	3.97 a	4.24 a	3.18 b
Stride length (m)	2.98 a	3.02 a	2.31 b
Stride frequency (stride/s)	1.33 a	1.40 b	1.38 b
Stride symmetry (%)	97	97	96
Stride regularity (/200)	185 a	182 a	174 b
Dorsoventral displacement (10^{-2} cm)	13 a	10 b	10 b
Dorsoventral activity (g^2/Hz or W/kg)	24.33 a	22.01 a	19.76 ab
Percentage of 2-beat rhythm (%)	89 ab	90 a	87 b
Propulsion acceleration vector (g)	8.49 a	7.39 b	9.22 a
Propulsion duration (%)	26 a	29 b	29 b
Longitudinal activity (g^2/Hz or W/kg)	2.35 a	1.43 b	2.42 a

GER Hannoverian + Oldenburger + Westphalian
SF Selle Français
PRE Pura Raza Espaniola
Means followed by different letters are significantly different at $P < 0.05$.

Table 12.5 Heritabilities of the gait variables measured by the Equimetrix system in French saddle horses. The moderate and high heritabilities are indicated in bold

Gait variables	h^2 (SE) for walk	h^2 (SE) for trot	h^2 (SE) for gallop
Stride characteristics			
Speed	0	**0.30 (0.14)**	NA
Stride length	0	**0.29 (0.13)**	NA
Stride frequency	0	**0.20 (0.15)**	**0.32 (0.19)**
Dorsoventral motion			
Symmetry	0.10 (0.08)	0.12 (0.08)	NA
Regularity	0.10 (0.13)	0.12 (0.09)	NA
Displacement	0.16 (0.12)	0.14 (0.08)	NA
Dorsoventral activity	**0.41 (0.12)**	**0.22 (0.10)**	**0.50 (0.13)**
Gait rhythm	**0.29 (0.10)**	0.05 (0.07)	NA
Longitudinal motion			
Mean propulsion vector	0.19 (0.07)	**0.20 (0.11)**	NA
Propulsion duration	**0.69 (0.13)**	**0.38 (0.15)**	NA
Longitudinal activity	0	**0.44 (0.14)**	**0.46 (0.20)**

h^2 Heritability
SE Standard error of heritability
NA Non-available data

because they form the basis of passage and piaffe, movements which are performed at the upper levels of dressage competition. According to the FEI standards, the trot should be a two-beat gait with free, active and regular steps. Regularity and elasticity of the steps and engagement of the hindquarters are important qualities of the trot. The same cadence and rhythm should be maintained during trot variations. The trot characteristics of the German horses were consistent with the FEI standards: slow stride frequency, high regularity, large dorsoventral displacement and activity. Activity is considered good when the horse diplays elasticity and good propulsion (Table 12.4). Spanish horses have shorter stride length, higher stride frequency and lower dorsoventral displacement and activity than German horses. Spanish horses exhibited elevated movements (large flexion of carpus and tarsus) rather than extended movements of the limbs. It has been shown that purebred Spanish horses have larger elbow and carpus angular range than Dutch Warmblood horses.[85] Spanish and German groups have high propulsion and longitudinal activity which should be an advantage for collecting the trot to passage and piaffe. Spanish groups exhibited gaits with lower regularity than the German group but this could be explained by the lower training level of the Spanish horses at this age. Traditionally, purebred Spanish horses are broken in at the age of 4 years instead of 2–3 years for German horses.

The mean heritability of dressage performance was rather low ($h^2 = 0.04–0.27$) as reported by several authors because non-genetic effects like training have a large influence on outcome.[86–88] Consequently, early selection using gait tests could be more efficient than selection based on performance results. Moderate and high heritabilities have been found for trot and gallop variables such as stride length, stride frequency, dorsoventral displacement and propulsion variables (Table 12.5).[83] Some of the gait variables such as stride frequency, dorsoventral and longitudinal activity which have moderate to high heritability, could be used for improving gait collection ability by genetic selection. Most of the trot variables had a moderate to high heritability (mean heritability $h^2 = 0.24$). The trot characteristics are very important for dressage ability and should be used for early selection at 2 or 3 years old. Slow stride frequency, high dorsoventral activity and high propulsion vector and longitudinal activity are the trot characteristics required for performing in dressage. Gallop variables are highly heritable (mean heritability $h^2 = 0.43$) and could also be used for genetic selection. Slow stride frequency and high longitudinal activity are required. Walk heritabilities were rather low (mean heritability $h^2 = 0.15$) except for vertical activity, longitudinal propulsion and percentage of four-beat walk which were highly heritable. The low heritabilities could be explained because the walk is a complex gait which could be modified by many environmental factors.

Specific locomotion in racing and equestrian sports

Galloping race

Maximum gallop velocity is primarily determined by stride length. An increase in this component is obtained by decreasing the overlap duration of the lead hindlimb and non-lead forelimb stance phase.[58] The movements of the hindlimbs and forelimbs are dissociated and the length between the footfalls of the diagonal increases. Overlap time of the diagonal decreases linearly down to about 50 ms as galloping speed increases.[68,69] In poorly performing Thoroughbreds tested on an inclined treadmill (10% slope) at a maximum velocity of 12 m/s, stride length and velocity at maximum

heart rate were the variables most highly correlated to running speed.[89]

The racing career of a Thoroughbred is short and the number of racing opportunities is limited. To maximize an individual horse's potential for winning, it should be entered in races appropriate for its racing ability. To help make optimal decisions about entering horses in races, a profile may be developed for each horse while in early training. The profile should include indicators of the animal's speed, endurance, preferred track conditions and locomotor variables that help determine these characteristics. Locomotor variables of the racing gallop while at maximal speed can only be obtained on a race track because the temporal stride variables should be natural. On a high-speed treadmill maximal speed is limited to 14–15 m/s and the biomechanics of locomotion are modified by the driven belt.[23] However, the physiological variables such as respiratory variables are more accurately measured on an inclined treadmill at submaximal speed.[89]

A gallop test has been designed to determine the locomotor profile of Thoroughbreds. The gallop test is part of normal 'fast work' training, is easy to perform and provides locomotor variables to evaluate the racing capacity of Thoroughbreds in training. This test may be used for early evaluation of young horses as soon as they can gallop close to maximal speed on a race track. The results characterize the gallop and could assist the trainer in planning the training and racing program of the horse.

Several gait variables were related to race performance which was evaluated by the percentage of wins, placings and the logarithm of average earnings per start. The best performers had a higher stride frequency, stride regularity and diagonal dissociation. Stride length increase described most of the velocity increase but was negatively correlated with performance. Horses that appeared to be better adapted for short racing distances had higher stride frequency but longer ground contact duration which provided more time for propulsion. It has been found that suspension duration (= stride duration – ground contact duration) decreased at maximal velocities greater than 13–14 m/s.[69] A quick gallop acceleration at the start of the race is achieved intially by a high rate of stride frequency increase and then by stride lengthening.[66] During a race, a gallop acceleration is required at the finish to win. Consequently, horses that can increase their stride frequency to the highest value have a better chance to win. A locomotor test performed in harnessed Trotters on a track confirmed that the best race performances were obtained by horses that had the highest maximal stride frequency and a long stride length.[56]

These findings suggest that good race horses are able to trot or gallop at high speed using an optimal stride length and that they can accelerate by increasing their stride frequency in order to finish the race. The best performers reached high stride frequencies of 2.52 strides/s at trot and 2.81 strides/s at the gallop. However, stride length is negatively correlated with performance but stride frequency is positively correlated. Because of pendulum mechanics of the body, maximal stride frequency is dependent on the height of the horse (length of the limbs), weight distribution of the limbs (moment of inertia), elasticity of the limbs and rib cage (module of elasticity) and the percentage of fast-twitch muscle fibers (forces). Increased propulsive activity produced a much greater velocity. Dorsoventral loading of the limbs was increased at high speed probably because of the large effect of kinetic energy of the body. Dorsoventral displacement of the thorax decreased linearly with velocity and minimized the potential energy changes of the center of gravity which reduced the energy expenditure of locomotion. At the fastest speed, horses reached the 'wheel gallop' by lowering and keeping their center of gravity at the same height during the entire stride, even the suspension phase. The 'wheel gallop' is optimized to produce maximum energy for propulsive work in the longitudinal axis and avoid energy wastage for vertical oscillations of the body. Energy cost of the gallop increases as stride regularity decreases. This may make regularity of the stride one of the limiting factors which determine maximum galloping speed. Regularity was affected by the increase in speed as it has been found in harness Trotters and it is highly correlated with racing performance.[32]

Harness racing

In order to measure gait variables during training sessions on a race track, a mobile gait analysis system has been used in harness Trotters.[41,56] Good Trotters have a short stance phase duration with a longer stance phase in the hindlimbs than in the forelimbs.[90] A locomotor test performed in race Trotters on a track confirmed that the best race performances were obtained by Trotters that had the highest maximal stride frequency and a long stride length.[56] These findings suggest that good race Trotters are able to trot at high speed using an optimal stride length and that they can accelerate by increasing their stride frequency in order to finish the race.

Show jumping

During the 1988 Seoul Olympic Games, the kinematics of jumping over a high and wide obstacle (oxer) were analyzed in 29 horses and the relationship to the total penalty score was studied.[91] Fewer total penalties were associated with lower velocities during the jump strides, closer take-off hindlimb placements and closer landing forelimb placements. Another study on elite horses jumping a high vertical fence demonstrated that the push-off produced by the hindlimbs at take-off was associated with the mechanical energy required for clearing the fence.[92] The action of the forelimbs should be limited to positioning the horse's body into proper orientation with the jump before the final push-off of the hindlimbs. A more vertical component of the initial velocity was observed in the horses that successfully cleared a wide water jump (4.5 m).[93] The angle of the velocity (vector) relative to the horizontal was 15° in a successful jump compared to 12° in an unsuccessful jump and the vertical component of the velocity was about 0.5 m/s greater in a successful rather than an unsuccessful jump. This initial velocity was

generated by the impulse of the hindlimbs and determined the ballistic flight characteristics of the body.

These kinematic findings agree with another study which showed that poor jumpers had a lower acceleration peak of the hindlimb at take-off than good jumpers.[94] Poor jumpers brake too much with the forelimbs at take-off impulse and the hindlimbs produce an acceleration which is too weak for clearing the fence. This force is one of the main factors affecting a successful jump because it determines the ballistic flight of the center of gravity and also the characteristics of the body rotation over the obstacle during the airborne phase. The moment of inertia and its influence on body rotation were also studied in a group of jumping horses but no consistent relationship with the level of performance was found.[94] More penalties were recorded for horses that cantered at a low stride frequency (lower or equal to 1.76 stride/s) and suddenly reduced their stride frequency at take-off.

Dressage

In dressage the horse should easily execute complex exercises, gait variations and gait transitions while maintaining its equilibrium and suppleness. This discipline requires a high level of locomotor control of the horse by the rider which is achieved progressively through exercise and collecting the gaits. A horse's ability for collection is one of the main limiting factors for dressage because it is impossible to execute the more complex exercises correctly without having attained good basic collection of the gaits. The collected gaits have been extensively described in kinematic studies.[54,55,95,96]

The trot Among the normal variations of the trot in saddle horses, the speed of the gait and the stride length increase from collected, to medium and to extended trot. A slow stride frequency, including a long swing phase, is required for good trot quality. The time elapsing between hindlimb contact and diagonal forelimb contact defines the diagonal advanced placement and should be positive and high at the trot. The horse should place its hindlimbs as far as possible under itself. A large amplitude of vertical displacement of the body during collected trot is desired in the dressage horse. Vertical displacement of the trot is obtained through the storage of elastic strain energy in the fetlock, hock, stifle and pelvis. For extending the trot, having an inclined scapula (a steeper angle to the scapula) and the amplitude of the elbow joint appeared as important factors. The horses judged to have a good trot should have a large degree of flexion in the elbow and carpal joints at the beginning of the swing phase of the stride. A positive diagonal advanced placement measured at the collected trot was observed in elite dressage horses.[52,97] In these elite horses the hindlimb contacts the ground about 20–30 ms before the diagonal forelimb. This advanced foot placement could be a means for the hindlimbs to push off earlier during the stance phase.

The degree of collection at the trot could also be measured by the acceleration components of the body. Horses equipped with the Equimetrix system in a dressage test were recorded at all trot variations and passage. With increasing collection at the trot, the vertical component of acceleration increased.[83] At the same time, the forward component of acceleration decreased. This indicates that propulsion power in dressage horses is used to increase vertical displacement instead of longitudinal displacement.

The passage and piaffe Passage and piaffe are two dressage exercises derived from the collected trot but the kinetics of each are quite different. Differences in the temporal variables were demonstrated in kinetic analyses of the dressage finalists at the Olympic Games in Barcelona.[52] Stride duration is longer (i.e. stride frequency is slower) for piaffe (1.08 s) and passage (1.09 s) than for the collected trot (0.84 s). For most of the other temporal variables, collected trot and passage were very similar except for the suspension phase, which was shorter in passage.

Specific kinetics of passage and piaffe were analyzed on experienced horses using the Equimetrix system. Mean dorsoventral and longitudinal acceleration vectors were measured during the exercise. At the passage, the mean acceleration vector shows that the largest component of propulsion is dorsoventral instead of longitudinal as it is in the extended or working trot. The high collection of passage transforms forward propulsion into upward propulsion. The greatest propulsive activity in passage is from the forelimbs, while the hindlimbs provide for braking.

At the piaffe, the amplitude of dorsoventral acceleration during the stance phase is lower than at the passage because the amplitude of dorsoventral displacement is reduced. Hindlimbs have greater braking activity to avoid forward movement of the body. The forelimbs have moderate dorsoventral propulsion. The same type of results was observed in a horse at the piaffe with a force plate.[98] However, at the passage the longitudinal ground reaction force of the hindlimbs was higher than in the forelimbs.

The canter At slow speed the canter is a three-beat gait. At the canter, the diagonal stance phase is synchronized while at the gallop the footfalls of the diagonal are dissociated. The speed of the canter increases from the collected, to working, medium and extended canter by increasing stride length. While stride length increases, stride frequency remains nearly constant.[95] Stride length increase is due to increase of diagonal step length and distance covered during suspension.

Relationships between the total dressage competition score and canter characteristics in Olympic dressage horses revealed that the best horses were able to extend their canter strides by increasing their stride length without changing their stride frequency.[99] For three-day event horses at the Olympic games, extended canter stride length and velocity were positively associated with points awarded by judges. However, non-finishers of the event had higher extended canter stride lengths and velocities in the dressage phase than finishers.[100]

The lead change is the transition between the footfall sequence of two different canter leads. Normally the hindlimb sequence changes first, then the front limb sequence. In dressage the rider can elicit the canter lead change during the suspension phase. In a bad lead change, the change in forelimb placements occurs before the change of the hindlimbs, resulting in a disunited canter, which may be observed for

several strides. The canter during the two and one tempi lead change is slow (3.35–3.95 m/s) with a short stride length (2.08–2.44 m) and a stride frequency of 1.62 strides/s.[101] Two tempi changes result in a change in the canter lead every other stride and one tempi change results in canter lead changes on every stride.

During the canter pirouette, the canter footfall sequence is altered. The cadence is reduced from 1.58 stride/s at the collected canter to 1.13 stride/s.[96] The diagonal support is entirely dissociated and there is no suspension phase.

The walk In dressage horses, the speed of the walk increases from the collected walk (1.37 m/s) to the extended walk (1.82 m/s) and simultaneously there is a little increase in stride frequency.[54] The speed change was mainly the result of the stride lengthening by increasing the overtracking distance. Even in horses trained for dressage, the regular four-beat rhythm of the footfall was observed only in one of the six horses evaluated. The stride regularity could be assessed by dorsoventral acceleration recording. Extended walk has a more regular pattern than collected walk where the footfall sequence is slightly disturbed by the actions of the rider. Elite dressage horses usually have a very regular acceleration pattern at the walk. This is a sign of a high level of co-ordination and stability in the rhythm of footfall sequence.

Gait transitions A study of transitions from trot to walk showed a positive correlation between a higher level of training and a 'clean' transition without a short intermediate step.[60] The combination of gait analysis by accelerometric measurement and wavelet analysis allowed quantification of some of the temporal and kinetic characteristics of gait transitions.[61] Transition duration, dorsoventral activity and frequency were specific to each transition. Training improved smoothness of braking deceleration and frequency changes with a longer transition duration.

The transition duration increased significantly with training for trot–walk, canter–halt and canter–trot transitions. The lengthening of the transition duration allowed a slow decrease of stride frequency (canter–trot transition) and a smooth decrease of vertical activity (canter–halt and trot–halt transition). The rider adapted his technique to locomotion and training level of the horse. By lengthening transition duration, experienced horses could perform a smooth deceleration. In contrast, young horses could not adequately prepare their gait transition and suddenly brake their forward motion, which produced a high peak of deceleration. The amplitude of frequency change during the gait transition decreased with training for all transitions, especially for canter–halt and trot–walk transition.

Three-day eventing

The analysis of the gallop stride characteristics of three-day event horses during the steeplechase of the Seoul Olympic Games revealed optimal values for successful performance. The optimal stride length should range between 1.85 and 2.05 m while the optimal velocity should range between 13 and 14.3 m/s.[102]

Biomechanics of the hoof and lameness prevention in the athletic horse

Effects of the track

The kinetics of hoof impact is an interesting subject for lameness prevention because a relationship between repeated exposure to shock and the onset of chronic injuries has been established in human medicine[103] and in animal models.[104,105] The shoes and the track surface can be designed in order to minimize hoof shock intensity, especially for race and showjumping horses which undergo very large hoof decelerations at high speeds and landing, respectively. Hoof shock and vibration acceleration measurements after the moment of impact on the ground were used for testing the influence of the track surface on shock and vibration intensity of hoof impact at the trot.[34] The shock of deceleration can reach 707 m/s^2 on asphalt and 31 m/s^2 on sawdust mixed with sand. The subsequent transient vibrations have frequencies between 592 Hz and 41 Hz, respectively. The stiffness of the track surface directly influences these mechanical parameters and should be controlled to minimize vibration damage. In horses, as in human athletes, damping hoof impact with viscoelastic shoes and a soft track surface is useful to prevent overuse injuries of the distal joints.

Improvements in race track designs and surfaces for race horses exemplify the application of research for the betterment of horses and the racing industry. The limb kinematic studies on Standardbreds trotting on various types of race tracks (length, curves) made it possible to propose some recommendations regarding the ideal geometry for race tracks (Fig. 12.12).[106,107] The most important factor affecting comfort is the total length of the track, which determines the curve length and the horses' inclination to avoid any load disequilibrium between the lateral and medial sides of the limbs.

Effects of shoeing

Many shoeing techniques are available but any assumption concerning their effects on hoof biomechanics should be verified experimentally by locomotion analysis studies. The limb kinematics of six sound horses was studied at trot in hand to determine the effect of long toes and acute hoof angles.[108] In this study, no lengthening of the trotting strides was observed after reducing the hoof angle about 10° from the normal value. However, this hoof angle change resulted in toe-first impact and prolonged breakover, both of which are potentially disadvantageous for athletic performance and may predispose the horse to injury. In another study, the effect of an acute angulation of the hind hooves showed some changes in the limb co-ordination which could be interesting for reducing limb interference. The hind hoof breakover can be prolonged and the lift-off of the hindlimbs delayed, which could prevent interference with the ipsilateral forelimb.

Hoof shock and vibration acceleration measurements after the moment of impact on the ground were used to investigate the damping capacity of various hoof pads and shoes.[35] Compared to the reference steel shoe, shock

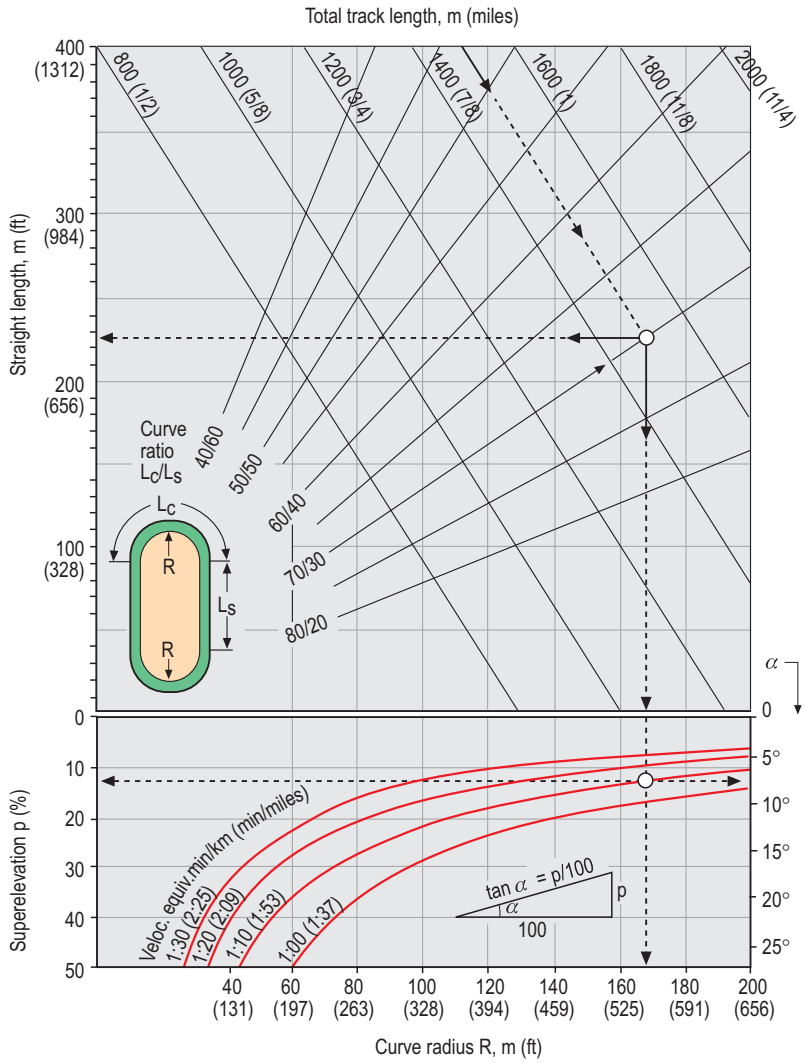

Fig. 12.12
Relationship between the geometric characteristics of a track with semicircular curves. Given a track length of 1500 m and a curve ratio (ratio of curve length to straight length) of 70/30, the length of each straight is read as 225 m and the curve radius as 167 m. For a velocity equivalent of 1:10 min/km the superelevation of the curve is read off on the scale as approximately 12.5% or 7°. (Reproduced from Fredricson et al.[106] with permission.)

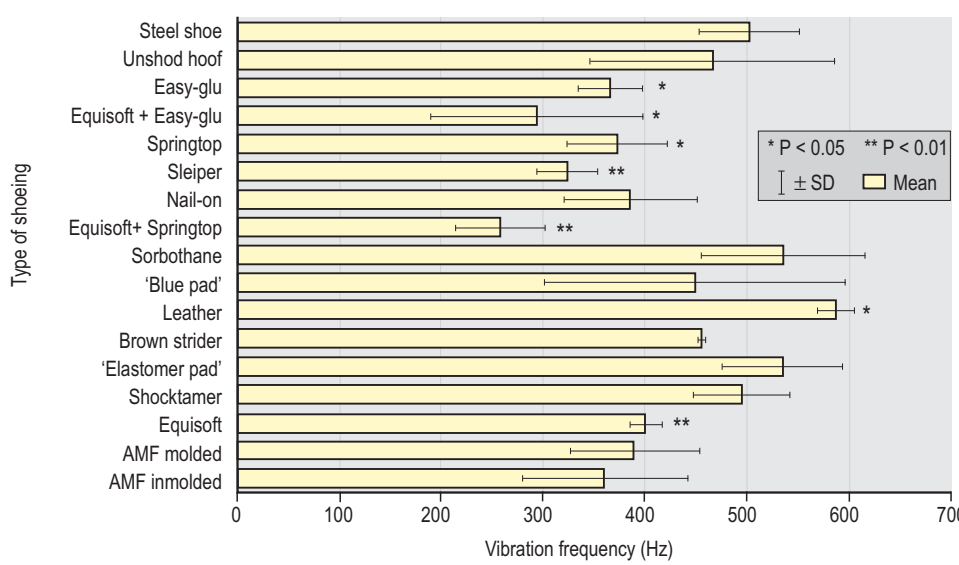

Fig. 12.13
Comparison of the hoof vibration recorded by an accelerometer at the trot on an asphalt road with different types of shoeing (shoe and pads). Better damping of the hoof vibrations after impact was observed with light shoes and soft pads. (Reproduced from Benoit et al.[35] with permission.)

reduction was higher for light shoes made of a polymer and/or aluminum alloy which had lower stiffness values and density than steel (Fig. 12.13). The use of viscoelastic pads contributed to shock reduction and attenuated the high-frequency vibrations up to 75%.

Damping hoof impact with viscoelastic shoes and a soft track surface is useful to prevent orthopedic overuse injuries of the distal joints. The shock damping potential of the track surface is higher than that of the shoes but when the track surface is too hard, the use of damping shoes is highly recommended for horses.

References

1. Jeffcott LB, Rossdale PD, Freestone J, et al. An assessment of wastage in Thoroughbred racing from conception to 4 years of age. Equine Vet J 1982; 14:185–198.
2. Rossdale PD, Hopes R, Wingfield Digby NJ, Offord K. Epidemiological study of wastage among racehorses 1982 and 1983. Vet Rec 1985; 11:66–69.
3. Fredricson I, Drevemo S, Dalin G, et al. The application of high-speed cinematography for the quantitative analysis of equine locomotion. Equine Vet J 1980; 12:54–59.
4. Langlois B, Froideveaux J, Lamarche L, et al. Analyse des liaisons entre la morphologie et l'aptitude au gallop, au trot et au saut d'obstacles chez le cheval. Annales de Génétique et de Sélection Animale 1978; 10:443–474.
5. Leach DH, Cymbaluk NF. Relationship between stride length, stride frequency, velocity and morphometrics of foals. Am J Vet Res 1986; 47:2090–2097.
6. Leach DH, Dyson S. Instant centres of rotation of equine limb joints and their relationship to standard skin marker locations. Equine Vet J 1988; 20(suppl 6):113–119.
7. Schamhardt HC, van den Bogert AJ, Hartman W. Measurement techniques in animal locomotion analysis. Acta Anat 1993; 146:123–129.
8. van Weeren PR, van den Bogert AJ, Barneveld A. A quantitative analysis of skin displacement in the trotting horse. Equine Vet J 1990; 22(suppl 9):101–109.
9. van Weeren PR, van den Bogert AJ, Barneveld A. Quantification of skin displacement in the proximal parts of the limbs of the walking horse. Equine Vet J 1990; 22(suppl 9):110–118.
10. Drevemo S, Johnston CJ. The use of a panning camera technique in equine kinematic analysis. Equine Vet J 1993; 25(suppl 17):39–43.
11. van Weeren PR, van den Bogert AJ, Barneveld A, et al. The role of the reciprocal apparatus in the hind limb of the horse investigated by a modified CODA-3 optoelectronic kinematic analysis system. Equine Vet J 1990; 22(suppl 9):95–100.
12. Peloso JG, Stick JA, Soutas-Little RW, et al. Computer assisted three dimensional gait analysis of amphotericin-induced carpal lameness in horses. Am J Vet Res 1993; 54:535–543.
13. Degeurce C, Dietrich G, Pourcelot P, et al. Three dimensional kinematic technique for evaluation of horse locomotion in outdoor conditions. Med Biol Engin Comp 1996; 34:1–4.
14. Holmström M, Fredricson I. High speed cinematographic gait analysis in riding horses. Proceedings of the 43th European Association for Animal Production – Horse Commission H 1; 1992:540–541.
15. Galloux P, Barrey E. Components of the total kinetic moment in jumping horses. Equine Vet J 1997; 29(suppl 23):41–44.
16. Springings EJ, Leach DH. Standardised technique for determining the center of gravity of body and limb segments of horses. Equine Vet J 1986; 18:43–49.
17. Kubo K, Sakai T, Sakuraoka H, Ishii K. Segmental body weight, volume, mass center in Thoroughbred horses. J Equine Sci 1992; 3:149–155.
18. Marey EJ, ed. La machine animale: locomotion terrestre et aérienne, 2nd edn. Paris: Librairie Gerner Baillere et Cie; 1873:145–186.
19. Pratt GW, O'Connor JT. A relationship between gait and breakdown in the horse. Am J Vet Res 1978; 39:249–253.
20. Quudus MA, Kingsbury HB, Rooney JR. A force and motion study of the foreleg of a Standardbred trotter. J Equine Med Surg 1978; 2:233–242.
21. Ueda Y, Niki Y, Yoshida K, Masumitsu H. A force plate study of equine biomechanics: floor reaction force of normal walking and trotting horses. Bull Equine Res Inst 1981; 18:28–41.
22. Schamhardt HC, Merkens HW, van Osch GJVM. Ground reaction force analysis of horses ridden at the walk and trot. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology, 3rd edn. Davis, CA: ICEEP Publications; 1991:120–127.
23. Merkens H. Quantitative evaluation of equine locomotion using force plate data. Dissertation, State University Utrecht, The Netherlands; 1987.
24. Weishaupt MA, Hogg HP, Wiestner T et al. Development of a technique for measuring ground reaction force in the equine on a treadmill. Third International Workshop on Animal Locomotion; 1996:1.
25. Weishaupt MA, Wiestner T, Hogg HP, et al. Assessment of gait irregularities in the horse: eye vs. gait analysis. Equine Vet J 2001; 33(suppl 33):135–140.
26. Björck G. Studies on the draught force of horse: development of a method using strain gauges for measuring between hoof and ground (PhD thesis). Acta Agri Scan 1958(suppl 4): 1–109.
27. Frederick FH Jr, Henderson JM. Impact force measurement using preloaded transducers. Am J Vet Res 1970; 31:2279–2283.
28. Ratzlaff MH, Grant BD, Frame JM, Hyde ML. Locomotor force of galloping horses. In: Gillespie JR, Robinson RE, eds. Equine exercise physiology, 2nd edn. Davis, CA: ICEEP Publications; 1987:574–586.
29. Barrey E. Investigation of the vertical hoof force distribution in the equine forelimb with an instrumented horseboot. Equine Vet J 1990; 22(suppl 9):35–38.
30. Roepstorff L, Drevemo S. Concept of a force-measuring horseshoe. Acta Anat 1993; 146:114–119.
31. Savelberg HCM, Vostenbosch MATM, Kamman EH, et al. The effect of intra-stride speed variation on treadmill locomotion. Proceedings of the 2nd World Congress of Biomechanics; 1994.
32. Barrey E, Hermelin M, Vaudelin JL, et al. Utilisation of an accelerometric device in equine gait analysis. Equine Vet J 1994; 26(suppl 17):7–12.
33. Galloux P, Richard N, Dronka T, et al. Analysis of equine gait using three-dimensional accelerometers fixed on the saddle. Equine Vet J 1994; 26(suppl 17):44–47.
34. Barrey E, Landjerit B, Wolter R. Shock and vibration during the hoof impact on different track surfaces. In: Persson SGB, Lindholm A, Jeffcott B, eds. Equine exercise physiology, 3rd edn. Davis, CA: ICEEP Publications; 1991:97–106.
35. Benoit E, Barrey E, Regnault JC, Brochet JL. Comparison of the damping effect of different shoeing by the measurement of hoof acceleration. Acta Anat 1993; 146:109–113.

36. Burns TE, Clayton HM. Classification of the temporal kinematics of the canter pirouette and collected canter. Equine Vet J 1997; 29(suppl 23):58–61.
37. Buchner HHF, Savelberg HCM, Schamhardt HC, et al. Habituation of horses to treadmill locomotion. Equine Vet J 1994; 26(suppl 17):13–15.
38. Fredricson I, Drevemo S, Dalin G, et al. Treadmill for equine locomotion analysis. Equine Vet J 1983; 15:111–115.
39. van Igen Schenau GJ. Some fundamental aspects of biomechanics of overground versus treadmill locomotion. Med Sci Sports Exerc 1980; 12:257–261.
40. Valette JP, Barrey E, Wolter R. Influence des deux composantes de la vitesse (fréquence et longueur des foulées) sur le métabolisme énergétique musculaire chez le poney. Annale de Zootechnie 1990; 39:187–192.
41. Couroucé A, Geoffroy O, Barrey E, et al. Comparison of exercise tests in French trotters under training track and treadmill conditions. Equine Vet J 1999; 31(suppl 30):528–532.
42. Sloet van Oldruitenborgh-Oosterbaan MM, Barneveld A, Schamhardt HC. Effect of treadmill inclination on kinematics of the trot in Dutch Warmblood horses. Equine Vet J 1997; 26(suppl 23):71–75.
43. Duboy J, Junqua A, Lacouture P. Vers le réexamen d'autres tests d'aptitude physique. In: Mécanique humaine. Paris: Revue EPS; 1994:157–159.
44. Kai M, Hiraga A, Kubo K, Tokuriki M. Comparison of stride characteristics in a cantering horse on a flat and inclined treadmill. Equine Vet J 1997; 29(suppl 23):76–79.
45. Leach DH. Locomotion analysis technology for evalution of lameness in horses. Equine Vet J 1983; 19:97–99.
46. Clayton HM. Terminology for the description of equine jumping kinematics. J Equine Vet Sci 1989; 9:341–348.
47. Leach DH. Recommended terminology for researchers in locomotion and biomechanics of quadrupedal animals. Acta Anat 1993; 146:130–136.
48. Muybridge E. Muybridge's complete human and animal locomotion, vol. 3. New York: Dover Publications; 1887.
49. Clayton HM. Locomotion. In: Jones WE, ed. Equine sports medicine. Philadelphia: Lea and Febiger; 1989:149–187.
50. Lenoble du Teil J. Les allures du cheval dévoilées par la méthode expérimentale. Paris: Berger Levrault; 1893:192–211.
51. Hildebrand M. Symmetrical gaits of horses. Science 1965; 191:701–708.
52. Clayton H. Classification of collected trot, passage and piaffe based on temporal variables. Equine Vet J 1997; 29(suppl 23):54–57.
53. Barrey E, Desbrosse F. Lameness detection using an accelerometric device. Pferdeheilkunde 1996; 12:617–622.
54. Clayton HM. Comparison of the stride kinematics of the collected, medium and extended walks in horses. Am J Vet Res 1995; 56:849–852.
55. Holmström M, Fredricson I, Drevemo S. Biokinematic effect of collection in the elite dressage horse trot. In: Holmström M, ed. Quantitative studies on conformation and trotting gaits in the Swedish Warmblood riding horse (PhD thesis). Dösjebro, Sweden: Hippo Vet AB; 1994:V1–V7.
56. Barrey E, Auvinet B, Couroucé A. Gait evaluation of race trotters using an accelerometric device. Equine Vet J 1995; 27(suppl 18):156–160.
57. Drevemo S, Dalin G, Fredricson I, Hjerten G. Equine locomotion 3: the reproducibility of gait in Standardbred trotters. Equine Vet J 1980; 12:71–73.
58. Leach DH. Locomotion of the athletic horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology, 2nd edn. Davis, CA: ICEEP Publications; 1987:516–535.
59. Leach DH, Ormrod K, Clayton HM. Standardised terminology for the description and analysis of equine locomotion. Equine Vet J 1984; 16:522–528.
60. Argue CK, Clayton HM. A preliminary study of transitions between the walk and trot in dressage horses. Acta Anat 1993; 146(2–3):179–182.
61. Biau S, Lemaire S, Barrey E. Analysis of gait transitions in dressage horses using wavelet analysis of dorsoventral acceleration. Pferdeheilkunde 2002; 4:343–350.
62. Hoyt DF, Taylor CR. Gait and energetics of locomotion in horses. Nature 1981; 292:239.
63. Farley CT, Taylor CR. A mechanical trigger for the trot-gallop transition in horses. Science 1991; 253:306–308.
64. Dusek J, Ehrlein HJ, von Engelhardt W, Hornicke H. Beziehungen zwischen trittlange, trittfrequenz und geschwindigkeit bei Pferden. Zeitschrift fur Tierzuechtung und Zuechtungsbiologie 1970; 87:177–188.
65. Ishii K, Amano K, Sakuraoka H. Kinetics analysis of horse gait. Bull Equine Res Inst 1989; 26:1–9.
66. Hiraga A, Yamanobe A, Kubo K. Relationships between stride length, stride frequency, step length and velocity at the start dash in a racehorse. J Equine Sci 1994; 5:127–130.
67. Leach DH, Springings EJ. Gait fatigue in the racing Thoroughbred. J Equine Med Surg 1979; 3:436–443.
68. Deuel NR, Lawrence LM. Effect of urging by the rider on equine gallop stride limb contacts. Proceedings of the 10th Equine Nutrition and Physiology Symposium; 1987:487–492.
69. Hellander J, Fredricson I, Hertén G, et al. Galloppaktion I – Basala gangartsvariabler i relation till hästens hastighet. Svensk Veterinärtidning 1983; 35(suppl 3):75–82.
70. Attenburrow DP. Time relationship between the respiratory cycle and limb cycle in the horse. Equine Vet J 1982; 14:69–72.
71. Hörnicke H, Meixner R, Pollmam U. Respiration in exercising horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1987:7–16.
72. Art T, Desmecht D, Amory H, Lekeux P. Synchronization of locomotion and repiration in trotting ponies. J Am Vet Med Assoc 1990; 37:95–103.
73. Evans DL, Silverman EB, Hodgson DR, et al. Gait and respiration in Standardbred horses when pacing and galloping. Res Vet Sci 1994; 57:233–239.
74. Persson SGB, Essen-Gustavsson B, Lindholm A. Energy profile and locomotor pattern of trotting on an inclined treadmill. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology, 3rd edn. Davis, CA: ICEEP Publications; 1991:231–238.
75. Roneus N, Essen-Gustavsson B, Johnston C, et al. Lactate response to maximal exercise on the track: relation to muscle characteristics and kinematic variables. Equine Vet J 1995; 26(suppl 18):191–194.
76. Rivero JLL, Clayton HM. The potential role of the muscle in kinematic characteristics. Pferdeheilkunde 1996; 12:635–640.
77. Valette JP, Barrey E, Auvinet B, et al. Comparison of track and treadmill exercise tests in saddle horses: a preliminary report. Annale de Zootechnie 1992; 41:129–135.
78. Back W, van den Bogert AJ, van Weeren PR, et al. Quantification of the locomotion of Dutch Warmblood foals. Acta Anat 1993; 146:141–147.
79. Back W, Barneveld A, Schamhardt HC, et al. Longitudinal development of the kinematics of 4-, 10-, 18- and 26-month-old Dutch Warmblood horses. Equine Vet J 1994; 26(suppl 17):3–6.

80. Back W, Barneveld A, Bruin G, et al. Kinematic detection of superior gait quality in young trotting Warmbloods. Vet Q 1994; 16:S91–96.
81. Corley JM, Goodship AE. Treadmill training induced changes to some kinematic variables measured at the canter in Thoroughbred fillies. Equine Vet J 1994; 26(suppl 17):20–24.
82. Barrey E, Holmström M, Biau S, et al. A new type of early performance test: gait and conformation measurements in 3 year old horses. Proceedings of 50th European Association of Animal Production; 1999.
83. Barrey E, Biau S. Locomotion of dressage horses. Proceedings of Conference on Equine Sport Medicine and Applied Science; 2002.
84. Barrey E, Desliens F, Blouin C, Langlois B. Mesures du modèle, des allures et du saut des étalons nationaux par la méthode Equimétrix. Proceedings of '28ème Journée d'étude', Les Haras Nationaux; 2002:157–176.
85. Galisteo AM, Vivo J, Cano MR, et al. Differences between breeds (Dutch warmblood vs Andalusian Purebred) in forelimb kinematics. J Equine Sci 1997; 8:43–47.
86. Langlois B. Estimation de la valeur génétique des chevaux de sport d'après les sommes gagnées dans les compétitions équestres françaises. Ann Génet Sel Anim 1980; 12:15–31.
87. Bruns E. Estimation of the breeding value of stallions from the tournament performance of their offspring. Livest Prod Sci 1981; 8:465–473.
88. Huizinga HA, van der Meij GJW. Estimated parameters of performance in jumping and dressage competition of the Dutch Warmblood horses. Livest Prod Sci 1989; 21:333–345.
89. Rose RJ, King CM, Evans DL, et al. Indices of exercise capacity in horses presented for poor racing performance. Equine Vet J 1995; 27(suppl 18):418–421.
90. Bayer A. Bewegungsanalysen an Trabrennpferden mit Hilfe der Ungulographie, Zentralblatt fur Veterinarmedizin Reihe A 1973; 20:209–221.
91. Deuel NR, Park J. Kinematic analysis of jumping sequences of olympic show jumping horses. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology, 3rd edn. Davis, CA: ICEEP Publications; 1991:158–166.
92. van den Bogert AJ, Janssen MO, Deuel NR. Kinematics of the hind limb push-off in elite show jumping horses. Equine Vet J 1994; 26(suppl 17):80–86.
93. Clayton HM, Colborne GR, Burns T. Kinematic analysis of successful and unsuccessful attempts to clear a water jump. Equine Vet J 1995; 27(suppl 18):166–169.
94. Barrey E, Galloux P. Analysis of the jumping technique by accelerometry. Equine Vet J 1997; 29(suppl 23):45–49.
95. Clayton HM. Comparison of the collected, working, medium and extended canters. Equine Vet J 1994; 26(suppl 17):16–19.
96. Burns TE, Clayton HM. Comparison of the temporal kinematics of the canter pirouette and collected canter. Equine Vet J 1997; 29(suppl 23):58–61.
97. Holmström M, Fredricson I, Drevemo S. Biokinematic differences between riding horses judged as good and poor at the trot. Equine Vet J 1994; 26(suppl 17):51–56.
98. Clayton HM. Performance in equestrian sport. In: Back W, Clayton H, eds. Equine locomotion. London: Saunders; 2001:211.
99. Deuel NR, Park J. The gait patterns of Olympic dressage horses. Int J Sport Biomech 1990; 6:198–226.
100. Deuel NR. Dressage canter kinematics and performances in an Olympic three-day event. Proceedings of 46th Annual Meeting of the European Association for Animal Production, Horse Commission H-2.3; 1995:341.
101. Deuel NR, Park J. Canter lead change kinematics of superior Olympic dressage horses. J Equine Vet Sci 1990; 10:287–298.
102. Deuel NR, Park J. Gallop kinematics of Olympic three-day-event horses. Acta Anat 1993; 146:168–174.
103. Taylor W, Brammer AJ. Vibration effects on the hand and arm in industry: an introduction and review. In: Brammer AJ, Taylor W, eds. Vibration effects on the hand and arm in industry. New York: Wiley-Interscience; 1982:1–12.
104. Radin EL, Parker HG, Pugh JW, et al. Response of joint to impact loading. III Relationships between trabecular microfractures and cartilage degeneration. J Biomech 1973; 6:51–57.
105. Radin EL, Martin RB, Burr DB, et al. Effects of mechanical loading on the tissues of the rabbit knee. J Orthop Res 1984; 2:231–234.
106. Fredricson I, Dalin G, Drevemo S, Hjerten G. A biotechnical approach to the geometric design of racetracks. Equine Vet J 1975; 7:91–96.
107. Drevemo S, Hjerten G. Evaluation of shock absorbing woodchip layer on a harness race-track. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology, 3rd edn. Davis, CA: ICEEP Publications; 1991:107–112.
108. Clayton HM. Comparison of the stride of trotting horses trimmed with a normal and a broken-back hoof axis. Proceedings of the 33rd Annual Convention of the American Association of Equine Practitioners 1987; 289–299.

CHAPTER 13

Kinematics of lameness

Joanne Kramer and Kevin G. Keegan

Introduction

Lameness is a frequent problem in the horse and the ability to detect lameness by observing movement is a skill that must be acquired by the equine clinician. With practice and experience equine clinicians develop this skill by recognizing how certain patterns of movement of the body and limbs correlate with lameness. However, there is no set of universally accepted rules about what to observe or how important different movements are in correctly evaluating lameness. We are all trained somewhat differently to identify lameness and this contributes to diversity in the developed skills of lameness recognition between equine clinicians.

It is not difficult to correctly detect and identify the affected limb in a lameness of moderate to severe intensity. There is little disagreement among equine clinicians and the diversity in our training poses little difficulty in these cases. However, when examining horses with intermittent lameness, lameness of mild intensity, or shifting-limb lameness, the diversity in our lameness training results in confusion, disagreement and, ultimately, disparate diagnosis. Even between skilled equine clinicians, interindividual agreement in recognition of mild to moderate lameness and the designation of the correct lame limb have been shown to be poor.[1] The success of treatments for various lameness conditions has traditionally been based on subjective evaluations, imprecise lameness scores computed by few individuals or broad classifications of recovery such as return to function. These evaluative techniques are all potentially influenced by numerous factors unrelated to lameness severity. A more objective methodology to detect and quantify lameness would make lameness evaluations more scientific and thus more reliable.

Kinematic gait analysis is an objective measurement of body movement. The movement is captured with video or cine cameras and a quantitative analysis of that movement is performed. Kinematic gait analysis can be used to detect and quantify lameness without the bias inherent in subjective evaluation. In its simplest form it allows the examiner to record history and compare movement at different points in time. Small differences in movement between separate examinations become apparent with simultaneous, side-by-side comparison of the different time periods. Also, most kinematic gait analysis techniques utilize cameras with high spatial resolution (< 1 mm), high frame rates (> 60 frames per second) and some form of computer-aided data collection and analysis. The high frame rates of the cameras plus the ability to review the motion at slower than normal speed improves the temporal resolution of the examiner. Increased temporal and spatial resolution enables one to detect small changes in stride parameters caused by lameness that would not normally be seen by simple observation alone.

Kinematic gait analysis technique is also conducive to evaluating numerous strides contiguously, a quality that is lacking in more traditional stationary force plate analysis of limb weight bearing. This enables a more accurate evaluation of lameness when there is significant stride-to-stride variance, a common finding in horses with bilateral lameness or lameness of mild severity (Keegan, unpublished data). Multiple measurements of multiple parameters can be made at the same time. Parameter relationships can be studied; for

example, how head or pelvic movement varies with footfall sequence. Changing relationships among multiple kinematic parameters may correlate significantly with lameness.

More importantly, kinematic gait analysis is fundamentally practical because it is intuitive. When equine clinicians evaluate lameness in the field they evaluate movement. We see movement (a kinematic measurement) directly. Force (a kinetic measurement) must be transduced for human perception. Therefore, what we learn about movement and how it changes with lameness can be easily described, taught and learned. Kinematic evaluation closely resembles the techniques used by equine clinicians and thus can be used to improve their understanding and clinical detection of lameness.

Although movement compensation occurs with lameness during many gaits, the ideal gait for kinematic evaluation is the trot. The trot is a symmetrical gait with simultaneous contralateral forelimb and hindlimb placement in each half-cycle of the full stride. Vertical movement of the body is sinusoidal with equivalent amplitudes in each half-cycle. One of the most characteristic features of lameness is its tendency to upset the simple periodicity of normal movement. This perturbation of movement is most easily appreciated at the trot against the normal background of symmetrical vertical movement. In addition, the total vertical movement of the trunk's center of gravity, and thus the resulting forces placed on the limbs during weight bearing, is greater during the trot than at a walk or canter.[2–4] Lameness exacerbated by weight bearing, which includes the majority of lameness in the horse, would therefore be more expressed at the trot than at a walk or canter. In this chapter the kinematic changes referred to as representative of lameness are those primarily observed and measured at the trot.

Methodology

The basic methodology of kinematic gait analysis requires that the horse be 'filmed' while moving. To facilitate calculations of kinematic parameters, the horse is 'marked', usually with light-reflective spheres, over specific body parts such as easily recognizable bony landmarks or joint centers (Fig. 13.1). Each camera used during filming generates two-dimensional images of the positions of the body markers. Multiple cameras set up with different fields of view generate multiple, two-dimensional images of the positions for each marker (Fig. 13.1). These images are then transformed into a sequence of three-dimensional positions for each marker. Data generation rate is high. For example, using cameras that capture at 120 frames per second, a horse marked with 20 light-reflective spheres, filmed for 30 seconds, will generate 216 000 ($120 \times 20 \times 30 \times 3$[$x$, y, z position]) pieces of data that precisely describe the horse's movement over that time period. From these data many different measurements relevant to the horse's movement (joint angle, maximum vertical head position, stride length, etc.) can be calculated.

Most kinematic systems, because of the need for processing and computation of large volumes of data, are computer assisted. Also, standard systems require the horse to move within the camera's limited fields of view. Therefore, most kinematic analysis is performed with the horse moving on a treadmill. This has an advantage of providing for the capture of multiple, consecutive strides of the horse traveling at a precisely controlled velocity. Controlling velocity of movement is necessary since many kinematic parameters are known to be velocity dependent.

Kinematic parameters of importance for the detection of lameness

It is not the purpose of this chapter to give a past synopsis of movement parameters thought to correlate with lameness. Much of what has been described in textbooks is subjective expert opinion. However, until recently much of this expert opinion was either inadequately described or misleading. One only has to try to define and then reconcile the term 'hip hike', a frequent descriptor of hindlimb lameness in horses,[5,6] with pelvic 'sinking' or excessive rotation towards the side of lameness that is described in other reports.[7,8] Some clinicians evaluate the 'head bob' as greater upward movement of the head during the stance phase of the lame limb[6] and others evaluate it as less downward movement during the stance phase of the lame limb.[9] Some evaluate

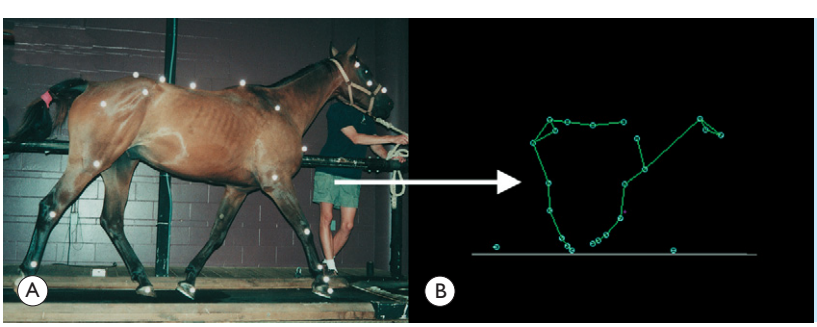

Fig. 13.1
Basic kinematic gait analysis methodology. (A) The horse is marked and filmed. (B) Data from multiple cameras are combined, resulting in the three-dimensional location of each marker in each video frame. Three-dimensional positional data for each marker are available for calculation of different kinematic parameters.

stride length and detect lameness when the length of stride seems to be short.[10] The shape of the hoof flight arc is said to be representative of lameness.[10] Joint angle excursions, during both the stance and swing phase of the stride, have been purported to be accurate indicators of lameness.[8,9,11] Recent objective evaluations have indicated that many of these parameters are either incorrect or, at best, insensitive.[12–14]

In this chapter we emphasize the parameters that are clearly significant and sensitive as indicators of lameness and that are easily seen by the unaided human eye. This necessitates a thorough description of the pattern of head movement for forelimb lameness and of pelvic movement for hindlimb lameness. All of the information necessary to detect lameness and identify it to the correct limb can be found in evaluation of the head and pelvic movement. For completeness, short descriptions of other kinematic parameters that have objectively been shown to correlate with lameness are described. We leave it to the reader to decide whether these other parameters are useful in detecting lameness in a standard clinical lameness examination.

Kinematic parameters used to detect and differentiate forelimb lameness

Vertical head movement

When the horse is trotting its head moves up and down twice during one complete stride. The head reaches a local maximum vertical position just before hoof contact of one forelimb and a local minimum vertical position near midstance of the same forelimb. Second local maximum and local minimum vertical positions are reached just before foot contact and at midstance of the other forelimb. In the sound horse the total vertical head excursion during the right and left forelimb stance phases is approximately equal so the local maximums and minimums are approximately the same heights relative to the ground.

Thus, the head moves up and down in a sinusoidal, temporally symmetrical pattern, with amplitude equivalent cycles corresponding to each half of the full stride cycle (Fig. 13.2). The familiar 'head nod', as an indicator of forelimb lameness in horses, is a disruption of this symmetrical movement. In most weight-bearing lameness conditions the downward head movement during weight bearing of the painful limb is reduced compared to that in the sound limb (Fig. 13.3). With increasing severity of lameness there is more reduction in the downward movement of the head (Fig. 13.4). With severe lameness there may be no downward movement of the head during the stance phase of the lame limb and with very severe lameness the head may actually move upward during the stance phase of the lame limb.

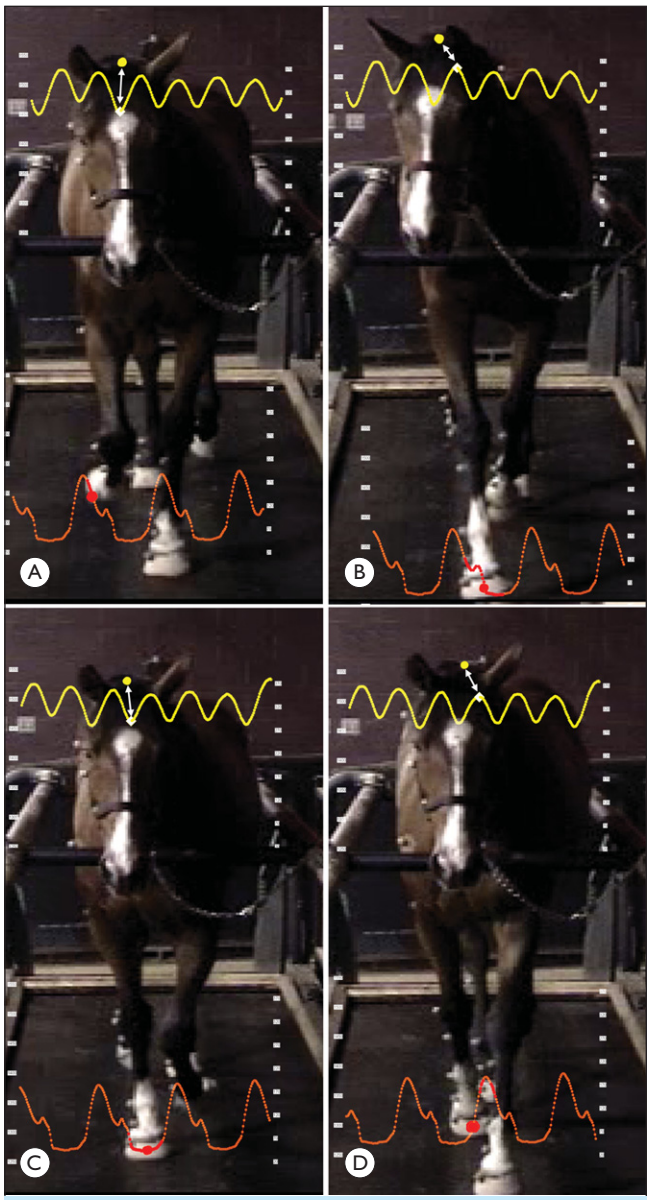

Fig. 13.2
Video frames and graphs depicting vertical head and right forelimb foot movement in a sound trotting horse. (A) First vertical minimum at midstance of the left forelimb. Right forelimb is at midswing. (B) First vertical maximum just after lift-off of the left forelimb foot and just before impact of the right forelimb foot. (C) Second vertical minimum at midstance of the right forelimb. Left forelimb is at midswing. (D) Second vertical maximum just after lift-off of the right forelimb foot and just before impact of the left forelimb foot. Curves at the top of each video frame (yellow) are the vertical head position. Arrows indicate points on the curve corresponding to video frame shown. Curves at the bottom of each video frame (orange) are the vertical position of the right forelimb foot. Orange circles on curve indicate the points corresponding to the video frame shown. Head and right forelimb foot heights are not in same scale. Approximately three full strides are indicated by the curves.

For purposes of categorization we have labeled lameness manifest by less downward movement of the head in the

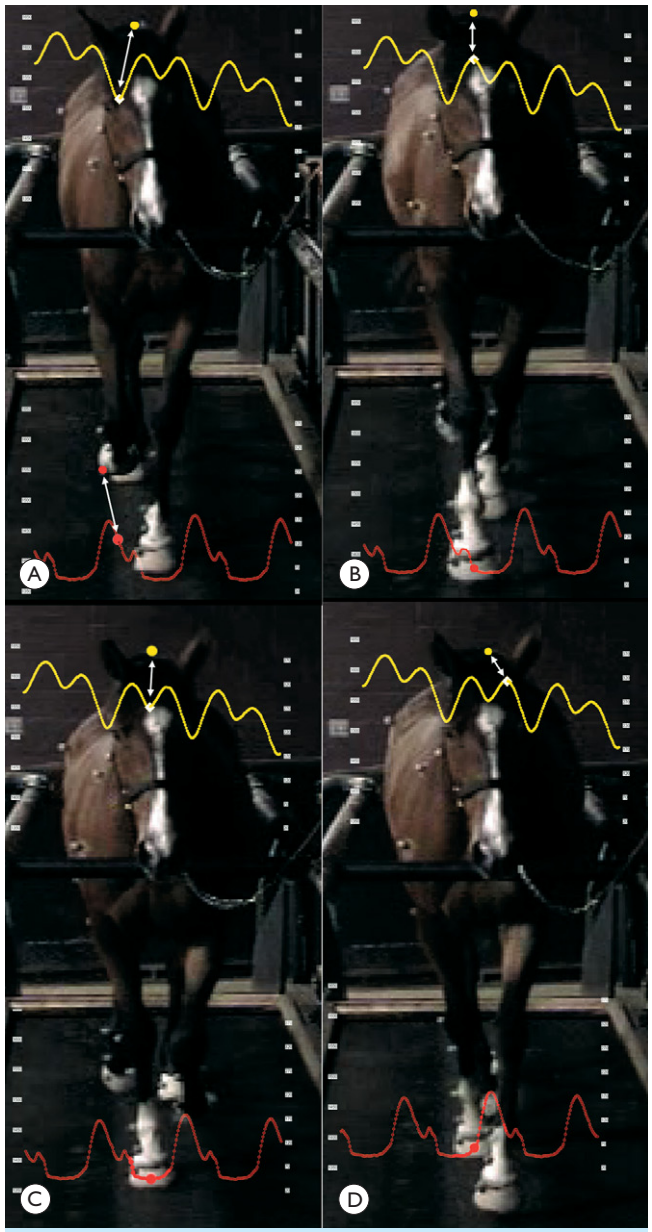

Fig. 13.3
Video frames and graphs depicting vertical head and right forelimb foot movement in a trotting horse with a unilateral (right) type-1 induced forelimb lameness. (A) First vertical minimum is lowest at midstance of the left forelimb. Right forelimb is at midswing. (B) First vertical maximum just after lift-off of the left forelimb foot and just before impact of the right forelimb foot. (C) Second vertical minimum at midstance of the right forelimb. Left forelimb is at midswing. There is less downward movement of the head compared to the minimum in left forelimb stance. (D) Second vertical maximum just after lift-off of the right forelimb foot and just before impact of the left forelimb foot. Curves at the top of each video frame (yellow) are the vertical head position. Arrows indicate points on the curve corresponding to video frame shown. Curves at the bottom of each video frame (orange) are the vertical position of the right forelimb foot. Orange circles on curve indicate the points corresponding to the video frame shown. Head and right forelimb foot heights are not in same scale. Approximately three full strides are indicated by the curves.

stance phase of the lame limb as type-1 lameness. Frequently in horses with type-1 lameness there is also less upward movement of the head at the end of the stance phase of the lame limb (Fig. 13.4). The majority of horses with weight-bearing lameness exhibit type-1 lameness. Sometimes during a clinical examination it is easier to appreciate the greater downward movement of the head during the stance phase of the normal or least lame forelimb. 'Down on sound' is an aphorism frequently used to describe this phenomenon.

Occasionally horses with forelimb lameness will have greater upward movement of the head at the end and shortly following the stance phase of the lame forelimb (Fig. 13.5). We have labeled lameness with this variant of head movement as type-2 lameness. Type-2 lameness is much less common than type 1. Horses with pain occurring during the breakover portion of stance may more likely exhibit type-2 lameness, although this has not been confirmed objectively. Also, display of type-2 lameness may be more idiosyncratic, possibly related to an individual's pain tolerance or threshold. It seems also that there is a higher incidence of type-2 lameness with lameness of increasing severity.

In the authors' opinion vertical head position is the most applicable and accurate movement parameter for use in clinical examination of forelimb lameness. It can be evaluated equally from the front or side of the horse. It is frequently exacerbated and made more apparent at the beginning (when the horse is accelerating) and end (when the horse is decelerating) of a short trot and when lunging the horse in short circles. However, conditions sometimes arise that make evaluation using this parameter more difficult. The asymmetrical nature of the vertical head movement in some mild lameness conditions may not occur at every stride. As the intermittent nature of the lameness increases, the need to evaluate increasing numbers of strides becomes more important and the ability to detect overall asymmetric head movement becomes more difficult. In addition, extraneous head movement, especially in the curious or excitable horse in an unfamiliar environment, may obscure small perturbations in vertical head movement. It is especially important not to jump to conclusions after a few strides and instead try to determine the overall predominant head movement pattern before committing oneself to a final decision. Algorithms to remove extraneous vertical head movement have been described and can be used in objective analysis of kinematic data to increase accuracy in detection of lameness.[15]

Temporal parameters (stance phase, swing phase and breakover durations)

Stance phase begins at hoof impact and ends after breakover, when the toe is lifted from the ground to start the swing phase of the stride. It is instinctive to suppose that stance-phase duration should be less in a lame compared to a sound limb and that it should decrease as lameness

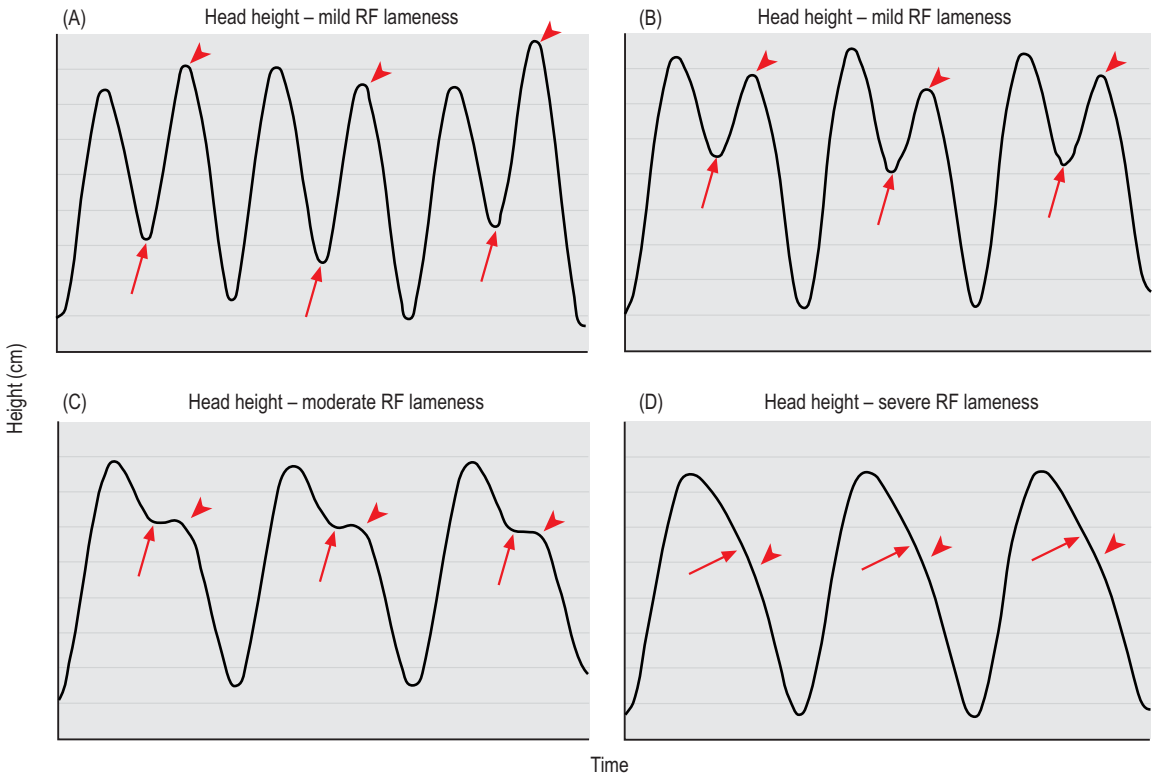

Fig. 13.4
Vertical head movement asymmetry with increasing severity of forelimb lameness. (A–C) Amount of downward movement during the stance phase of the lame limb becomes less and less, until (D) minimum vertical position during stance phase of lame limb disappears. Arrows indicate approximate time of lame (right) forelimb midstance. Arrowheads indicate corresponding decreasing elevation of the head after the stance phase of the lame (right) forelimb.

worsens. After all, a horse with a non-weight-bearing lameness spends no time on the affected leg. However, except for horses with severe lameness, the opposite occurs. In horses with mild to moderate lameness, stance-phase duration is increased compared to the contralateral sound limb.[9] Consequently, stance-phase duration decreases after alleviation of lameness, such as after a regional nerve or joint block.[13] This correlation between stance-phase duration and severity of lameness, however, is true only if the horse is constrained to move at the same forward velocity before and after treatment. Ensuring the same velocity before and after treatment is not easy without special equipment and therefore is not reliable enough for practical purposes of subjective lameness observation.

Stance-phase duration increases in horses with mild to moderate lameness as a direct consequence of the horse attempting to lessen peak loads on the affected limb.[16] When a horse is trotting at a particular velocity a resultant force is applied to the affected limbs. Some force is relieved from the affected forelimb by shifting of weight to the contralateral hindlimb, but the amount is small and inconsequential in horses with mild to moderate lameness.[17,18] Therefore, the only way available to the horse to reduce peak load on the affected limb (and therefore ostensibly to reduce pain) is to spread the total load over a longer period of time.

Despite being a good indicator of lameness, it is doubtful that subjective measurement of stance-phase duration would be of much use to the equine practitioner in the field. In a horse trotting at about 4 m/s the stance duration is less than 1 second and the increase in stance duration with moderate lameness is less than 20 ms.[13] Changes in duration of such small magnitude cannot be appreciated by simple observation.

As a direct consequence of an increase in stance-phase duration in mild to moderate lameness, there is an equivalent decrease in the swing-phase duration.[12] This may be more readily apparent during direct observation of a trained eye than the increased stance-phase duration. The decreased swing-phase duration may cause the observer to think that there is a decrease in the length of the stride or in the swing-phase height of the foot, two parameters commonly associated with lameness. It has also been shown that with unilateral forelimb lameness there is a shortened suspension-phase duration (the time during the stride when no feet are in contact with the ground) after the stance phase of the lame limb.[19] This asymmetry in suspension-phase duration is generally not present with hindlimb lameness.[19]

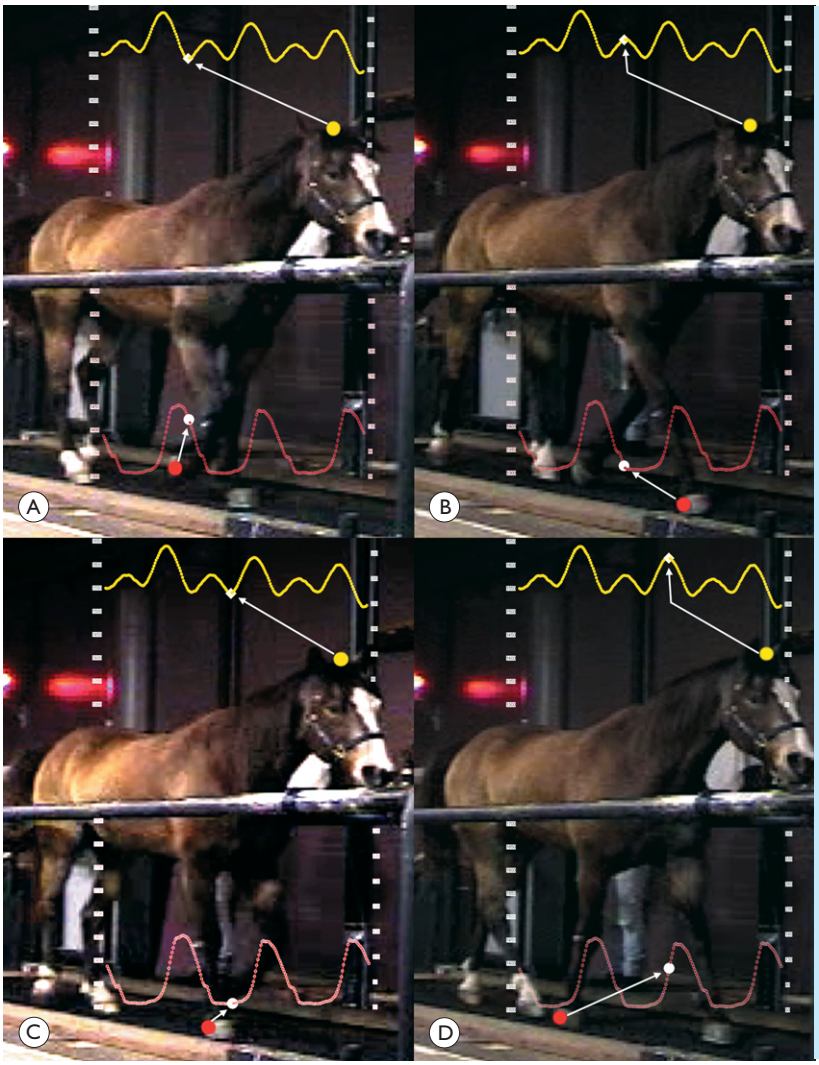

Fig. 13.5
Video frames and graphs depicting vertical head and right forelimb foot movement in a trotting horse with a unilateral (right) induced type-2 forelimb lameness. (A) First vertical minimum at midstance of the left forelimb. Right forelimb is at midswing. (B) First vertical maximum just after lift-off of the left forelimb foot and just before impact of the right forelimb foot. (C) Second vertical minimum at midstance of the right forelimb. Left forelimb is at midswing. (D) Second vertical maximum just after lift-off of the right forelimb foot and just before impact of the left forelimb foot. Head vertical position is at the highest point in the stride. Curves at the top of each video frame (yellow) are the vertical head position. Arrows indicate points on the curve corresponding to video frame shown. Curves at the bottom of each video frame (orange) are the vertical position of the right forelimb foot. Arrows indicate points on curve corresponding to the video frame shown. Head and right forelimb foot heights are not in same scale. Approximately three full strides are indicated by the curves.

An important limitation to remember when using these parameters is the changing velocity of the horse between sessions of a lameness examination. All temporal gait parameters are velocity dependent. When lame, the horse will naturally attempt to travel at a slower velocity. After a successful nerve or joint block and alleviation of the pain the horse will then naturally be more comfortable at a higher velocity. The handler may inadvertently increase forward velocity between evaluation sessions or the horse may move faster because of pain alleviation. An increase in velocity after alleviation of pain may be noticeable as an increased willingness of the horse to move, an inexact but subjective supporting piece of evidence indicating lameness improvement that is generally appreciated by the examiner.

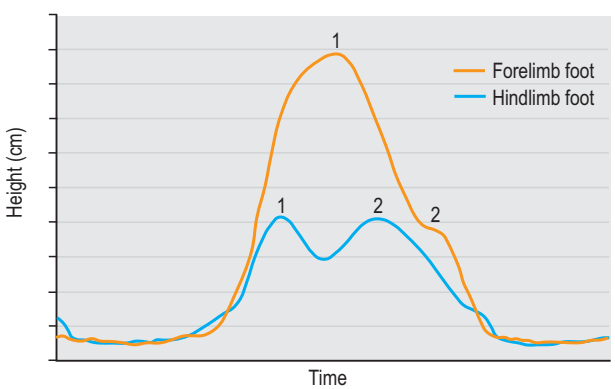

Fig. 13.6
Typical foot-flight pattern in the forelimb and hindlimb. Forelimb foot-flight pattern has a predominant peak (1) just before midswing and sometimes a small peak (2) at the end of the swing phase of the stride. Hindlimb foot-flight pattern has two prominent peaks, (1) the first within the first half and (2) the second in the last half of the swing phase of the stride.

Hoof movement in the swing phase of the stride (foot-flight pattern, swing-phase height, limb protraction and retraction)

Hoof flight pattern in the forelimb[20] is different from that in the hindlimb (Fig. 13.6). In the forelimb, maximum hoof height occurs before midswing and then gradually lowers as the foot moves toward impact, sometimes having a second, smaller peak at the end of the swing phase of the stride. In the hindlimb, maximum hoof height frequently also occurs before midswing, but it is followed by a lowering of the foot at midswing and a second prominent peak in the second half that may be almost as high as the peak in the first half of the swing phase of the stride.

There is much confusion concerning the effect of lameness on hoof movement in the horse during the swing phase of the stride. In experimentally induced forelimb lameness, an absolute higher hoof flight arc is seen in the sound limb with no change in the lame forelimb.[12] In experimentally induced hindlimb lameness, an absolute lower hoof flight arc is seen in the lame hindlimb with no change in the sound hindlimb.[12] Both of these combinations give rise to the impression of lower hoof flight arc with lameness.

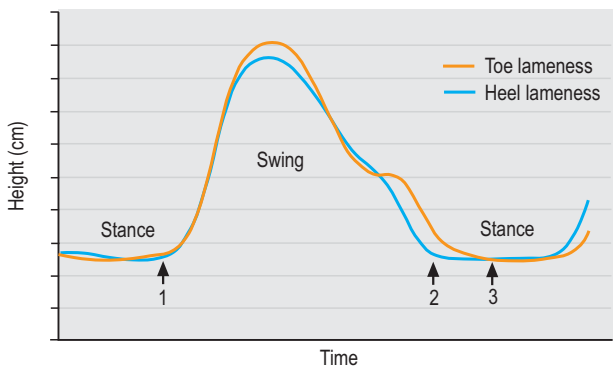

Fig. 13.7
Forelimb hoof-flight pattern after induction of toe and heel lameness. (1) Breakover is lined up in time to show the increased protraction with toe lameness. (2) Hoof impact after heel lameness. (3) Hoof impact after toe lameness.

Fig. 13.8
Fetlock extension at midstance (limb axis perpendicular to the ground). Dorsal angle decreases as fetlock extends.

However, there are over-riding biomechanical factors that make evaluation of this parameter problematic when observing horses for lameness. During lameness, the trunk height after push-off of the lame limb is reduced, causing a corresponding decrease in absolute limb and hoof height. However, in order to move the limb forward without ground interference the horse must increase flexion of the limb joints. This increased flexion results in higher relative foot height during the swing phase of the stride. Decreased hoof height resulting from decreased trunk height is partially canceled by the increased flexion of the limb joints. In the authors' opinion, absolute hoof height during the swing phase of the stride is not a reliable parameter for evaluating lameness in horses.

Lame forelimbs show a reduction in the extent of retraction at the end of the stance phase of the stride.[12] The extent of protraction is diminished only with severe lameness.[21] Some lameness conditions, specifically lameness of the toe of the foot, have even been shown to increase protraction of the lame forelimb (Fig. 13.7).[9] One only has to consider the typical gait of a horse with severe toe pain from laminitis, which is mostly protraction and little retraction, to understand this.

Joint angle changes

Fetlock extension at midstance, when the limb is perpendicular to the ground, is a very sensitive indicator of the amount of ground reaction force on the limb in both forelimbs and hindlimbs (Fig. 13.8).[22,23,39] When compared to the sound limb in a unilateral lameness condition, the fetlock is relatively less extended in the lame limb.[12] In a lameness of moderate severity this difference can be up to 5° in the sagittal plane at the fast trot.[13] With lameness, maximum coffin joint flexion within the first half of the stance phase of the stride is also reduced.[12] Although these changes are consistent and can be measured by sophisticated kinematic or goniometric techniques it is questionable whether they can be reliably detected by direct visual observation.

Kinematic parameters used to detect and differentiate hindlimb lameness

Vertical pelvic movement

Analysis of pelvic movement is frequently used in the identification of hindlimb lameness and varying descriptions of how to do this have been published.[24–27] The

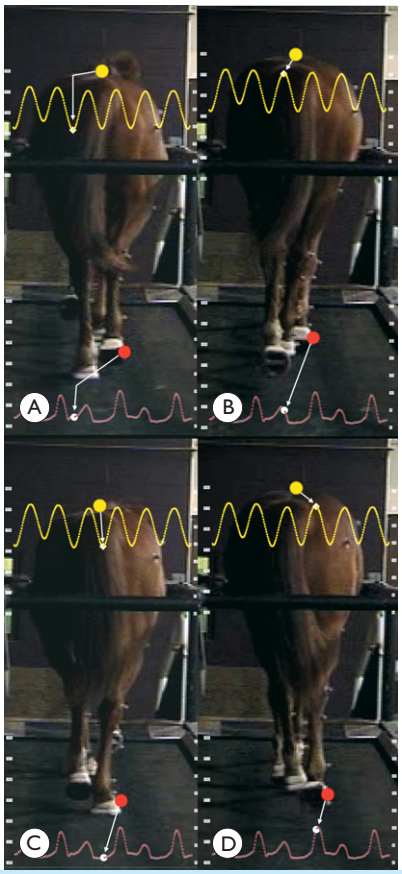

Fig. 13.9
Video frames and graphs depicting vertical pelvic and right hindlimb foot movement in a sound trotting horse. (A) First vertical minimum at midstance of the left hindlimb. Right hindlimb is at midswing. (B) First vertical maximum just after lift-off of the left hindlimb foot and just before impact of the right hindlimb foot. (C) Second vertical minimum at midstance of the right hindlimb. Left hindlimb is at midswing. (D) Second vertical maximum just after lift-off of the right hindlimb foot and just before impact of the left hindlimb foot. Curves at the top of each video frame (yellow) are the vertical pelvic position. Arrows indicate points on the curve corresponding to video frame shown. Curves at the bottom of each video frame (orange) are the vertical position of the right hindlimb foot. Arrows indicate points on the curve corresponding to the video frame shown. Pelvic and right hindlimb foot heights are not in same scale. Approximately three full strides are indicated by the curves.

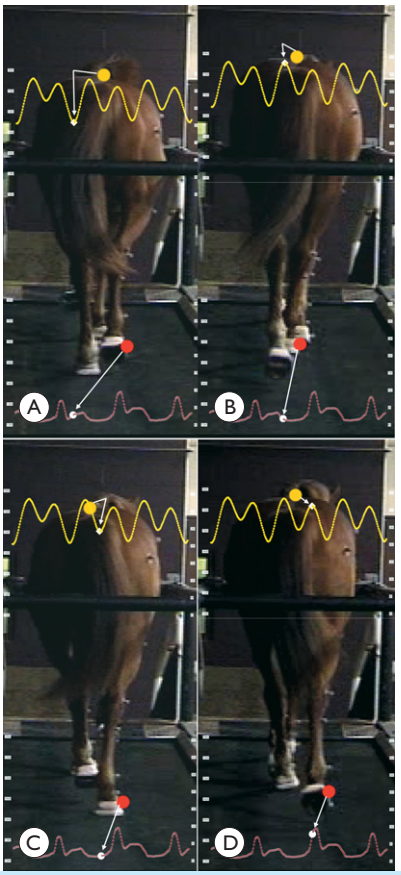

Fig. 13.10
Video frames and graphs depicting vertical pelvic and right hindlimb foot movement in a trotting horse with an induced right hindlimb lameness. (A) First vertical minimum is lowest at midstance of the left hindlimb. Right hindlimb is at midswing. (B) First vertical maximum just after lift-off of the left hindlimb foot and just before impact of the right hindlimb foot. (C) Second vertical minimum at midstance of the right hindlimb. Left hindlimb is at midswing. There is less downward movement of the pelvis compared to vertical minimum at left hindlimb stance. (D) Second vertical maximum just after lift-off of the right hindlimb foot and just before impact of the left hindlimb foot. Curves at the top of each video frame (yellow) are the vertical pelvic position. Arrows indicate points on the curve corresponding to video frame shown. Curves at the bottom of each video frame (orange) are the vertical position of the right hindlimb foot. Arrows indicate points on the curve corresponding to the video frame shown. Pelvic and right hindlimb foot heights are not in same scale. Approximately three full strides are indicated by the curves.

pattern of vertical movement of the pelvis is similar to that of the head seen in trotting horses.[7] Vertical pelvic movement has a sinusoidal pattern with two cycles occurring during one complete stride. The first minimum height is reached during the middle of one of the limb's stance phase and the first maximum height at the end of this stance phase. A second symmetrical oscillation occurs during the stance phase of the contralateral limb (Fig. 13.9). Although extraneous vertical movement of the pelvis (unassociated with normal inertial changes due to mechanics of movement) does occur, its contribution to total vertical movement of the pelvis is much less than that seen in the head.[7] However, as in the forelimb, algorithms can be applied to eliminate extraneous pelvic movement and evaluate only movement due to the biphasic vertical excursion.

Unilateral hindlimb lameness changes the symmetry of pelvic movement.[7,25,28,29] During lameness the entire pelvis exhibits less lowering during the stance phase and less lifting at the end and following the stance phase of the lame limb (Fig. 13.10). Using the classification scheme described above, this describes a typical type-1 lameness. These changes are proportional to the degree of lameness. Severe hindlimb

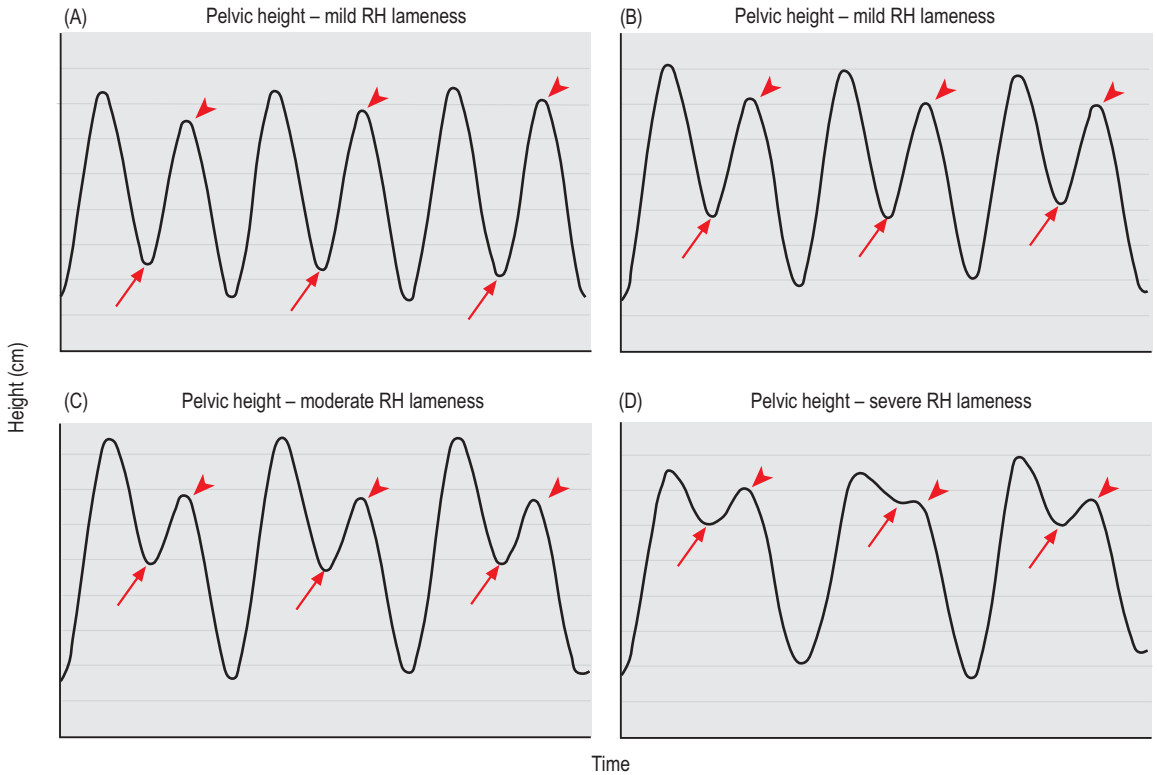

Fig. 13.11
Vertical pelvic movement asymmetry with increasing severity of hindlimb lameness. (A–C) Amount of downward movement during the stance phase of the lame limb becomes less and less, until (D) minimum vertical position during stance phase of lame limb almost disappears. Arrows indicate approximate time of lame (right) hindlimb midstance. Arrowheads indicate corresponding decreasing elevation of the pelvis after the stance phase of the lame (right) hindlimb.

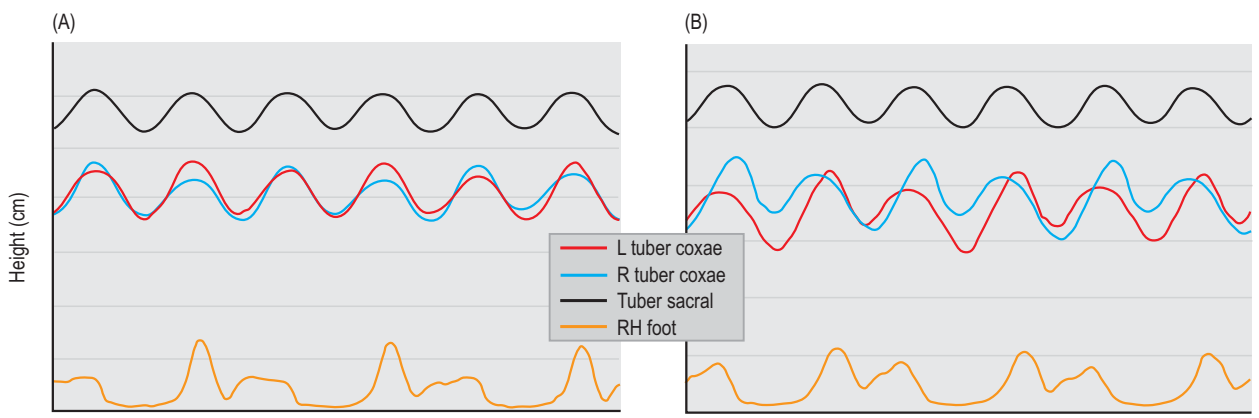

Fig. 13.12
Vertical tuber coxae movement in two sound horses. Tuber sacral movement is symmetric. (A) In horse 1, tuber coxae vertical movement is only slightly asymmetric, indicating little pelvic rotation. (B) In horse 2, tuber coxae vertical movement is very asymmetric, indicating greater pelvic rotation.

lameness may change the degree of symmetry to the extent that there is very little downward movement of the pelvis during the stance phase of the lame limb (Fig. 13.11). It is instructive to note that, in contrast to what is occasionally seen with head movement in forelimb lameness, increased pelvic movement at the end of the stance phase of the lame limb (a type-2 lameness) has not been described.

Tuber coxae movement

Vertical movement of the tuber coxae is normally slightly asymmetric in time. The vertical movement of the tuber coxae has the same basic pattern as the entire pelvis, but the two oscillations are not completely symmetric. The first minimum height is reached during the middle of one limb's

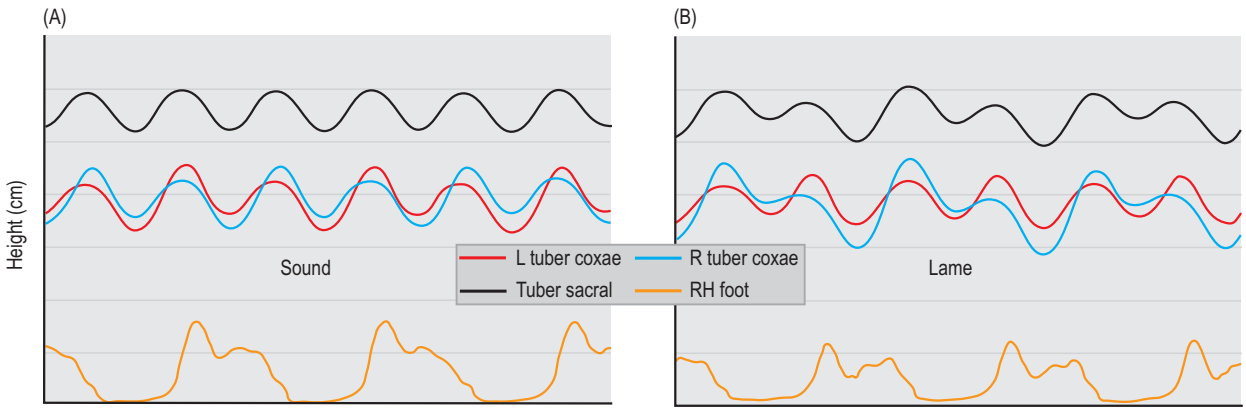

Fig. 13.13
Vertical tuber coxae movement in a (A) sound horse and in (B) the same horse after induction of a right hindlimb lameness. Note the increased vertical movement asymmetry in the right tuber coxae after induction of lameness. Note also the development of asymmetry of vertical tuber sacral movement after induction of lameness.

stance phase and first maximum height is reached at the end of this stance phase. The second oscillation occurs during and shortly following the stance phase of the contralateral hindlimb. However, the vertical movement of the tuber coxae is greater during and shortly after the stance phase of the contralateral hindlimb than that of the ipsilateral hindlimb. The tuber coxae reaches its lowest height at midstance and its maximum height just following the stance phase of the contralateral limb (Fig. 13.12). The asymmetrical movement of the tuber coxae has been attributed to rotational movements of the pelvis around the longitudinal axis of the vertebral column.[7,28] If the pelvis did not rotate the pattern of vertical movements of both tuber coxae would be identical to each other and to the entire pelvis.

The degree of tuber coxae vertical movement asymmetry seen normally in the sound horse is exaggerated in the lame horse (Fig. 13.13). In lame horses the tuber coxae of the lame limb has less downward movement during and less upward movement at the end and shortly following the stance phase of the lame limb. During the stance phase of the sound limb the contralateral tuber coxae has more downward movement during and more upward movement at the end and shortly following the stance phase of the sound limb. This increased upward movement after the stance phase of the sound limb may be what is referred to as 'hip hike'.

Clinically, tuber coxae movement has been described to be useful in the diagnosis of hindlimb lameness.[25] Because of pelvic rotation, total vertical movement of the tuber coxae is greater than total vertical pelvic movement and thus may be easier to observe. Total vertical movement of the tuber coxae is greater on the side of hindlimb lameness. This asymmetry in the amplitudes of left and right vertical tuber coxae movements has been measured and used to diagnose hindlimb lameness in horses.[7,8,14,25] One explanation for the exaggerated tuber coxae movement on the lame side has been

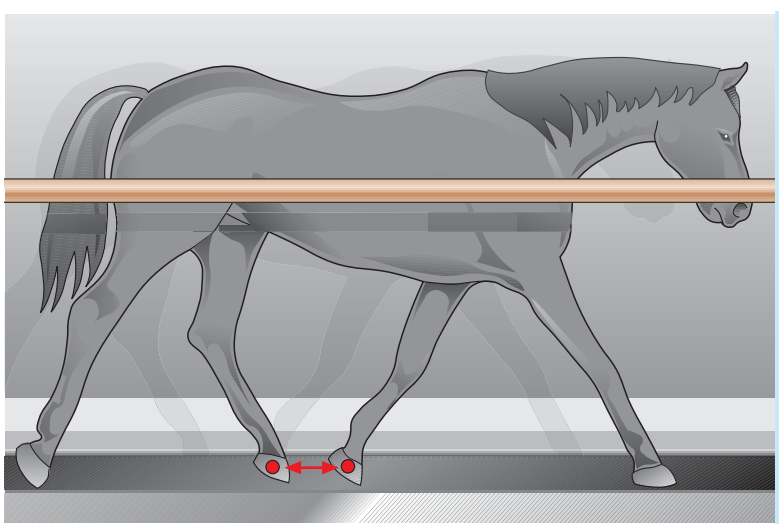

Fig. 13.14
Evaluation of hindlimb protraction at the trot by observing the distance between ipsilateral fore- and hindlimb feet.

offered by Buchner et al.[7] In a right hindlimb lameness the right tuber coxae during right stance has mainly vertical movements. These excursions are enlarged during left stance by rotational movements in the spine. Exaggerated back rotation during the stance of the lame limb may reduce lifting effort during lame limb stance phase.

Although total vertical tuber coxae movement may be observed more easily than total pelvic vertical movement, observing only total vertical tuber coxae movement in some cases may be misleading. Individual horses have varying amounts of vertical tuber coxae movement asymmetry, likely due to different rotational flexibilities of the pelvis and vertebral columns. In some horses tuber coxae movement is primarily due to vertical movement of the trunk and is equally symmetrical as total pelvic vertical movement. In other horses with more significant pelvic rotational movement there is greater vertical tuber coxae movement asymmetry (see Fig. 13.12). Mild asymmetries between right and left tuber coxae vertical movement have been identified in clinically sound horses,[8,28] suggesting that the degree of acceptable asymmetry has not yet been determined. Horses with pre-existing pelvic shape asymmetry unassociated with lameness may also have fairly dramatic vertical tuber coxae movement.

Hindlimb protraction

Decreased hindlimb protraction is a useful indicator of hindlimb lameness. With hindlimb lameness of the tarsus and foot, reduced protraction of the lame hindlimb has been measured.[12,14,30] This change may be a method of decreasing load on the hindlimb by placing it further away from the center of gravity.[12] The decreased protraction of the hindlimb is an easy gait parameter to evaluate at the trot and walk because of the reference point provided by the simultaneous backward movement of the ipsilateral forelimb. The space between the maximally retracted forelimb and the maximally protracted hindlimb on one side of the body can be easily compared to that on the other side during the next half of the stride (Fig. 13.14).

The difference between forelimb and hindlimb protraction and retraction accommodation with lameness can be most easily explained by differences in the timing of load on the limb. In the forelimb the load is greatest during the second half of the stance phase when the limb is more directly under the center of gravity of the trunk. In the hindlimb the highest load occurs in the first half of stance phase. The horse attempts to restrict the forward motion of the hindlimb so that hoof impact is farther from the trunk's center of gravity.

Joint angle changes

Changes in the maximum flexion and extension of various joint angles have been measured in the sound and affected limbs of horses with unilateral hindlimb lameness.[8,12,14,30,31] In general the flexion and extension patterns of the distal joints seem to be primarily affected by ground reaction forces or differences in the loading of the limbs.[32] Several researchers have documented significant decrease in fetlock joint extension of the lame hindlimb.[12,14] Comparing the relative extension of the right and left fetlock joint during stance has also been described in visual descriptions of lameness.[24,33] Changes in the pattern of fetlock and coffin joint movement mimic closely the pattern of changes in vertical ground reaction forces.

Tarsal flexion increases during the swing phase of the lame limb after sole-induced lameness (Fig. 13.15).[12] The increase is attributed to an effort by the horse to avoid dragging the toe after push-off in the lame limb, resulting in lower trunk height. If the trunk is not raised to the normal degree after push-off of the lame limb then increased flexion of the joints during swing may be necessary to avoid dragging the toe during the swing phase of the lame leg. However, in a study of induced distal tarsal lameness, fetlock flexion

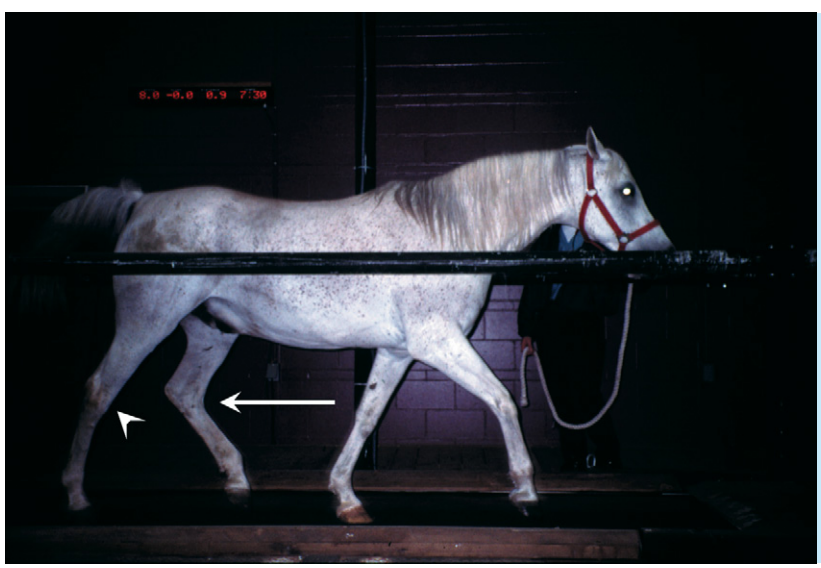

Fig. 13.15
Maximum tarsal flexion during the swing phase of the stride (arrow). Maximum tarsal extension at the end of stance (arrowhead).

increased but tarsal angle during the swing phase of the affected limb was unchanged.[14]

Decreased flexion of all limb joints during the swing phase of the lame hindlimb resulting in an increase in tuber coxae height during the swing phase of the stride has been described, but to the authors' knowledge this has not been measured directly. All present data suggest that, in weight-bearing lameness, flexion of the proximal joints is increased or unchanged.

By contrast, the tarsal joint during stance tends to flex more (extend less) during lameness of the hindlimb.[12,14] Tarsal angle during stance is influenced by ground reaction force, as in the fetlock, but being a proximal joint it is also under heavy influence of large proximal limb muscle groups. With pain during weight bearing in a lame limb, the large proximal muscle groups act to provide gentler and less sudden braking of the limb at the onset of weight bearing. In a study of induced distal tarsal lameness that resulted in the development of mild to moderate lameness, mean hock flexion during the stance phase of the stride was 3° greater after lameness induction than before.[14] This small degree of change is probably not apparent to the naked eye.

Changes in hindlimb abduction/adduction

Changes in hindlimb abduction and adduction have been reported in subjective, observational descriptions of lameness evaluation.[34,35] The most common description is that of tarsal adduction or medial swinging of the hindlimb during protraction and a lateral hoof wall landing pattern, which is reported to be specific for lameness involving the distal tarsal joints.[34,35] To the authors' knowledge, this parameter has not been measured directly and the same hindlimb movement pattern is seen in lameness emanating from other foci within the hindlimb.

Foot-flight pattern

As described previously, the foot-flight pattern of the hindlimb in horses has two peaks, with a depression or lowering occurring about midswing. Maximum height and pattern of hoof flight may be affected by lameness. In one study, maximum hoof height during the swing phase of the stride was lower after sole pressure-induced lameness.[7] A lower hoof flight arc has also been described in a single case report of distal tarsal degenerative joint disease.[30] A decrease in the height of the hoof-flight arc with hindlimb lameness may be due to an overall decrease in trunk height after push-off of the lame limb. In one study of induced distal tarsal arthritis, hoof height during swing increased in the lame limb.[14] As in the forelimb, hoof-flight arc is likely to be simultaneously affected by decreased trunk elevation and increased proximal limb joint flexion. Determination of lameness based upon hoof height or pattern alone is not reliable.

Interlimb co-ordination

In most trotting horses the forelimb and contralateral hindlimb contact the ground surface simultaneously.[34,36] At high forward trunk velocities or during elite performance, slight dissociation between the normal co-ordination of limb pairs may occur.[34,37] Dissociation of simultaneous forelimb and hindlimb impact in one forelimb–hindlimb pair may be a sign of lameness. In cases of moderate to marked hindlimb lameness the forelimb contacts the ground surface before the lame hindlimb.[36,38]

Kinematic parameters associated with bilateral lameness

Many musculoskeletal problems in horses present as bilateral lameness, two common examples being navicular disease and distal tarsal degenerative joint disease. The evaluation of bilateral lameness is complicated by two factors. Symmetry of movement between the right and left sides of the body is maintained to some extent with bilateral lameness.[31,38] Often the magnitude of pain and dysfunction in one limb is only slightly more or less intense than in the similarly affected other side. Careful observation is necessary to detect the small differences in symmetry of movement between the affected sides. A second factor complicating the detection of bilateral lameness is the propensity for the lameness to shift sides during the lameness examination. In some cases of bilateral lameness local, regional or joint anesthesia may be used to temporarily reduce lameness on one side. Frequently, after local anesthesia of one limb, the lameness will become more unilateral, simplifying lameness detection. In other cases the source of lameness may not be amenable to local anesthesia or the effects of local anesthetics may actually interfere with the detection of mild changes in lameness.[40,41]

The characteristic stride described for a horse with a bilateral lameness is a short, 'stiff' and 'shuffling gait'.[26,42] Attempts to objectively measure these changes in stride parameters during bilateral lameness have been made and described.[31,35] In one study utilizing a bilateral hoof-induced lameness model, horses exhibited some characteristic gait compensations. Total stride duration was reduced, relative stance duration was increased and a diagonal advanced placement (placing forelimbs earlier than hindlimbs) was initiated.[36]

Without pre-existing control data from a horse with bilateral lameness of equivalent severity between the right and left sides, diagnosis of lameness based upon kinematic parameters would be challenging. Kinematic detection of such cases requires analysis of multiple stride sequences to evaluate the limb-shifting nature of the lameness and precise detection of subtle asymmetries between left and right sides. A database of kinematic evaluation of normal sound horses

to establish accepted asymmetry measurements for relative comparison would also be needed.

Kinematic parameters in compensatory lameness

Horses with true hindlimb lameness will frequently appear to have false, ipsilateral forelimb lameness (Fig. 13.16).[43] The hindlimb lameness causes a compensatory asymmetric vertical movement of the head, with the head moving down less when the ipsilateral forelimb is in stance. Sometimes rather mild hindlimb lameness will cause a more apparent severe but false forelimb lameness on the ipsilateral side. Conversely, sometimes horses with true forelimb lameness will appear to have false, contralateral hindlimb lameness (Fig. 13.17). The forelimb lameness causes a compensatory asymmetric vertical movement of the pelvis. The pelvis will move down less when the contralateral hindlimb is in stance phase. The biomechanical compensation mimicking hindlimb lameness only occurs when the forelimb lameness is moderate to severe. Therefore, it is a good rule of thumb,

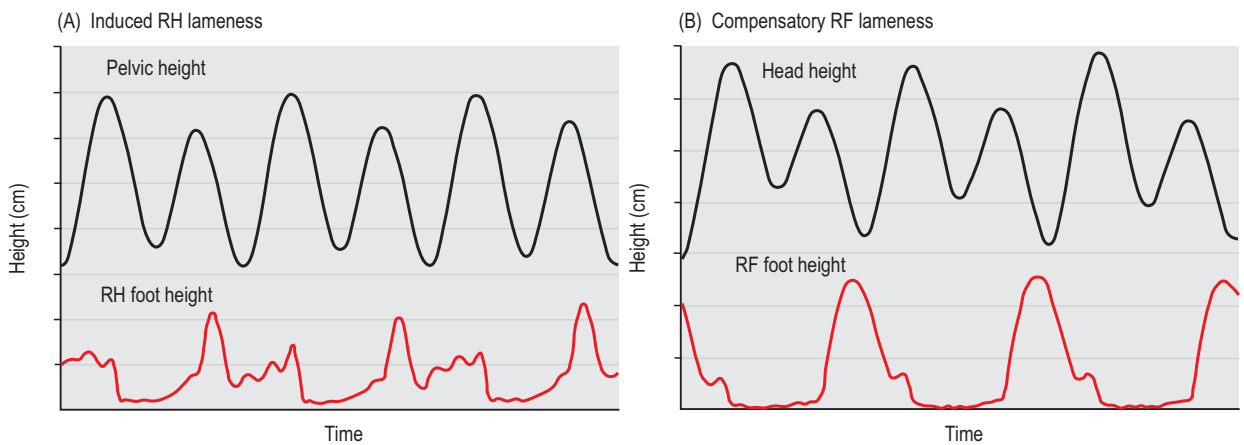

Fig. 13.16
(A) Mild induced right hindlimb lameness causing a (B) moderate to severe compensatory right forelimb lameness. Notice less downward movement of the pelvis during the stance phase of the right hindlimb in (A) and less downward movement of the head during the stance phase of the right forelimb in (B).

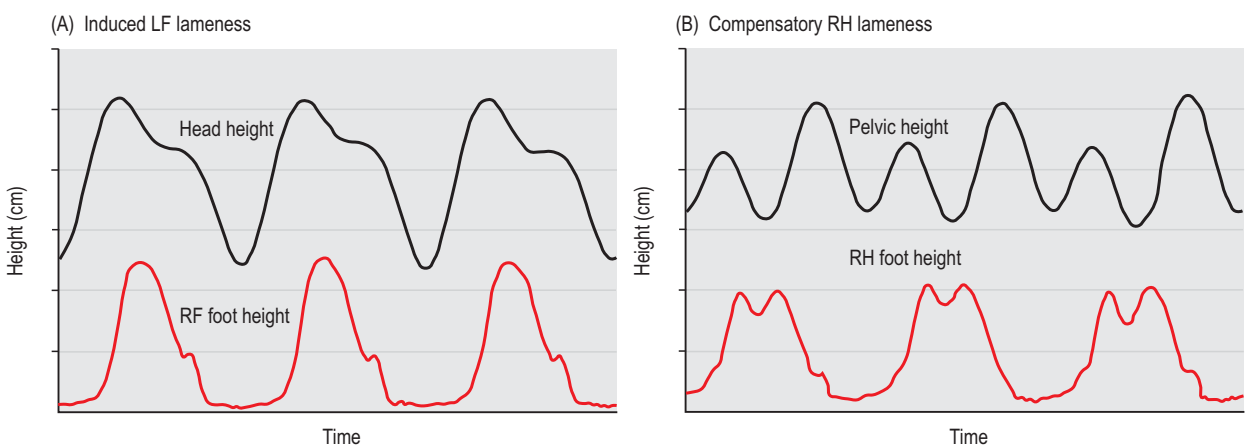

Fig. 13.17
(A) Severe induced left forelimb lameness causing a (B) mild compensatory right hindlimb lameness. Notice less downward movement of the head during the swing phase of the right forelimb (stance phase of the left forelimb) in (A) and slightly less downward movement of the pelvis during the stance phase of the right hindlimb in (B).

when presented with what appears to be an ipsilateral forelimb and hindlimb lameness, to assume first that the hindlimb lameness is primary and when presented with what appears to be a contralateral forelimb and hindlimb lameness, to assume that the forelimb lameness is primary. This rule of thumb has sometimes been termed 'the rule of sides'.

Future directions for kinematic analysis of lameness in horses

Advances in camera and computer technology are resulting in more clinically useful kinematic evaluation techniques. Kinematic analysis has identified objective and specific changes in movement indicative of lameness. This knowledge is improving our understanding and therefore teaching of normal and abnormal locomotion. As our knowledge and ability to detect gait compensations increase further, the possibilities for earlier and more accurate detection of lameness increase.

Future directions in the kinematic analysis of gait for the detection of lameness should concentrate on isolating parameters useful in localizing the site of lameness within an affected limb. Preliminary evidence indicates this may be possible with the aid of advanced signal and data processing techniques. As additional investigative endeavors and further study of known lameness conditions continue, automatic classification of lameness to the affected limb, and possibly to the specific site within the affected limb, could be achieved. Development of new kinematic measurement techniques that free the horse from the treadmill should also be pursued. Acceleration of the head, pelvis and feet can be measured with small sensors[44,45] and the signals transmitted wirelessly to receivers attached to laptop or handheld computers. Acceleration can then be integrated to positional measurements and the analysis techniques already developed from standard video-based kinematic analysis could be utilized.[46] Such a system could be used by equine practitioners in a field setting.

Combining measurement of ground reaction forces with kinematic gait analysis allows calculation of joint torque and internal tendon forces through inverse dynamic analysis.[47,48] The parameters are affected by lameness[49] and knowledge of how these parameters change with lameness will be helpful in developing models for the detection of equine lameness. However, further development of ground reaction force measurement techniques will be required for them to be really useful for the detection of mild to moderate lameness condition in horses. Trotting the horse over stationary force plates does not control stride variability. Collection of multiple, contiguous strides will lessen trial variance when evaluating lameness conditions with significant stride-to-stride variation. Force-measuring treadmills[50] and shoes[51–54] have been designed and described, but the techniques are either in their infancy or have not been widely adopted. Further development of these kinetic techniques for simultaneous use with kinematic gait analysis should be pursued.[55]

References

1. Keegan KG, Wilson DA, Wilson DJ, et al. Evaluation of mild lameness in horses trotting on a treadmill: agreement between clinicians and interns or residents and correlation of their assessments with kinematic gait analysis. Am J Vet Res 1998; 59:1370–1377.
2. Nanua P, Waldron KJ. Energy comparison between trot, bound, and gallop using a simple model. ASME J Biomechanical Engineering 1995; 117:466–473.
3. Rubin CT, Lanyon LE. Limb mechanics as a function of speed and gait: a study of functional strains in the radius and tibia of horse and dog. J Exp Biol 1982; 101:187–211.
4. Hildebrand M. The mechanics of horse legs. Am Scient 1987; 75:594–601.
5. Stashak TS. Diagnosis of lameness. In: Stashak TS, ed. Adams' lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1985:106.
6. Wilson DA, Keegan KG. Pathophysiology and diagnosis of musculoskeletal disease. In: Kobluk CN, Ames TR, Geor RJ, eds. The horse: diseases and clinical management, vol. 1. Philadelphia, PA: Saunders; 1995:623–624.
7. Buchner HHF, Savelberg HHCM, Schamhardt HC, Barneveld A. Head and trunk movement adaptations in horses with experimentally induced fore- or hindlimb lameness. Equine Vet J 1996; 28:71–76.
8. Kobluk CN, Schnurr D, Horney FD, et al. Use of high-speed cinematography and computer generated gait diagrams for the study of equine hindlimb kinematics. Equine Vet J 1989; 21:48–58.
9. Keegan KG, Wilson DA, Smith BK, Wilson DJ. Changes in kinematic variables observed during pressure-induced forelimb lameness in adult horses trotting on a treadmill. Am J Vet Res 2000; 61(6):612–619.
10. Stashak TS. Diagnosis of lameness. In: Stashak TS, ed. Adams' lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1985:101.
11. Martinez-del Campo LJ, Kobluk CN, Greer N, et al. The use of high-speed videography to generate angle-time and angle-angle diagrams for the study of equine locomotion. Vet Clin Orthop Traum 1991; 4:120–131.
12. Buchner HHF, Savelberg HHCM, Schamhardt HC, Barneveld A. Limb movement adaptations in horses with experimentally induced fore- or hindlimb lameness. Equine Vet J 1996; 28:63–70.
13. Keegan KG, Wilson DJ, Wilson DA, et al. Effects of anesthesia of the palmar digital nerves on kinematic gait analysis in horses with and without navicular disease. Am J Vet Res 1997; 58:218–223.
14. Kramer J, Keegan KG, Wilson DA, et al. Kinematics of the hind limb in trotting horses after induced lameness of the distal intertarsal and tarsometatarsal joints and intra-articular administration of anesthetic. Am J Vet Res 2000; 61:1031–1036.

15. Keegan KG, Pai PF, Wilson DA, Smith BK. Signal decomposition method of evaluating head movement to measure induced forelimb lameness in horses trotting on a treadmill. Equine Vet J 2001; 33(5):446–451.
16. Morris EA, Seeherman HJ. Redistribution of ground reaction forces in experimentally induced equine carpal lameness. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:553–572.
17. Buchner HHF. Gait adaptation in lameness. In: Back W, Clayton H, eds. Equine locomotion. Philadelphia, PA: Saunders; 2001:265.
18. Vorstenbosch MATM, Buchner HHF, Savelberg HCM, et al. Modeling study of compensatory head movements in lame horses. Am J Vet Res 1997; 58:713–718.
19. Buchner HHF. Gait adaptation in lameness. In: Back W, Clayton H, eds. Equine locomotion. Philadelphia, PA: Saunders; 2001:254.
20. Clayton HM. Comparison of the stride of trotting horses trimmed with a normal and a broken-back hoof axis. Proceedings of the American Association of Equine Practitioners; 1987:289–299.
21. Back W, Barneveld A, van Weeren PR, van den Bogert AJ. Kinematic gait analysis in equine carpal lameness. Acta Anat 1993; 146:86–89.
22. Riemersma DJ, van den Bogert AJ, Schamhardt HC, et al. Kinetics and kinematics of the equine hind limb: in vivo tendon stain and joint kinematics. Am J Vet Res 1988; 49:1353–1359.
23. Riemersma DJ, Schamhardt HC, Hartman W. Kinetics and kinematics of the equine hind limb: in vivo tendon loads and force plate measurement in ponies. Am J Vet Res 1988; 49:1344–1352.
24. Stashak TS. Diagnosis of lameness. In: Stashak TS, ed. Adams' lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1987:100–106.
25. May SA, Wyn-Jones G. Identification of hindleg lameness. Equine Vet J 1987; 3:185–187.
26. Gough M, Munroe G. Decision making in the diagnosis and management of bone spavin in horse. In Practice 1998; 2:252–258.
27. Dyson S. An approach to hindlimb lameness 2: gait assessment, flexion tests and what to do next. In Practice 1997; 1:14–20.
28. Buchner HHF, Kastner J, Girtler D, et al. Quantification of hind limb lameness in the horse. Acta Anat 1993; 146:196–199.
29. Peham C, Licka T, Girtler D, et al. Hindlimb lameness: clinical judgement versus computerized symmetry measurement. Vet Rec 2001; 61:750–752.
30. Clayton HM. Cinematographic analysis of the gait of lame horses IV: degenerative joint disease of the distal intertarsal joint. J Equine Vet Sci 1987; 7:274–278.
31. Pourcelot P, Audigie F, Degueurce C, et al. Kinematic symmetry index: a method for quantifying the horse locomotion symmetry using kinematic data. Vet Res 1997; 28:525–538.
32. Merkens HW, Schamhardt HC. Relationships between ground reaction force patterns and kinematics in the walking and trotting horse. Equine Vet J 1994; 17(suppl):67–70.
33. Schneider RK. Slow motion video analysis of gait abnormalities in horses. Proceedings of the 8th Annual American College of Veterinary Surgeons Symposium, 1998; 97–98.
34. Seeherman HJ. Lameness evaluation. In: Auer JA, Stick JA, eds. Equine surgery. Philadelphia, PA: Saunders; 2001:251–280.
35. Bohanon TC. Pain associated with the distal tarsal joints of the hock. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia, PA: Saunders; 1997:88–93.
36. Buchner HHF. Gait adaptation in lameness. In: Back W, Clayton H, eds. Equine locomotion. Philadelphia, PA: Saunders; 2001:251–280.
37. Clayton HM. Classification of collected trot, passage and piaffe based on temporal variables. Equine Vet J 1997; 23(suppl):54–57.
38. Caron JP. Objective and subjective gait analysis techniques. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness. Philadelphia, PA: Saunders; 1998:501–506.
39. Bucher HHF, Savelberg HHCM, Schamhardt HC, Barneveld A. Bilateral lameness in horses – a kinematic study. Vet Q 1995; 17:103–105.
40. Drevemo S, Johnston C, Roepstorff L, Gustås P. Nerve block and intra-articular anaesthesia of the forelimb in the sound horse. Equine Vet J 1999; 30(suppl):266–269.
41. Keg PR, Schamhardt HC, van Weeren PR, Barneveld A. The effect of diagnostic regional nerve blocks in the fore limb on the locomotion of clinically sound horses. Vet Q 1996; 18(2):103–105.
42. Stashak TS. Diagnosis of lameness. In: Stashak TS, ed. Adams' lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1987: 100–156, 731, 840–847.
43. Uhlir C, Licka T, Kübber P, et al. Compensatory movements in horses with a stance phase lameness. Equine Vet J 1997; 23(suppl):102–105.
44. Barrey E, Hermelin M, Vaudelin JL, et al. Utilisation of an accelerometric device in equine gait analysis. Equine Vet J 1994; 17(suppl):7–12.
45. Barry E, Desbrosse F. Lameness detection using an accelerometric device. Pferdeheilkunde 1996; 12:617–622.
46. Keegan KG, Yonezawa Y, Pai PF, Wilson DA. Telemeterized accelerometer-based system for the detection of lameness in horses. 39th International ISA Biomedical Sciences Instrumentation Symposium 2002. Vol. 419, p. 112.
47. Colbourne GR, Lanovaz JL, Springings EJ, et al. Forelimb joint moments and power during walking stance phase of horses. Am J Vet Res 1998; 59:609–614.
48. Clayton HM, Schamhardt HC, Willemen MA, Lanovaz JL, Colborne GR. Net joint moments and joint powers in horses with superficial digital flexor tendinitis. Am J Vet Res 2000; 61:197–201.
49. Buchner HHHF, Savelberg HHCM, Becker CK. Load redistribution after desmotomy of the accessory ligament of the deep digital flexor tendon in adult horses. Vet Q 1996; 18(suppl):70–74.
50. Weishaupt MA, Hogg HP, Wiestner T, Denoth J, Stussi E, Auer JA. Instrumented treadmill for measuring vertical ground reaction forces in horses. Am J Vet Res 2002; 63:520–527.
51. Ratzlaff MH, Hyde ML, Grant BD, et al. Measurement of vertical forces and temporal components of the strides of horses using instrumented shoes. J Equine Vet Sci 1990; 10:23–35.
52. Roepstorff L, Drevemo S. Concept of a force-measuring horseshoe. Acta Anat 1993; 146:114–119.
53. Judy CE, Galuppo LD, Snyder JR, Willits NH. Evaluation of an in-shoe pressure measurement system in horses. Am J Vet Res 2001; 62:232–238.

54. Kai M, Aoki O, Hiraga A, Oki H, Tokuriki M. Use of an instrument sandwiched between the hoof and shoe to measure vertical ground reaction forces and three-dimensional acceleration at the walk, trot, and canter in horses. Am J Vet Res 2000; 61:979–985.

55. van den Bogert AJ. Computer-assisted gait analysis in equine orthopaedic practice: the case for inverse dynamic analysis. Equine Vet J 1998; 30:362–363.

CHAPTER 14

Diagnosis of lameness

Andris J. Kaneps

Introduction

The evaluation of lameness includes the following steps:

- history
- visual examination at rest
- in motion examination
- manipulations
- localization
- diagnostic imaging.

A horse without gait abnormalities should move in a balanced manner with all limb movements in equilibrium. If lameness is present, it is the examiner's task to identify the gait abnormality, its location and the likely causes and to recommend appropriate treatment. Evaluation of lameness requires an ability to visualize gait abnormalities, skill in applying techniques that localize the abnormality to a specific site, and obtaining and interpreting appropriate images of the site. These findings must be consolidated to determine a diagnosis.

Experience in observing and interpreting the equine gait is a hard-fought and ongoing process. The science of gait evaluations (see Chapters 12 and 13) may help us understand how and why a horse moves in a particular fashion, but visual examination by a trained and experienced examiner remains the basis for most lameness examinations.

History

A complete anamnesis of a horse presented for evaluation of gait abnormality helps to narrow the list of differential diagnoses, determines the effect of previous treatment or shoeing protocols and may help to narrow the focus of the examination. The signalment of the horse (age, sex, breed and use of the horse) should be clearly elucidated. The list of potential diagnoses will be different for a 2-year-old Warmblood horse in early training as opposed to a 2-year-old Thoroughbred that has started three races.

Specific questions to ask during the history

When did you (or your trainer) first notice a lameness problem and how long has it been present?

Acute onset of lameness may indicate abnormalities such as severe subsolar bruising or osteochondral fracture. Prolonged, insidious onset of lameness may be due to wear-and-tear disorders such as navicular syndrome or bone spavin.

Describe what you noticed initially

Owners and trainers may make an incorrect interpretation of the initial signs of subtle lameness, but their interpretations may still be very useful. For example, a short and choppy forelimb gait associated with heel pain is often described by clients as 'sore in the shoulders' because of the shuffling gait. Also, advanced riders may notice subtle abnormalities in their horse's gait that may be extremely difficult to observe during the lameness examination. An example would be reluctance of a dressage horse to enter a round frame while being ridden.

When is the lameness most obvious?

Lameness that is first evident when the horse comes out of the stall or early in an exercise period (when the horse is 'cold') may be associated with synovitis or arthritis. Lameness that decreases in severity as the horse warms up during exercise is also often associated with arthritis. Lameness that becomes more pronounced with longer periods of exercise may be indicative of tendon or ligament inflammation. The lameness may be more evident on different types of surfaces. Deep footing may make soft tissue injuries more apparent, while very firm footing will cause greater concussion and may exacerbate lameness due to arthritis.

Have you noticed any swelling or thickenings?

Some effusions and soft tissue swellings may be transient. Joint effusion with carpal osteochondral fracture often is pronounced near the time of occurrence and then gradually subsides. Soft tissue swelling due to tendinitis is often observable for prolonged periods of time.

Has the horse undergone any treatment for this condition?

For example, has the horse had rest, medication, change in level of use or shoeing modifications?

When was your horse last shod?

Changes in hoof angle and paring of a thin sole may be a cause of transient lameness. Excessive wear of the hoof or shoes soon after a farrier visit may be indicative of a more severe gait abnormality.

Any previous history of lameness?

Is this a new condition or a continuation of a previous injury?

Visual examination at rest

Before observing the horse in motion, a careful appraisal of the horse's conformation and close visualization of its stance and limbs should be made. Start by evaluating the horse from a distance to allow appreciation of its stance, general conformation, areas of swelling or atrophy and attitude. Evaluate wear patterns of the hoof or shoes. Closer inspection should always involve palpation of each limb in its entirety. Subtle effusion of the carpal joints and medial femorotibial joints may only be noticed with palpation. Swollen regions should be palpated to evaluate tissue temperature and the degree of sensitivity to deep palpation. A swelling that is sensitive to touch and is warmer than surrounding areas is likely undergoing active inflammation. A cold, insensitive swelling may be a lesion that has healed and is no longer actively inflamed.

The digital pulses should always be palpated at the level of the proximal sesamoid bones or in the pastern region of each distal limb. Elevated pulses are associated with injury or inflammation in the distal limb and may help localize the lesion to medial or lateral aspects of the limb.

Tendons and ligaments should be palpated with the limb in both weight-bearing and flexed positions. Tendon sheath effusions are best evaluated with the limb bearing weight. When the limb is flexed the tendons and ligaments on the palmar or plantar surface are more easily defined and separated. Deep palpation of the mid- to proximal suspensory ligament often elicits some discomfort in the normal horse. Compare contralateral limbs if there is a concern regarding palpation sensitivity.[1]

In motion examination

Examination of the lame horse in motion is necessary to characterize the nature and intensity of the gait abnormality. The lameness should be graded using a consistent scale (Table 14.1).[2] Conducting the in motion examination in controlled surroundings will add consistency to the findings. The ideal location in which to examine a horse for lameness is a flat, firm surface where the horse may by jogged for 30–40 meters without encountering obstructions or distractions.[3] An asphalt surface has the advantage of allowing the examiner to both visualize and listen to the horse's footfalls. The sound of the lame limb impacting the surface will be diminished when compared to the unaffected contralateral limb. A common finding with subtle gait abnormalities is the unaffected limb of a pair impacting the surface louder than the affected limb.

A safe place to work the horse in a circle, preferably on a lunge line, should be available (Fig. 14.1). The surface should be firm, but safe enough to permit circles from 10 to 20 meters in diameter without risk of the horse slipping.

Table 14.1 Lameness grading scale

Grade	**Lameness grading scale** (after AAEP scale[2])
0	Lameness is not observed
1	Intermittent or inconsistent lameness at the trot that is difficult to discern under any circumstance
2	Lameness is difficult to observe at a walk or trot in a straight line, but is consistently apparent under special circumstances such as with manipulation, lunging or riding
3	Lameness is consistently observed at the trot under all conditions
4	Lameness is obvious with marked asymmetry of gait at the trot without manipulation
5	Minimal or no weight bearing on the affected limb, horse is reluctant to move

Fig. 14.1 Evaluating lameness on the lunge line may be used to exacerbate mild gait abnormalities and to determine how a horse performs during transitions of gait.

Horses with subtle gait abnormalities may need to be observed while being worked in normal tack. In select circumstances an examiner with sufficient experience may find it useful to work or ride the horse. This is particularly useful in harness race horses that only demonstrate their gait abnormalities at speed.

Watch the horse initially at a walk to evaluate footfall patterns and to familiarize the horse with the environment in which the examination will take place. Each foot should normally land heel first, then toe with the lateral and medial aspects of the hoof landing nearly equally in time.[4] Deviations from normal footfall may indicate dynamic imbalance of the limb that could be due to abnormalities of conformation, hoof shape, shoeing or pain. The swinging phase of the limb in a correctly conformed horse should be a straight track without any tendency to swinging in or out. Toe-in or toe-out conformations predispose the horse to swinging out ('paddling') or swinging in ('winging in'), respectively.[3]

The trot is the most useful gait to evaluate lameness because it is a symmetrical, two-beat gait where diagonal limb pairs are simultaneously in the stance phase. The horse should be trotted at a comfortable, unhurried speed with the head allowed to move freely up and down. The horse should be trotted directly away and returned directly toward the examiner. Subtle imbalances in gait may easily be missed if the examiner is not directly aligned with the center of the long axis of the horse (the vertebral column). The examiner should also observe the horse from the side as it trots by for characteristics of stride length and to determine if there is any toe dragging. Viewing the horse from the side at the trot may provide better evaluation of rear limb lameness.[5]

Lameness is evident to the observer as an asymmetry of the gait. Forelimb lameness is usually evident as a head bob: the head rises immediately prior to and during weight bearing of the lame limb. Conversely, the head drops as the sound limb contacts the ground and bears weight.[6] Stride length may also be altered by gait abnormalities. A shortened anterior phase to the stride (shuffling gait) may be associated with heel pain as the horse is reluctant to extend the affected limb and bear full weight on the heel.[3] This type of change in the stride may also occur due to pain during the swing phase of the gait, such as may be encountered with bicipital bursitis/tendinitis of the forelimb. Subtle forelimb lameness may only be evident as an unequal shift in weight with the unaffected limb bearing more weight than the lame limb. Such subtle weight shifts are best observed with the horse trotting directly toward the examiner.

Rear limb gait abnormalities may be evident as elevation of the hip (hip hike, gluteal rise), dropping of the hip (hip drop, gluteal drop), toe dragging and decreased stride length.[3] These responses to rear limb lameness are mechanisms the horse uses to avoid discomfort during various portions of the stride and are due to the nature of the abnormality. Elevation of the hip occurs when the horse shifts weight away from the lame limb during the weight-bearing phase of the stride. Dropping of the hip occurs if pain is most acute during the posterior phase of the weight-bearing portion of the stride. Often this movement is associated with abnormalities of the caudal/plantar aspect of the rear limb such as suspensory desmitis, flexor tendinitis, desmitis of the distal suspensory apparatus and injury to the semimembranosus/semitendinosus muscle group. Dragging of the toe is associated with reluctance to raise the limb during the swing phase of the stride and usually suggests upper rear limb joint lameness such as bone spavin and abnormalities of the stifle or coxofemoral joints.

Stashak describes 'gluteal rise and use' as characteristics observed from the rear of the horse at the trot. Gluteal rise is observed during the swing phase of the stride and use is observed during weight bearing.[3] Three characteristics of rear limb lameness in relationship to the gluteals were described.

1. Depressed gluteal rise and use is associated with upper rear limb (usually hip region) lameness.
2. Symmetric gluteal rise, but decreased gluteal use, is seen in subtle rear limb lameness and is non-localizing.
3. Rapid increased gluteal rise with decreased gluteal use is found in horses with marked discomfort during weight bearing and is often associated with a noticeable head bob.[3]

During the trot the pelvis normally rocks symmetrically from left to right in the sound horse when observed from the rear. In a study of induced right distal tarsal lameness, the right limb had greater vertical displacement of the tuber coxae than did the left (unaffected) limb, but the difference was not significant.[5] However, the ratio of left to right tuber coxae vertical displacement decreased 20% with the induction of distal tarsal lameness.[5] The change in ratio was evidence that tuber coxae asymmetric movement is a sensitive indicator of rear limb lameness at the trot.[5] A practical application of these findings is that when a rear limb lameness is observed at the trot from the rear of the horse, the tuber coxae of the lame limb usually has greater up-and-down motion compared to the tuber coxae of the sound limb.

Severe rear limb lameness (≥ grade 3) is often associated with a head bob. At the trot the rear limb and the contralateral forelimb are simultaneously in the same stride phase (working as a diagonal pair). If lameness of the rear limb is severe enough, as the affected limb contacts the ground the horse will shift weight forward (off the lame rear limb) using its neck, resulting in an observable head drop as the contralateral forelimb enters the weight-bearing phase of the stride. Kinematic analysis has found a measurable head bob with even mild rear limb lameness.[7] The examiner needs to be

aware of this process as moderate to severe rear limb lameness may be confused with a lameness of the ipsilateral forelimb.[3,7]

When the examiner has difficulty in determining which limb is lame, it may be easier to determine which limb is sound. At times it is simpler to visualize and/or hear which limb is bearing more weight (the sound limb). Manipulative tests should be used when lameness is subtle.

Manipulative tests and techniques

Manipulations that enhance or localize lameness include:

- work on the lunge line
- hoof tester application
- flexion tests
- riding or working with tack
- rectal palpation.

Lunge line

Most sport horses may be safely worked in a circle on a lunge line. Working the horse in a 10–20 meter diameter circle will put additional weight and stress on the innermost limbs and the medial aspect of the outermost limbs (see Fig. 14.1). The additional stress on the limbs helps the examiner identify subtle lamenesses and in some cases will help localize the region of soreness to a portion of the limb. A round pen of appropriate size may be similarly used.

Use of hoof testers

Hoof testers are squeezed on the sole and hoof capsule to determine if there are any sensitive areas present. Hoof tester pressure on normal hoof or sole does not result in a significant withdrawal response. If a sensitive area is found the hoof tester pressure should be repeated to verify the finding, then pressure should be maintained for 20–30 seconds and the horse should be trotted off to determine if pressure on the sensitive area causes an exacerbation of the lameness. Significant sensitive areas should be closely evaluated by paring out the foot.

While using the hoof testers the foot should also be evaluated for balance, general condition of the hoof and sole and the degree of wear of shoes and hoof walls. Abnormalities such as dished hoof, long toe, low heels, sheared heels, contracted heels, hoof cracks, thrush, flaky sole, hard sole, sole bruising and white line disease should be noted. Percuss the hoof wall with the hoof tester or a hammer. Hollow-sounding areas may correspond to a deep abscess or hoof wall separation. Areas of pain on concussion may be indicative of a tightly clinched nail or a nail that has penetrated the sensitive laminae and is causing a local abscess.

Flexion tests

Flexion tests are used to apply stress or pressure on an anatomic region of the limb for a set period of time. Following the flexion period the horse is trotted off and observed for the effects of the test on gait. Recalling the baseline level of lameness during both trotting on the lead rope and on the lunge line (if appropriate) is crucial to objectively evaluating the results of both flexion tests and diagnostic local anesthesia. The amount and duration of pressure applied may affect the outcome of flexion tests.[8] Consistency of application is also a key to correct interpretation of flexion tests. The flexion test, particularly of the distal limb, should not be overinterpreted. More than 60 of 100 horses determined to be sound prior to application of manipulative tests had some degree of lameness evident after distal limb flexion.[9]

Each flexion test should be completed in anatomic pairs (for example, distal flexions of both forelimbs) with the sound limb flexed first. Tests should progress from the distal to proximal aspect of the limbs. Moderate and equal pressure should be applied for each flexion test. Consistency is improved by having the same individual perform all of the tests during an examination. One study found a 12% coefficient of variation between multiple distal forelimb flexion tests applied by one clinician and a 20% coefficient of variation between different clinicians.[10]

Flexion tests used for lameness evaluation are described in Table 14.2. Results of flexion tests may be recorded as:

- *negative:* no change in lameness
- *slight positive:* slight exacerbation of lameness following flexion that is noticed during only a portion of the trotting course
- *moderate positive:* lameness is exacerbated while the horse is trotting away from the examiner, but not on the return
- *severe positive:* marked exacerbation of lameness during the outbound and return portions of the trotting course.

Other tests

Other aids to localizing lameness include rectal palpation of the pelvis for upper rear limb lameness, manipulations of the back (see Chapter 21) and working the horse in its given discipline with full tack. Working horses in circumstances that are similar to those when lameness is noticed by the owner or trainer is especially important for evaluation of subtle lamenesses or those that only occur under special circumstances.

Localization with diagnostic local anesthesia

Diagnostic local anesthesia ('nerve block') is performed to localize lameness. Important considerations are:

Table 14.2 Manipulative tests for lameness evaluation

Sequence of flexion tests	Technique	Duration of test
Forelimb		
Distal limb	Stand to the front or side of the horse with the carpus relaxed. Grasp the toe with one hand, using the other hand placed on the palmar aspect of the distal metacarpus as a fulcrum (Fig. 14.2A). Alternatively, stand in front of the horse and grasp the toe with both hands, placing the dorsal aspect of the fetlock on your knees and flexing the distal joints (Fig. 14.2B). Distal limb flexion stresses the metacarpophalangeal, proximal interphalangeal and distal interphalangeal joints and the navicular region	60 seconds
Carpus	Stand to the side of the horse and grasp the distal dorsal aspect of the metacarpus with one hand. Flex the carpus maximally. A full range of motion is evident when the palmar metacarpus contacts the caudal aspect of the antebrachium. The metacarpus may be adducted and abducted during flexion to provide more stress to the medial and lateral aspects of the joints	60 seconds
Metacarpus	Direct pressure on the flexor tendons or suspensory ligament	30 seconds
Proximal forelimb	The shoulder and elbow are difficult to isolate. The bicipital bursa of the shoulder may be evaluated by applying direct pressure over the bicipital tendon at the point of the shoulder or by retracting the upper forelimb caudally to its full extent. The upper limb should be abducted and adducted to stress the medial and lateral support structures of the joints	30–60 seconds
Rear limb		
Distal rear limb	Techniques are similar to that used in the forelimb. Flexion is performed with the tarsus and stifle relaxed. See Fig. 14.3A and B for two techniques	60 seconds
Full rear limb	Also referred to as the spavin test, this flexion test stresses all of the rear limb joints to some degree because of their connection via the reciprocal apparatus. However, the tarsus and stifle joints are stressed more than others. The rear limb is grasped with both hands around the distal metatarsus and the full limb is flexed maximally	90 seconds
Stifle	This joint is stressed during application of the full limb flexion. The cruciate ligaments may be stressed by abruptly forcing the tibial crest caudally using a hand on the tibial crest while the horse is fully weight bearing on the limb. The medial collateral ligament of the stifle may be stressed by picking up the limb, grasping the mid-metatarsus and placing the examiner's shoulder over the lateral aspect of the stifle. Abruptly abduct the distal limb, using the examiner's shoulder as the fulcrum	15–30 seconds
Coxofemoral joint	With the limb not bearing weight and nearly extended, 'stir' the limb in an arc. An alternative method is to adduct the limb. For example, to stress the right coxofemoral joint, stand on the horse's left, pick up the right rear limb while maintaining limb extension and pulling the distal limb to the horse's left side (Fig. 14.4)	30 seconds

Fig. 14.2
(A) Distal forelimb flexion using one hand as the fulcrum on the palmar aspect of the fetlock and one hand pulling on the toe of the hoof. (B) Distal forelimb flexion with the dorsal aspect of the fetlock resting on the operator's knees and both hands used to pull on the toe. Excessive force during this manipulation may lead to false-positive results.

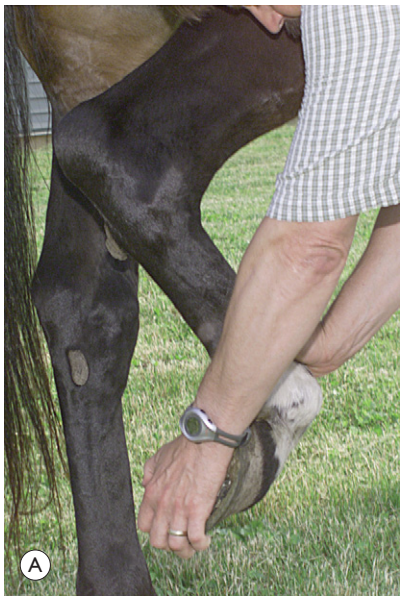

Fig. 14.3
(A) Distal rear limb flexion with the limb nearly extended and one hand on the plantar aspect of the fetlock acting as the fulcrum and the other hand flexing at the toe of the hoof. (B) An alternative method of applying a distal rear limb flexion test by tucking the tuber calcis under the operator's inside arm pit and using both hands to flex the toe.

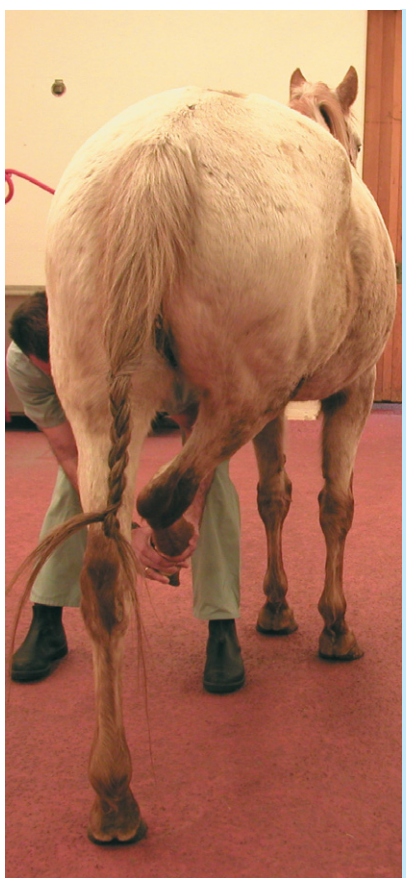

Fig. 14.4
Manipulative test of the coxofemoral joint by adduction of the rear limb. An assistant can initially pick up the limb and hand it to the operator.

1. understanding the anatomy to provide accurate placement of the anesthetic
2. being aware of different options for administering anesthetic to a site as clinical situations may dictate one technique over another
3. maintaining strict asepsis when penetrating synovial spaces.

Mepivacaine HCl 2% is the preferred local anesthetic for regional and joint anesthesia in horses. Compared to lidocaine (lignocaine), it is less irritating to tissues and has a comparable onset, yet a longer duration of action.[11,12] Local anesthetics cause blockade of sodium channels that results in inhibition of nerve conduction.[13] The effectiveness of local anesthesia depends on local tissue pH (local anesthetics are much less effective in acid pH), accuracy of deposition and the size of nerves being blocked (small, unmyelinated fibers are more sensitive than large, myelinated fibers).[13] The toxic dose is approximately 13 mg/kg (~6 mg/lb). Overdose of local anesthetics may result in heart block, bradycardia and convulsions.[14] Toxicity is usually only a concern in smaller animals. Onset of action for regional nerve blocks is 10–25 minutes with smaller diameter nerves desensitized earlier than larger nerves. Onset of intra-articular analgesia is 5–10 minutes with a gradual increase in analgesia over that time. Check the effects of the local anesthetic in most joints at 20 min-utes and in complex joints, such as the stifle, in 30 minutes. Mepivacaine inhibits nerve sensation for 90–180 minutes.[13]

Strict aseptic techniques should always be followed when injecting joints or synovial structures. A fresh bottle of local anesthetic should always be used. The site to be injected may be clipped, but in a study of various methods of preparing the site of intra-articular injections, clipping of the site was not found to improve results of skin surface bacteriological cultures.[15] A 7–10 minute scrub with povidone-iodine or chlorhexidine should be made of the injection site. Immediately prior to injection the site should be carefully wiped with 70% isopropyl alcohol. The operator should wear sterile surgical gloves. Adequate assistance should be available for restraining the horse. The most painful portion of the injection is needle penetration of the skin and joint capsule. Confident, quick insertion of the needle in the correct anatomic site minimizes discomfort for the horse. A skin bleb of local anesthetic may be helpful in making the joint

Table 14.3 Forelimb diagnostic local anesthesia

Sequence of diagnostic local anesthesia	Anatomic site of injection	Region desensitized	Needle size and anesthetic volume	Onset of action
Palmar digital nerves (PDN)	Palmar aspect of pastern, immediately proximal to the collateral cartilages	Palmar heel, entire sole	25–22 g × 1 inch 0.5–0.7 × 16 mm 1.5–2 mL/nerve	10–15 minutes
Dorsal branch of PDN	Same as above, redirect needle dorsally approximately 1 inch (25 mm)	All structures within the hoof	As above	As above
Abaxial sesamoid (palmar nerves)	Abaxial aspect of proximal sesamoid bones (may use either dorsal branch or abaxial sesamoid block)	All structures within the hoof and most of structures from midpastern distal	25–22 g × 1 inch 0.5–0.7 × 16 mm 2–2.5 mL/nerve	As above
Low four-point (palmar nerves and palmar metacarpal nerves)	At the level of the distal aspect of MCII and MCIV (splint bones). Palmar nerves are injected subcutaneously between the suspensory branch and the deep digital flexor tendon immediately proximal to the digital sheath. Palmar metacarpal nerves are injected subcutaneously immediately dorsal and distal to the splint buttons	Fetlock joint and all distal structures	22 g × 1 inch 0.7 × 25 mm 4–5 mL per palmar nerve, 3 mL per palmar metacarpal nerve	15 minutes
High four-point (palmar nerves and palmar metacarpal nerves)	At the most proximal aspect of the metacarpus that a palpable groove between the deep digital flexor tendon and suspensory ligament is palpable. The palmar nerves are injected in this groove. The palmar metacarpal nerves are injected by redirecting the needle to the axial surface of MCII and MCIV	All structures distal to the point of injection. Inadvertent injection of the carpometacarpal joint may occur[18]	22 g × 1 inch 0.7 × 25 mm 4–5 mL per palmar nerve, 3 mL per palmar metacarpal nerve	15 minutes
Base of the accessory carpal bone	The lateral and medial palmar metacarpal and lateral palmar nerves lie together at a site between the flexor retinaculum and the carpal sheath at a point midway between the head of MCIV and the base of the accessory carpal bone and immediately distal to the accessoriometacarpal ligament. The medial palmar nerve is injected as previously described[19]	All structures distal to the point of injection including the origin of the suspensory ligament. Inadvertent injection within the carpal canal may occur[18]	22 g × 1 inch 0.7 × 25 mm 3–4 mL at base of accessory carpal bone, 3 mL at medial palmar nerve	15 minutes
Suspensory ligament origin	The needle is inserted directly into the origin of the suspensory ligament. A large needle is used to reduce the chance of breakage. (High four-point, base of accessory carpal and suspensory origin blocks may be interchanged depending on operator preference)	The entire suspensory ligament and structures distal to the injection point. Inadvertent injection within the carpometacarpal joint may occur[18]	18 g × 1–1.5 inch 1.2 × 25–40 mm 4–6 mL	First check in 10 minutes, then again after 20 minutes
Median/ulnar/ musculocutaneous	The median nerve is injected on the caudomedial aspect of the radius immediately distal to the pectoral muscle mass. The needle is partially removed and redirected subcutaneously to a point just cranial to the cephalic vein for the musculocutaneous nerve. The ulnar nerve is injected 25 mm deep to the skin at a point 6–8 cm proximal to the accessory carpal bone between the flexor carpi ulnaris and ulnaris lateralis muscles	The entire limb distal to points of injection including the carpus, suspensory origin	22–20 g × 1.5 inch 0.7–0.9 × 40 mm 6–8 mL at median nerve, 4–6 mL at musculocutaneous nerve, 4–6 mL at the ulnar nerve	20–30 minutes

injection less uncomfortable to the horse, particularly when a larger gauge needle must be used.[16]

The sequence of diagnostic local anesthesia begins with the most distal nerves being injected first and gradually working proximally until the lameness has been localized. Regional anesthesia usually results in less effective analgesia of intra-articular soreness than direct intra-articular anesthesia. If the lameness has been improved noticeably, but not completely,

Table 14.4 Rear limb diagnostic anesthesia

Sequence of diagnostic local anesthesia	Anatomic site of injection	Region desensitized	Needle size and anesthetic volume	Onset of action
Palmar digital nerves (PDN)	Plantar aspect of pastern, immediately proximal to the collateral cartilages	Plantar heel, entire sole	25–22 g × 1 inch 0.5–0.7 × 16 mm 1.5–2 mL/nerve	10–15 minutes
Dorsal branch of PDN	Same as above, redirect needle dorsally approximately 1 inch (25 mm)	All structures within the hoof	As above	As above
Abaxial sesamoid (plantar nerves)	Abaxial aspect of proximal sesamoid bones (may use either dorsal branch or abaxial sesamoid block)	All structures within the hoof and most of structures from midpastern distal	25–22 g × 1 inch 0.5–0.7 × 16 mm 2–2.5 mL/nerve	As above
Low six-point (plantar, plantar metatarsal and dorsal metatarsal nerves)	At the level of the distal aspect of MTII and MTIV (splint bones). Plantar nerves are injected subcutaneously between the suspensory branch and the deep digital flexor tendon immediately proximal to the digital sheath. Plantar metatarsal nerves are injected subcutaneously immediately dorsal and distal to the splint buttons. Dorsal metatarsal nerves are injected immediately lateral and medial to the common extensor tendon	Fetlock joint and all distal structures	22 g × 1 inch 0.7 × 25 mm 4–5 mL per plantar nerve, 3 mL per plantar metatarsal nerve, 3 mL per dorsal metatarsal nerve	15 minutes
High six-point (plantar, plantar metatarsal and dorsal metatarsal nerves)	At the most proximal aspect of the metatarsus a palpable groove between the deep digital flexor tendon and suspensory ligament is palpable. The plantar nerves are injected in this groove. The plantar metatarsal nerves are injected by redirecting the needle to the axial surface of MTII and MTIV. Dorsal metatarsal nerves are injected immediately lateral and medial to the long digital extensor tendon	All structures distal to the point of injection. Inadvertent injection within the tarsometatarsal joint may occur[20]	22 g × 1 inch 0.7 × 25 mm 4–5 mL per plantar nerve, 3 mL per plantar metatarsal nerve, 3 mL per dorsal metatarsal nerve	15 minutes
Suspensory ligament origin	The needle is inserted directly into the origin of the suspensory ligament. A large needle is used to reduce the chance of breakage. (High six-point, and suspensory origin blocks may be interchanged depending on operator preference)	The entire suspensory ligament and structures distal to the injection point. Inadvertent injection within the tarsometatarsal joint may occur[20]	18 g × 1–1.5 inch 1.2 × 25–40 mm 4–6 mL	First check in 10 minutes, then again after 20 minutes
Tibial/peroneal	The tibial nerve is injected subcutaneously on the medial aspect of the limb approximately 6–8 cm proximal to the tuber calcis and immediately deep to the calcaneal tendon. The peroneal nerves are injected on the lateral aspect of the tibia with the needle inserted between the muscle bellies of the lateral and long digital extensor muscles. Injections are made 25 mm deep to the skin (deep peroneal n.) and subcutaneously (superficial peroneal n.)	The entire limb distal to points of injection including the tarsus, suspensory origin	20 g × 1.5 inch 0.9 × 40 mm 6–8 mL at tibial nerve, 4 mL at each peroneal nerve	20–30 minutes

following regional nerve anesthesia, intra-articular anesthesia of the suspect joint should be conducted. Regional nerve blocks are described for the forelimb (Table 14.3) and rear limb (Table 14.4). Distribution of the peripheral nerves is represented for the forelimb (Fig. 14.5) and rear limb (Fig. 14.6).

Intra-articular anesthesia

Navicular bursa

Strict asepsis must be adhered to at this site because of its close proximity to the ground and the attendant

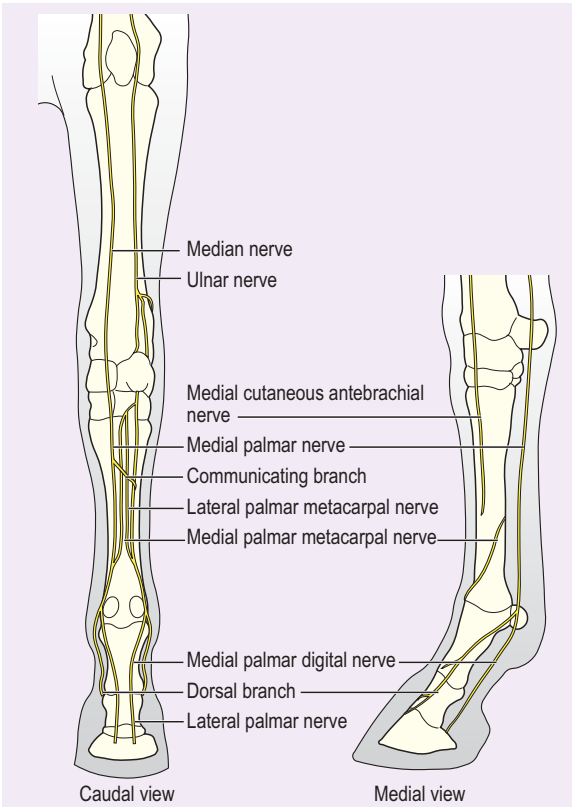

Fig. 14.5
Peripheral nerve distribution of the forelimb. Modified from Schmotzer & Timm,[16] with permission.

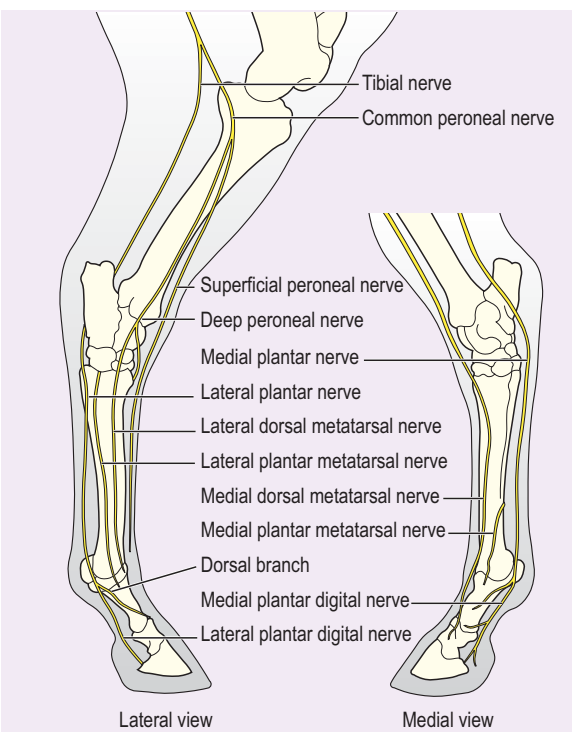

Fig. 14.6
Peripheral nerve distribution of the rear limb. Modified from Schmotzer & Timm,[16] with permission.

contaminants. A subcutaneous bleb of local anesthetic should be placed on the palmar aspect of the distal pastern in the midsagittal cleft immediately proximal to the heel bulbs. An 18 gauge, 3 inch (1.2 × 90 mm) spinal needle is advanced parallel to the bearing surface of the hoof until it contacts the flexor surface of the navicular bone. The needle should be aimed at a point 1 cm distal to the coronary band and midway between its most dorsal and palmar extent.[21] Correct placement of the needle should be confirmed with radiography or fluoroscopy before 3–5 mL of local anesthetic is injected.[22]

Comparing the results of navicular bursa, distal interphalangeal joint and palmar digital nerve local anesthesia may aid localization of distal limb lameness.[22] However, mepivacaine has been found to diffuse widely following injection in the distal equine limb, potentially confounding efforts to specifically localize the site of lameness.[25]

Distal interphalangeal joint

The distal interphalangeal (DIP) joint has a large dorsal pouch that is easily entered with a needle.[23] The joint may also be approached immediately cranial to the collateral cartilage.

Anesthetic injected in the DIP joint will desensitize other nearby structures. The proximal suspensory ligament of the navicular bone, distal extent of the palmar digital nerves, navicular bursa and impar ligaments are directly adjacent to palmar aspects of the DIP joint.[24] Thirty minutes after mepivacaine was injected in the DIP, local anesthetic concentrations sufficient to result in analgesia were found in the navicular bursa synovial fluid (10 of 10 horses) and in the medullary cavity of the navicular bone (six of 10 horse).[25] Mepivacaine diffused from the distal interphalangeal joint into the navicular bursa and vice versa in 25 of 25 joints evaluated.[25] Ten minutes following distal interphalangeal joint anesthesia lameness induced by tightening a set screw on the sole was resolved.[17]

Dorsal approach This injection is best made with the horse fully weight bearing using a 20–18 gauge, 1½ inch (0.9–1.2 × 40 mm) needle. The needle is inserted 1.5–2 cm proximal to the coronary band and a similar distance lateral or medial to the extensor process of the distal phalanx and directed toward the extensor process.[16] A skin bleb may be made at this site to facilitate needle placement. Alternatively, the needle may be directed perpendicular to the dorsal cortex of the second phalanx and 'walked' distally until the joint is entered. The needle usually penetrates the skin approximately 1 inch (25 mm) before entering the joint. Four to 6 mL of anesthetic is injected.

Hemorrhage often occurs from the coronary corium when the needle is withdrawn. Counterpressure and a light bandage will control any bleeding and help protect the region from contamination until the needle puncture seals.

Lateral approaches Two dorsolateral approaches have been described with the needle inserted either cranial[26] or proximal[23] to the collateral cartilage. The most cranial extent of the collateral cartilages is palpated and the needle is

inserted at that point approximately 1–1.5 cm proximal to the coronary band with the horse fully weight bearing. The needle is first inserted parallel to the bearing surface of the hoof, then immediately angled 30° distally and 30° toward the midline.

Needle placement proximal to the collateral cartilage may be performed with the horse non-weight bearing. The needle is inserted just proximal to the collateral cartilage midway between the dorsal and palmar aspect of the second phalanx and is directed along the palmar surface of the second phalanx by aiming at the center of the frog.[23]

Proximal interphalangeal joint

A dorsolateral or palmar approach may be used to enter the proximal interphalangeal (PIP) joint. The dorsal approach is made with the horse weight bearing. A large palmar pouch of the PIP joint is readily entered with the limb non-weight bearing and with the distal joints flexed.[27]

Dorsal approach The horse should be weight bearing for this approach. A 20 gauge, 1½ inch (0.9 × 40 mm) needle is directed through the skin approximately 1–1.5 cm distal to the distal eminence of the first phalanx and under the extensor tendon. Orient the needle parallel with the dorsal joint surface. Inject 4–5 mL of local anesthetic.[16]

Palmar approach The limb should be picked up and held with the distal joints in moderate flexion. The palmar pouch of the PIP joint is bounded by the palmar first phalanx, the palmarodistal eminence of the first phalanx and the insertion of the lateral branch of the superficial digital flexor tendon. When the pastern is moderately flexed these structures form a 'V' on the palmar first phalanx. Retract the palmar digital neurovascular bundle that lies directly over the needle insertion site in a palmar direction, using the operator's thumb. The needle is placed through the skin dorsal to the neurovascular bundle within the region of the distal 25% of the first phalanx and directed distally and toward the midline. Joint fluid is commonly aspirated.[27]

Metacarpophalangeal/metatarsophalangeal joint

The fetlock joint is commonly injected for diagnostic and therapeutic reasons. Three approaches may be used: dorsal, palmar/plantar pouch and palmar/plantar approach through the collateral sesamoidean ligament. The collateral sesamoidean ligament approach is best used if arthrocentesis is an objective because synovial fluid free of blood contamination is more readily obtained.[28] Administration of local anesthesia is most easily performed using the palmar/plantar pouch approach.

Palmar/plantar pouch The approach is made with the horse weight bearing. The palmar/plantar pouch is bounded by the third metacarpus/metatarsus dorsally, distally by the apex of the sesamoid bone, and palmar/plantar by the suspensory ligament. A 20 gauge, 1½ inch (0.9 × 40 mm) needle is inserted through the skin in the center of this site and directed distally and toward the midline. Synovial fluid commonly will drip from the needle if effusion is present, but aspiration with a syringe often results in plugging of the needle with synovial tissue. Four to 6 mL of local anesthetic is injected.[16]

Dorsal approach This approach should only be used if effusion is present because of the possibility of abrading joint cartilage with the needle. The horse should be weight bearing. The needle is placed from the lateral side into the proximal aspect of the dorsal joint capsule and directed toward the midline and under the extensor tendon. Care should be taken not to abrade the sagittal ridge.[16]

Collateral ligament approach The limb should be held up with the fetlock joint flexed. This procedure is facilitated by having an assistant hold the limb. The lateral palmar aspect of the distal metacarpal/metatarsal condyle and the dorsal surface of the proximal sesamoid bone are palpated. The collateral sesamoidean ligament may be rarely palpated. The neurovascular bundle over the abaxial surface of the sesamoid bone does not interfere with this approach because it is displaced palmar when the joint is flexed. The needle is inserted in the palpable space between the third metacarpus/metatarsus and the proximal sesamoid bone. Entry into the joint is easily determined because the needle may be inserted up to its hub.[28]

Carpal joints

The radiocarpal joint is always separate from the middle carpal and carpometacarpal joints, which always communicate.[29] Complete intra-articular anesthesia of the carpus necessitates injecting local anesthetic into the radiocarpal and middle carpal joints. The joints are traditionally injected with the limb flexed, but may also be injected with the horse weight bearing on the limb.

Dorsal approach The limb is flexed and the joint spaces of the middle and radial carpal joints are easily palpated medial or lateral to the extensor carpi radialis tendon.[16] A 20 gauge, 1–1½ inch (0.9 × 25–40 mm) needle is most often inserted medial to the extensor carpi radialis tendon. If the needle is inserted lateral to the extensor carpi radialis tendon care must be taken to avoid the common digital extensor tendon and its sheath. The most common difficulty encountered when inserting the needle is penetrating into articular cartilage. To avoid this, visualize the plane of the carpal articular surfaces distal to the intended needle insertion site. Direct the needle parallel to the joint surfaces on insertion. Inject 10 mL of local anesthetic per joint.

Caudolateral approach The carpal joints may also be injected with the horse weight bearing on the limb. By inducing slight carpal flexion, the joint spaces may be identified by palpation of the lateral aspect of the carpus. The radiocarpal joint is approached immediately cranial to the accessory carpal bone at roughly 50% of its proximal–distal length. The middle carpal joint is approached immediately cranial to the distal aspect of the accessory carpal bone.[30]

Cubital (elbow) joint

The cubital joint is injected on the lateral aspect of the limb just cranial to the lateral collateral ligament.[31] The joint

space may be palpated in most horses by identifying the humeral condyle and tracing its margin. The procedure may be done with the horse standing or by having an assistant elevate the forelimb slightly to open the joint space dorsally.[31] An 18–20 gauge, 1½ inch (0.9–1.2 × 40 mm) needle is inserted perpendicular to the limb and 15–20 mL of local anesthetic is injected. An alternative approach is to insert the needle on the cranial aspect of the olecranon at a point approximately 3 cm distal to its most proximal extent. The needle is directed distally and axially.[3]

Scapulohumeral (shoulder) joint

Craniolateral approach This is the most common approach used to inject the scapulohumeral joint. Identify the cranial and caudal parts of the greater tubercle on the craniolateral aspect (point) of the shoulder. An intradermal bleb of anesthetic will facilitate insertion of the spinal needle. An 18 gauge, 3½ inch (1.2 × 90 mm) spinal needle with a stylet is inserted in the notch between the cranial and caudal parts of the greater tubercle and directed slightly distally and toward the opposite tarsus (roughly a 30–40° angle to the long axis of the horse). The needle is inserted 2–3 inches (50–75 mm) to reach the joint. Synovial fluid is rarely aspirated to confirm the needle is within the joint. Injection of 10–20 mL of anesthetic with minimal resistance initially, followed by increased resistance as the joint fills, confirms that the needle is correctly positioned.[31] Excessive diffusion of local anesthetic into the surrounding tissues may cause temporary anesthesia of the suprascapular nerve. While this nerve is desensitized, the horse will lack use of the infraspinatus and supraspinatus muscles, which results in abaxial displacement of the shoulder during weight bearing. This may be avoided by injecting the minimum volume of anesthetic necessary to effect joint desensitization and by minimizing multiple needle punctures of the joint capsule.[3,31]

Lateral approach A skin bleb of anesthetic may be placed immediately caudal to the infraspinatus tendon at the level of the proximal humerus. The needle is inserted immediately caudal to the infraspinatus tendon, roughly perpendicular to the long axis of the horse and directed slightly distally. The needle is inserted 1.5–2 inches (40–50 mm) to enter the joint. Synovial fluid is more commonly obtained with this approach.[3]

Bicipital bursa The bicipital bursa lies between the bicipital tendon and the dorsoproximal aspect of the humerus. The bursa is injected using an 18 gauge, 1½ inch (1.2 × 40 mm) needle entering perpendicular to the skin at a point proximal to the deltoid tuberosity and distal to the proximal humeral tuberosity.[31] Ten to 15 mL of local anesthetic is injected.

Tarsal joints

It is commonly accepted that the tarsocrural (tibiotarsal) and proximal intertarsal (PIT) joints always communicate. Communication between the distal intertarsal (DIT) and tarsometatarsal (TMT) joints is reported to occur 8–38% of the time.[20,32,33] For accurate diagnosis or complete treatment of the distal tarsal joints, separate injections must be made in the DIT and TMT joints.

Use of 22 gauge (0.7 mm) needles with metal hubs facilitates injections of the distal tarsal joints, particularly when medications are being administered. The small needle size makes placement within the joint easier and the syringe is more securely seated in a metal than a plastic hub needle. The more secure syringe attachment decreases the inadvertent leakage of costly medications.

Tarsocrural (tibiotarsal) and proximal intertarsal joints These joints are approached on the dorsomedial aspect of the proximal tarsus. An 18–20 gauge, 1½ inch (0.9–1.2 × 40 mm) needle is inserted either lateral or medial to the medial saphenous vein at a point 1–3 cm distal to the medial malleolus.[16] Eight to 10 mL of local anesthetic is injected. If joint effusion is present, the needle may be inserted in the plantarolateral pouch of the tarsocrural joint.

Tarsometatarsal joint The TMT joint may be injected from a plantarolateral or medial approach. The plantarolateral approach is the easiest method because the landmarks are readily palpated and the needle can usually be inserted securely into the joint. The site for plantarolateral injection is directly proximal to the head of the lateral splint bone (metatarsal IV). The plantar edge of the splint and the indentation at its head is identified. A 22–20 gauge, 1 inch (0.7–0.9 × 25 mm) needle is directed toward the opposite forelimb and distally at approximately 10–15°.[32] When correctly placed, the needle is inserted nearly to its hub and 3–4 mL of local anesthetic is injected.

No landmarks are palpable when injecting the TMT from the medial approach. The needle is inserted perpendicular to the medial surface of the tarsus approximately 1 cm distal to the DIT joint (see below). A 22 gauge (0.7 mm) needle should be used and the joint is found by probing with the needle until it enters the joint.

Distal intertarsal joint The DIT joint is injected by placing a 22 gauge, 1 inch (0.7 × 25 mm) needle in a small space between the fused first and second tarsal bones, and the third and central tarsal bones. The space is immediately distal to the cunean tendon on the medial aspect of the tarsus. Firm digital pressure is necessary to identify the space. The needle is inserted perpendicular to the medial tarsal surface and some probing is often necessary to fall into the joint space.[33] If the needle does not enter the joint easily, inject 1–2 mL of local anesthetic subcutaneously. This will make repeated needle insertions more comfortable for the horse. Probing for the joint space often causes a burr to form on the needle tip, necessitating changing of the needle. Formation of a burr will be obvious because of the increased friction and rough feel of the needle during continued probing. Inject 3–4 mL of local anesthetic.

Stifle joints

The stifle includes three large-volume joints: the femoropatellar, lateral femorotibial and medial femorotibial. The

femoropatellar and medial femorotibial joints communicate in 60–80% of horses.[34,35] The lateral and medial femorotibial joints do not communicate under normal circumstances.[34] Each joint should be separately injected to ensure complete analgesia of the stifle.[35]

Femoropatellar joint Insert an 18 gauge, 3½ inch (1.2 × 90 mm) spinal needle at the cranial aspect of the stifle between the middle and medial or middle and lateral patellar ligaments at a point approximately 2 cm proximal to the tibial crest with the limb fully weight bearing. Direct the needle slightly proximal to a depth of approximately 2–3 inches (50–75 mm). Synovial fluid is rarely aspirated using this approach, but entry into the joint is assumed when there is minimal resistance during injection of 30–50 mL of local anesthetic.

An alternative approach may be used to enter the lateral proximal pouch of the femoropatellar joint. With the limb fully weight bearing, an 18 gauge, 1½ inch (1.2 × 40 mm) needle is placed immediately caudal to the proximal aspect of the lateral trochlear ridge and the lateral patellar ligament. The needle is directed lateral to medial and somewhat distal. The insertion point is approximately 5 cm proximal to the lateral tibial condyle. This approach avoids abrasion of articular cartilage with the needle and facilitates aspiration of synovial fluid.[36]

Lateral and medial femorotibial joints For needle placement in the lateral femorotibial joint have the limb fully weight bearing and identify the space between the proximal tibia and the distal trochlear ridge of the femur between the lateral patellar ligament and the lateral collateral ligament. The space is a small triangle of soft tissue that you may indent on digital palpation. An 18–20 gauge, 1½ inch (0.9–1.2 × 40 mm) needle is inserted perpendicular to the skin and may be placed nearly to its hub.[31] Inject 15–20 mL of local anesthetic. The approach is similar for the medial femorotibial joint with the needle being placed between the medial patellar and medial collateral ligaments.

Coxofemoral joint

Accurately injecting local anesthetic into the coxofemoral joint is not easily accomplished. The landmarks may be difficult to palpate in heavily muscled horses and the joint is very distant to the insertion point of the needle.

The horse should be standing squarely in stocks and a bleb of local anesthetic in the skin should be placed at the needle insertion point. The paired eminences of the major trochanter of the femur lie on a line approximately two-thirds of the distance from the tuber coxae to the tuber ischium. The proximal aspect of the cranial part of the greater trochanter lies approximately 5 cm distal to the proximal extent of the caudal part. A 16 gauge, 5–8 inch (1.5 mm × 15–20 cm) needle is inserted immediately proximal to the cranial part of the greater trochanter. The needle is directed in nearly a horizontal plane, slightly cranial and distal, toward the coxofemoral joint. The joint capsule is thick and may require vigorous pressure on the needle to penetrate. A volume of 20–40 mL of local anesthetic is injected.[31]

Imaging

When the lameness has been localized with manipulations and/or diagnostic local anesthesia, the region should have appropriate images obtained to allow a diagnosis of the lameness. Most often, this would involve radiography or ultrasonography but occasionally nuclear scintigraphy, computed tomography, magnetic resonance imaging or thermography may be used.

References

1. Denoix J-M. Diagnostic techniques for identification and documentation of tendon and ligament injuries. Vet Clin North Am Equine Pract 1994; 10(2):365–407.
2. AAEP. Guide for veterinary service and judging of equestrian events, 4th edn. Lexington, KY: American Association of Equine Practitioners; 1991:19.
3. Stashak TS. Adams' lameness in horses, 5th edn. Philadelphia, PA: Lippincott, Williams and Wilkins; 2002:113–183, 664–680.
4. Back W, Schamhardt HC, Hartman W, et al. Kinematic differences between the distal portions of the forelimbs and hindlimbs of horses at the trot. Am J Vet Res 1995; 56(11):1522–1528.
5. Kramer J, Keegan KG, Wilson DA, et al. Kinematics of the hind limb in trotting horses after induced lameness of the distal intertarsal and tarsometatarsal joints and intra-articular administration of anesthetic. Am J Vet Res 2000; 61(9):1031–1036.
6. Buchner HH, Savelberg HH, Schamhardt HC, et al. Limb movement adaptations in horses with experimentally induced fore- or hindlimb lameness. Equine Vet J 1996; 28(1):63–70.
7. Buchner HH, Savelberg HH, Schamhardt HC, et al. Head and trunk movement adaptations in horses with experimentally induced fore- or hindlimb lameness. Equine Vet J 1996; 28(1):71–76.
8. Keg PR, van Weeren PR, Back W, et al. Influence of the force applied and its period of application on the outcome of the flexion test of the distal forelimb of the horse. Vet Rec 1997; 141(18):463–466.
9. Busschers E, van Weeren PR. Use of the flexion test of the distal forelimb in the sound horse: repeatability and effect of age, gender, weight, height and fetlock range of motion. J Vet Med A Physiol Pathol Clin Med 2001; 48(7):413–427.
10. Keg PR, van Weeren PR, Schamhardt HC, et al. Variations in the force applied to flexion tests of the distal limb of horses. Vet Rec 1997; 141(17):435–438.
11. Specht TE, Nixon AJ, Moyer DJ. Equine synovia after an intra-articular injection of lidocaine or mepivacaine. Vet Surg 1988; 17:42.
12. Moore DC, Bridenbaugh DL, Bridenbaugh PO, et al. Bupivacaine for peripheral nerve block: a comparison with mepivacaine, lidocaine and tetracaine. Anesthesiology 1970; 32:462–463.
13. Mama KR, Steffey EP. Local anesthetics. In: Adams HR, ed. Veterinary pharmacology and therapeutics, 8th edn. Ames: Iowa State University Press; 2001:343–359.
14. Riebold TW, Geiser DR, Goble DO. Large animal anesthesia: principles and techniques, 2nd edn. Ames: Iowa State University Press; 1995:205–209.

15. Hague BA, Honnas CM, Simpson RB, et al. Evaluation of skin bacterial flora before and after aseptic preparation of clipped and nonclipped arthrocentesis sites in horses. Vet Surg 1997; 26:121–125.
16. Schmotzer WB, Timm KI. Local anesthetic techniques for diagnosis of lameness. Vet Clin North Am Equine Pract 1990; 6(3):705–728.
17. Schumacher J, Steiger R, Schumacher J, et al. Effects of analgesia of the distal interphalangeal joint or palmar digital nerves on lameness caused by solar pain in horses. Vet Surg 2000; 29:54–58.
18. Ford TS, Ross MW, Orsini PG. A comparison of methods for proximal palmar metacarpal analgesia in horses. Vet Surg 1989; 18:146–150.
19. Wheat JD, Jones K. Selected techniques of regional anesthesia. Vet Clin North Am Large Animal Pract 1981; 3:223–246.
20. Dyson SJ, Romero JM. An investigation of injection techniques for local analgesia of the equine distal tarsus and proximal metatarsus. Equine Vet J 1993; 25(1):30–35.
21. Schramme MC, Boswell JC, Hamhougias K, et al. An in vitro study to compare 5 different techniques for injection of the navicular bursa in the horse. Equine Vet J 2000; 32(3):263–267.
22. Dyson SJ, Kidd L. A comparison of responses to analgesia of the navicular bursa and intra-articular analgesia of the distal interphalangeal joint in 59 horses. Equine Vet J 1993; 25(2):93–98.
23. Vazquez de Mercado R, Stover SM, Taylor KT, et al. Lateral approach for arthrocentesis of the distal interphalangeal joint in horses. J Am Vet Med Assoc 1998; 212(9):1413–1418.
24. Bowker RM, Linder K, van Wulfen KK, et al. Anatomy of the distal interphalangeal joint of the mature horse: relationships with navicular suspensory ligaments, sensory nerves and neurovascular bundle. Equine Vet J 1997; 29:126–135.
25. Keegan KG, Wilson DA, Kreeger JM, et al. Local distribution of mepivacaine after distal interphalangeal joint injection in horses. Am J Vet Res 1996; 57:422–426.
26. Moyer W, Carter GK. Techniques to facilitate intra-articular injection in equine joints. Proceedings of the American Association of Equine Practitioners 1996; 42:48–54.
27. Miller SM, Stover SM, Taylor KT, et al. Palmaroproximal approach for arthrocentesis of the proximal interphalangeal joint in horses. Equine Vet J 1996; 28(5):376–380.
28. Misheff MM, Stover SM. A comparison of two techniques for arthrocentesis of the equine metacarpophalangeal joint. Equine Vet J 1991; 23(4):273–276.
29. Ford TS, Ross MW, Orsini PG. Communication and boundaries of the middle carpal and carpometacarpal joints in horses. Am J Vet Res 1988; 49:2161–2164.
30. Kiely RG, McMullen W. Lateral arthrocentesis of the equine carpus. Equine Practice 1987; 9:22.
31. Lewis RD. Techniques for arthrocentesis of equine shoulder, elbow, stifle and hip joints. Proceedings of the American Association of Equine Practitioners 1996; 42:55–63.
32. Sack WO, Orsini PG. Distal intertarsal and tarsometatarsal joints in the horse: communication and injection sites. J Am Vet Med Assoc 1981; 179(4):355–359.
33. Kraus-Hansen AE, Jann HW, Kerr DV, et al. Arthrographic analysis of communication between the tarsometatarsal and distal intertarsal joints of the horse. Vet Surg 1992; 21(2):139–144.
34. Vacek JR, Ford TS, Honnas CM. Communication between the femoropatellar and medial and lateral femorotibial joints in horses. Am J Vet Res 1992; 53(8):1431–1434.
35. Reeves MJ, Trotter GW, Kainer RA. Anatomical and functional communications between the synovial sacs of the equine stifle joint. Equine Vet J 1991; 23(3):215–218.
36. Hendrickson DA, Nixon AJ. Comparison of the cranial and a new lateral approach to the femoropatellar joint for aspiration and injection in horses. J Am Vet Med Assoc 1994; 205(8):1177–1179.

CHAPTER 15

Diseases of the foot

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A thorough examination and assessment of the equine foot forms an essential part of both the physical and lameness evaluation. Because foot problems are the most common cause of lameness in horses, the examiner must have an accurate knowledge of foot anatomy and must be willing to take a 'hands-on' approach to fully identify any problems the horse might be experiencing.

There are numerous causes of pain in the foot of the horse. These can be divided arbitrarily into: (1) conditions of the hoof wall and horn-producing tissues; (2) conditions of the distal phalanx; and (3) conditions of the podotrochlear region:

1. Hoof problems include: hoof-wall defects, such as cracks that involve the sensitive tissue; laminitis (systemic); laminar tearing (local, due to hoof imbalance); separation or inflammation of the sensitive laminae from the insensitive laminae; abscess formation; contusions of the hoof causing bruising or corn formation; neoplasia; and pododermatitis (thrush or canker).
2. Distal phalanx problems include: fractures of the coffin bone (types I–VII), deep digital flexor insertional tenopathy, pedal osteitis (generalized or localized inflammation of the bone), disruption of the insertions of the collateral ligaments, cyst-like lesion formation, and remodeling disease.
3. Conditions of the podotrochlear region have been reported to include: distal interphalangeal synovitis/capsulitis, deep digital flexor tendonitis, desmitis of the impar (distal navicular ligament) or collateral sesamoidean ligaments, navicular osteitis or osteopathy, and vascular disease of the navicular arteries, and navicular fractures.

The common denominator of all these conditions is that they are characterized by pain that can be localized to the hoof.

Anatomy

- The hoof capsule is comprised of tubular and intertubular keratin arranged as a laminated composite material.
- Ninety per cent of the energy input is dissipated by the hoof capsule and its associated structures.
- The lamellae of the inner layer of the hoof capsule provide a large surface area (13.75 sq ft; 1.28 sq meters) to suspend the coffin bone.

The hoof capsule is an amazing design that not only provides strength but also supports the horse's skeletal column. Keratin is the main structural protein of the epidermis in the animal kingdom and is present in skin, hair, nail, claw, wool, horn, feather, and scale, as well as hoof. The keratins can be loosely grouped into the 'soft' keratins of skin and the 'hard' keratins of horn, hair, etc. In the horse, the tubular hoof of the wall is composed of hard keratin and is rich in disulfide bonds, and so has great physical strength. The frog and the white zone are rich in sulfhydryl groups but poor in disulfide bonds, and therefore have lower physical strength but greater elasticity. The strength, hardness, and insolubility of keratin are due to disulfide bonds between and within the molecules. The sulfur-containing amino acids methionine and cysteine are incorporated into the keratinocytes in the final stages of its maturation and hence these amino acids (or their sulfur-containing precursors) are a necessary part of the diet.

New hoof is made continuously because there is continual loss of hoof wall from the ground surface. Continual regeneration of the hoof wall occurs at the coronary band where germinal cells (epidermal basal cells) produce populations of daughter cells (keratinocytes or keratin-producing cells), which mature and keratinize, continually adding to the hoof wall. It takes these cells anywhere from 6 to 12 months to reach the ground surface.

Two types of horn are produced from the coronary band. Tubular horn arises from cells surrounding papillae (finger-like projections from the coronary band) and become organized into thin, elongated, cylinders or tubules. In cross-section the keratinocytes of individual hoof wall tubules are arranged around a central hollow medulla in nonpigmented concentric layers. Each hair-like tubule is continuous, from its origin at the coronary band all the way to the ground surface (a distance of 5–15 cm, depending on the breed). The keratinocytes generated between the papillae mature into intertubular hoof, thus forming a keratin matrix in which tubules are embedded. The intertubular horn is formed at right angles to the tubular horn and bestows on the hoof wall the unique property of a mechanically stable, multidirectional, fiber-reinforced composite. Interestingly, hoof wall is stiffer and stronger at right angles to the direction of the tubules, a finding that is at odds with the usual assumption that the ground reaction force is transmitted proximally up the hoof wall parallel to the tubules. The hoof wall appears to be reinforced by the tubules but it is the intertubular material that accounts for most of its mechanical strength stiffness and fracture toughness. The tubules are three times more likely to fracture than intertubular horn. Thus hoof wall is considered to have an anatomical design that confers strength in all directions. During normal locomotion the hoof wall only experiences one-tenth of the compressive force required to cause its structural failure.

The fully keratinized cells of the tubular and intertubular hoof, cemented firmly to each other, form a continuum; the tough yet flexible stratum medium of the hoof wall. When mature, these cells, which are firmly cemented together, form a tough protective barrier preventing the passage of water and water-soluble substances inwards and the loss of body fluids, imparted by the highly vascular dermis, outwards. In addition to acting as a permeability barrier, the hoof wall ultimately is responsible for supporting the entire weight of the horse.

The tubules of the equine hoof wall are not arranged randomly. The tubules of the hoof wall are arranged in four distinct zones based on the density of tubules in the intertubular horn. The zone of highest tubule density is the outermost layer and the density declines stepwise towards the internal lamellar layer. As the force of impact with the ground (the ground reaction force) is transmitted proximally up the wall, the tubule density gradient across the wall appears to be a mechanism for smooth energy transfer, from the rigid (high tubule density) outer wall to the more plastic (low tubule density) inner wall, and ultimately to the coffin bone (third phalanx). The gradient in tubule density mirrors the gradient in water content across the hoof wall and together these factors represent an optimum design for equine hoof-wall durability. The zones confer on the hoof wall the design properties of a laminated composite; the interface between zones absorbs energy and prevents the propagation of cracks towards sensitive inner structures. In addition, the fact that the hoof wall is stronger in one direction ensures that cracks, when they occur, propagate from the bearing surface upwards and parallel with the tubules (that is, they propagate along the weakest plane). They do not extend to the innermost layers of the hoof wall because in this region the relatively high water content confers high crack resistance (the hoof wall is more pliable). The hoof wall also has a powerful dampening function on vibrations generated when the hoof wall makes contact with the ground during locomotion. It is able to reduce both the frequency and maximal amplitude of the vibrations. In fact, by the time the shock-wave of impact with the ground reaches the coffin bone, around 90% of the energy has been dissipated.

The corium is the region of the foot that nourishes the hoof-wall cells. There are several distinct zones, the coronary corium, lamellar corium, solar corium, and frog corium. The coronary corium fills the coronary groove and blends distally with the lamellar corium. Its inner surface is attached to the extensor tendon and the cartilages of the coffin bone by the subcutaneous tissue of the coronary cushion. Collectively the coronary corium and the germinal epidermal cells that produce the hoof wall are known as the coronary band. A feature of the coronary corium is the large numbers of hair-like papillae projecting from its surface. Each tapering papilla fits into one of the holes on the surface of the epidermal coronary groove and in life, is responsible for nurturing an individual hoof wall tubule.

The innermost layer of the hoof wall and bars is named the stratum lamellatum after the 550–600 primary epidermal lamellae that project from its surface in parallel rows. Examination of the hoof capsule, with its contents removed, shows that the lamellae of the dorsal hoof wall are shaped like long, thin, rectangles approximately 7 mm wide and 50 mm long. One edge of the rectangle is incorporated into the tough, heavily keratinized hoof wall proper and the opposite end faces the outer surface of the coffin bone. The proximal end is curved and forms the curved shoulder of the coronary groove. The distal end merges with the sole and becomes part of the white zone visible at the ground surface of the hoof (white line).

In common with all epidermal structures, the lamellae of the inner hoof wall are avascular and depend on capillaries in the microcirculation of the adjacent corium for nutrition. The lamellar corium covers the coffin bone. The primary function of the lamellar hoof is to suspend the coffin bone within the hoof capsule. It reserves its proliferative potential for the healing of injuries.

Because the role of the lamellae is suspension of the distal phalanx, an anatomical specialization increasing the surface area for the attachment of the multitude of collagenous fibers arising from the outer surface of the coffin bone would be expected. The secondary epidermal lamellae are just such a specialization. These folds form an extra 150–200 secondary lamellae along the length of each of the 550–600 primary lamellae.

The tips of the lamellae (both primary and secondary) all orientate towards the distal phalanx, thus indicating the lines of tension to which the lamellar suspensory apparatus is subjected. The surface area of the equine inner hoof wall has been calculated to average 13.75 square feet (1.28 square meters). This means that the lamellae (contained inside the hoof capsule) have a surface area roughly equal to two-thirds the size of a standard door. This large surface area for suspension of the coffin bone and the great compliance of the interdigitating

lamellar architecture helps reduce stress and ensures even energy transfer during peak loading of the equine foot. In life, this hoof wall/coffin bone interface is amazingly strong and can be separated only under the direst circumstances.

Examination of the distal limb

Six steps should be taken in the evaluation of foot pain:

1. history
2. subjective evaluation of the hoof
3. objective assessment of hoof balance
4. assessment of pain
5. the response to diagnostic analgesia
6. imaging of the foot.

History

Any examination begins by obtaining a history.[1] More information than age, breed, and sex is necessary. Obviously, the questions that should be answered would apply to any lameness examination, but some will have greater significance when dealing with foot problems.

The examiner must know what the presenting problem is and how long it has been apparent. It is an excellent idea to ask what the owner/trainer suspects is wrong. The examiner then can address these concerns while ascertaining the problem. The history-taker then needs to ask about the pattern of lameness (intermittent or constant) and, if the lameness is intermittent, under what conditions it is likely be seen, i.e. at the beginning of exercise or after hard work.

An appreciation of the breed and the use of the horse will also provide information relative to the incidence of certain foot problems. Thoroughbred and Quarter Horse racehorses have a relatively high incidence of foot bruising, pedal osteitis, distal phalanx fractures, heel bulb damage from overreaching, quarter cracks, nail problems, underrun and sheared heels. Standardbred racehorses have similar foot problems but also have a much higher incidence of quarter cracks. Racing combines extraordinary speed with surfaces that are more conducive to speed than to cushion, thus creating tremendous force on the hoof. Quarter Horses, Thoroughbreds, Standardbreds and the Warmblood breeds have the highest incidence of navicular problems, whereas Arabians and ponies have the least issue with the navicular bone. Horses that participate in agility sports such as roping, cutting, reining, barrel racing, and polo have frequent problems with pulled shoes and associated hoof wall loss. Distal phalangeal fractures occur but with less frequency than in racing. Palmar foot pain syndrome is a frequent diagnosis in this group as well. Horses used over fences, such as showjumpers and eventers, suffer frequently from foot bruising, pulled shoes and hoof-wall loss, quarter cracks, and palmar foot pain syndrome. Gaited horses such as Morgans, American Saddlebreds, Tennessee Walking Horses, Arabians, and Hackneys (horses and ponies) are often purposely shod with longer hooves, heavier shoes and pads, which alters the biomechanics of the hoof capsule for animation and frequently results in problems with hoof-wall breakage, hoof cracks, and thrush. Sand cracks (coronary quarter cracks) occur more often in Saddlebreds and Tennessee Walking Horses than any other breed.

Laminitis is seen frequently in older horses of all breeds, Morgans, ponies of all breeds, and heavily campaigned overweight show horses. Horses that are turned out to pasture for extended periods of time frequently show hoof-wall loss, superficial hoof cracks, and subsolar infections. The larger draft breeds (Clydesdales, Percherons, Belgians) that work in harness often injure the coronet and associated tissues by stepping on their feet. There is reportedly a high incidence of canker in these draft breeds.

It is helpful to determine when the horse was last shod or trimmed; to evaluate the shoeing you must know when it was performed. Often, a normal healthy hoof will grow over the shoe when it is due for a reset. The hoof also does not necessarily grow uniform, so the way the horse was shod by the farrier might not be what you see as an examiner weeks later. Foot problems that arise within a few days of shoeing can indicate sole pressure, a poorly placed or overclinched nail(s), or excessive trimming. Find out whether the farrier encountered any recent problems or has had to deal with ongoing shoeing problems. This might include horses that are difficult to shoe because of behavioral problems, thin walls, continual evidence of bruising, or thrush.

It is important to ascertain the environment in which the horse lives, trains, and competes. The environment plays a major role in the quality of the horn of the hoof and, as such, serves as the catalyst of many foot problems. The time of year and the surface can dramatically change the feet as well as the shoes. For instance, a horse training on a stone dust track will show very rapid wear of the shoes, the groove or fullering might be completely gone in less than 2 weeks; whereas, the shoes of a horse training on a deep, soft sand track might show very little evidence of wear in as many as 6 to 8 weeks. Foot bruising, pedal osteitis, and distal phalanx fractures are much more likely on hard 'fast' surfaces than on grass or deeper surfaces. Horses that are subjected to wet grass in the morning and hot, dry conditions later in the day often develop weak hoof walls and lose shoes easily. Adverse environmental factors can negatively influence the outcome of some foot problems. When horses move from one environment to another the feet often become a problem. This has been a particular problem of horses moving in the USA from the Midwest (soft, moist surfaces) to the Rocky Mountain region (hard, dry surfaces). The horse's foot is simply too slow to adapt to a change in stress. We have occasionally seen the same problem in horses coming from Europe. The hoof appears to need acclimatizing to the new environment.

Look at the current type of shoe being used, as well as the type of shoe used in the past. Is it steel or aluminum? The answer might be as simple as the horse appears to perform best with one particular type of shoe and poorly with another. However, the farrier might also have recognized a problem and begun to make adjustments. On the other hand,

the shoe could simply be a trainer's preference without a good reason for using it. Enquire why any special shoe or addition to a shoe (calk, grabs, extensions, or bars) was used. Bar shoes, for example, are often useful in treating various foot problems but can be essentially useless for some horses trying to race, in other instances, bar shoes might be a fad (e.g. all the dressage horses in a barn wearing egg-bar shoes). Is the bar shoe fitted appropriately? First and foremost it must be remembered that a shoe has no magical properties and how the shoe is applied is more important than the type of shoe, i.e. 'the application is more important than the appliance'. Some horses simply do not get sufficient traction on some surfaces or travel as well in certain types of shoes. Prior knowledge of a shoeing history as it affects an individual horse is useful information. It should suggest to the examiner that an alternative should be sought or that an individual horse should be trained at speed to see if he or she can 'handle' the surface with the type of shoe that is employed.

Information regarding previous foot problems must be obtained. The horse might have experienced a foot abscess 3 or 4 weeks earlier, or 'foundered' 1–2 years earlier, all of which would suggest to the examiner that the same problem might have resurfaced. Obtaining reasonable detail on the previous treatments is essential when examining an ongoing problem for the first time. This will help to prevent the use of a similar but previously unsuccessful treatment.

Subjective evaluation of the hoof

Like any physical examination, this involves more than simply measuring a few parameters and determining where on the scale of normality they fall; it should be a systematic evaluation of the hoof capsule and the structures within that tell the examiner about the general health of the hoof, the stresses that have been placed on it and how the hoof has responded to these stresses. The hoof is a dynamic structure that grows continuously and therefore has the ability to deform continuously to stresses that are applied to it.

The examination begins simply by looking at the hoof, preferably from sufficient distance to compare all four feet at once.[1] The size, shape, toe length, heel length, hoof pastern axis, and position of each foot relative to each limb and to each other are assessed. This is the best time to evaluate the horse's 'balance', i.e. the differences in each of the horse's legs and how the horse stands on the hoof.[2] One could consider this a conformational analysis but in fact the examiner is simply evaluating the position of the hoof on the end of the limb. This analysis must be evaluated from three directions: the front (dorsal), the side (lateral), and the back (palmar/plantar).[3] From the front, the hoof needs to be assessed for symmetry and alignment. Is the hoof centered under the cannon bone or is it offset? If the hoof is offset then the stresses on the hoof will change. Does the hoof rotate on the leg (toe-in or toe-out)? If it does rotate, what is the origin of the rotation, knee, fetlock, pastern, or hoof? This will determine where the torque is occurring in the hoof. Does the ground surface of the hoof appear symmetrical? If not, this indicates stresses on the hoof. Most commonly, one sees the medial hoof wall more upright. Is the coronary band straight and parallel to the ground surface? If not, this indicates a stress on the wall below the coronet.

The next factor to observe is the hoof alignment. This is viewed form the dorsal and lateral aspect.[2] The average horse (60%) will have a hoof angle between 50 and 55°. The alignment of the pastern and dorsal hoof wall is referred to as the hoof axis. Ideally, when the horse is standing square; the

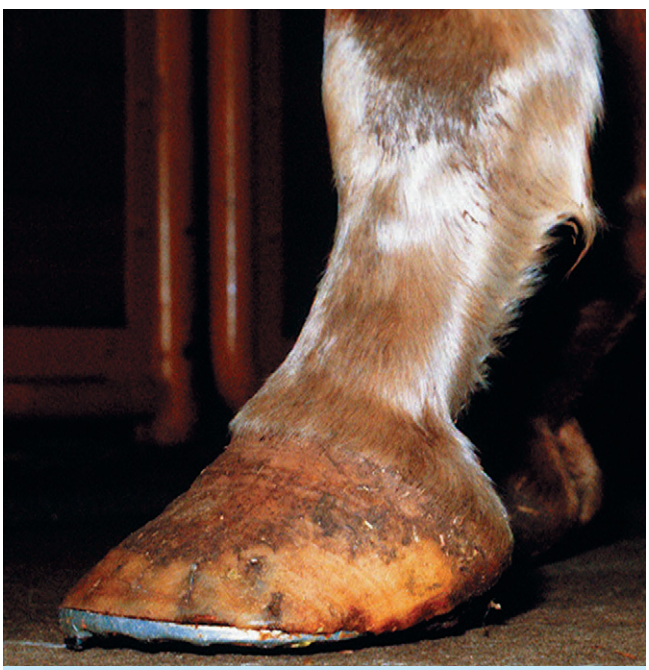


Fig. 15.1
Underrun heels. Note how the bearing surface of the hoof and the caudal extent of the shoe is well cranial of the optimal position. Less heel stress would occur in this foot if the hoof were trimmed to bring the bars caudally and the shoe was set with its caudal aspect in line with the bulbs of the heel.

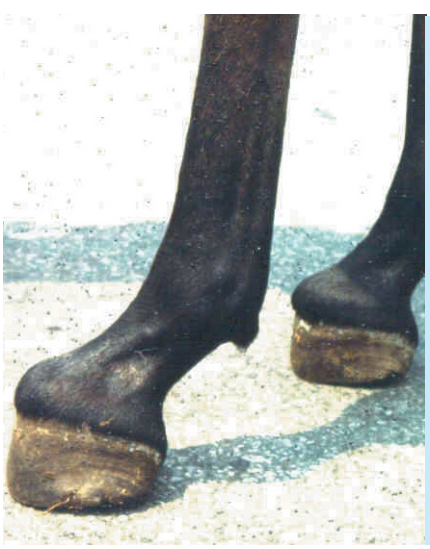


Fig. 15.2
Bilateral club-footed confirmation due to flexural contracture of the deep digital flexor tendon.

cannon bone, pastern, and hoof should line up straight as seen from the front. From the side, the pastern and hoof should be straight with the angle created by the dorsal hoof wall the same angle as the pastern and the angle of the heels within 5° of the angle of the toe.[4] Horses that have a low hoof angle compared to the pastern have a broken-back hoof axis (Fig. 15.1). This hoof conformation is also called 'long toe and low heel'. On the other hand, horses with a steep hoof angle and sloping pastern have a broken-forward axis. This hoof conformation is also called 'club foot' or 'clubby' (Fig. 15.2). Unfortunately, horses do not normally stand with their cannon bones perpendicular to the ground, so evaluation of hoof alignment must be done with the horse standing comfortably.

The next area to evaluate is hoof shape and level. Generally, the front hoof should be round or circular in shape, whereas the rear hoof is more triangular or pear-shaped. Front and rear hooves should be shaped like inverted cones. Both hooves should be evaluated for differences in length and width. Hooves of equal width and length tend to look circular but as hoof capsule length increases the width of the hoof wall in the quarters becomes more upright and the stresses on the hoof will naturally be different. There are two aspects to hoof levelness. First, is the ground-bearing surface flat? This determines how evenly the hoof wall will bear weight. Second, is the ground-bearing surface perpendicular to the upper limb? This determines how the leg is loaded during weight bearing. These factors are the basis for determining medial to lateral hoof orientation.

The final observation is to evaluate the heel support. This is done by evaluating the location of the ground-bearing surface of the heels relative to the remaining hoof capsule, relative to the pastern and relative to the fetlock and cannon bone. Does the ground-bearing surface provide sufficient support to the palmar (plantar) aspect of the digit? Are the heels of the hoof centered under the cannon bone (from the palmar/plantar aspect) or are they offset. This can be important in determining how the horse loads the heels, whether they are landing simultaneous or whether one heel might strike before the other. These observations are helpful for understanding how the hoof capsule has grown and remodeled to adapt to the forces on it.

Watching the horse at a walk will enhance these previous observations. Observing the foot in motion should determine the manner the horse lands and breaks over, as well as the path of the foot during the flight phase of the stride. Toe-first landing or excessively heel-first landing indicates either compensation for pain or dorsopalmar hoof imbalance. Similarly, medial or excessively lateral heel-quarter-first landing suggest either compensation for limb conformation or pain leading to mediolateral hoof imbalance. The flight of the foot during the stride is correlated with rotational deviation of the limb and imbalance of the foot. The horse that wings-in or 'dishes' is either toed-out or breaking over the inside toe. Conversely, the horse that paddles or wings-out is either toed-in or breaking over the outside toe.

Once the above observations have been made the examiner needs to make a closer evaluation of the hoof. This evaluation needs to be performed first with the horse in weight-bearing position and then with the foot in non-weight-bearing position.

This begins by palpating the pastern to determine if there is any obvious heat, pain, or swelling. More subtly, the examiner needs to palpate the bones and tendinous structures. Generally, the flexor tendons are not as wide as the pastern bones and there is a finger's-width difference medially and laterally. Follow the tendons down the leg until they disappear at the heel bulb.

Next palpate the digital arteries, vein, and nerve. It is normal to feel a digital pulse but not a bounding pulse, which is abnormal and an indicator of foot inflammation. The strength of the pulse can be compared to other limbs if one is in doubt. A symmetrical abnormal pulse indicates generalized inflammation, whereas an asymmetric pulse indicates the inflammatory process on the side of the stronger pulse. In addition, the skin should to be carefully palpated for the presence of neurectomy scars.

Palpation is then continued to the coronet (hairline/hoof capsule junction). Normally one should appreciate a 'spongy' feel to this area and abnormalities such as swelling, discharge, focal pain or heat, or absence of tissue (loss of sponginess or a 'trough') should be examined more closely. The examiner should feel that the hairline forms a smooth edge with the hoof capsule. Any area where the hoof capsule is prominent indicates an area of stress. Prominent edges of the coronary band indicate proximal movement of the hoof capsule ('jamming') into the hairline. In many breeds, particularly in the gaited breeds that carry longer lengths of hoof, this seems to be normal. As the edge becomes more prominent the examiner can be sure that the vertical distance from the hairline to the extensor process of the third phalanx is increasing (measurement that is made from a lateral radiograph).

From the coronet the examiner moves to the collateral cartilages where they are palpated and manipulated. The palmar and proximal edges should be easily defined. The thickness, density, and pliability of the cartilages need to be assessed. Palpation of this area will not only determine if there is any pain but also can give an impression of the flexibility of the hoof. For instance, a very stiff inflexible collateral cartilage is associated with a narrow, upright hoof. On the other hand, flimsy cartilages are commonly seen in the hoof with collapsed heels and a narrow, convex frog.

The entire hoof wall must be examined for the presence of cracks, fissures, bulges, growth abnormalities, focal heat, wall loss, or breakage. A high percentage of quarter and heel cracks begin as small, very fine fissures at the coronet. They might extend less than 1 cm distally and are easily missed if this area is not examined carefully. These small fissures are a definite cause of foot pain and usually associated with deeper injury to the coronet and/or lamina below.

The exit of all shoeing nails from the hoof capsule needs to be evaluated. The higher the exit point the more likely the nail is impinging on sensitive tissue. This is an excellent time to use the hammer and gently percuss the hoof wall to determine if wall defects, hollow sounds, or painful areas are present.

From this point it is natural to begin manipulating the foot in the non-weight-bearing position.[1] Begin by cleaning the bottom of the hoof and lightly paring away any debris that

obscures visualization of the frog, sulci of the frog, sole, and white line if the horse is unshod. Once the foot is clean, examine it in its entirety. The frog should be examined for size, shape, and consistency, and to determine whether it is securely attached to the underlying tissue and its sulci (collateral and central). The examiner needs to determine how much of the structure could actually bear weight and how much represents loose tissue. The frog should be resilient and rubbery, rather than hard and flaky, and the caudal two-thirds should be nearly level with the ground surface of the hoof wall. The frog should not be recessed deep into the sulci of the foot and nor should the frog be convex at its apex. The receded frog is often associated with upright narrow feet, whereas the convex frog is associated with weak and underrun heels. I have long thought that this conformation is associated with a poorly constructed digital cushion and therefore a poor hoof support mechanism but this has yet be proven.

The medial and lateral bars of the foot usually require light paring with a hoof knife to appreciate problems such as bar cracks. Do not pare the bars away totally as this weakens the foot. The entire sole of the foot should be carefully examined for fissures, punctures, consistency, discoloration (bruising), and the degree of concavity. The shape of the sole should be concave. A flat sole might signify either poor hoof conformation (a weak hoof) or distal coffin bone displacement. A convex (dropped) sole indicates a displaced coffin bone (Fig. 15.3). The consistency (relative degree of stiffness) of the sole is determined using digital pressure as well as hoof testers. At this point it is necessary to evaluate the texture of the sole. By grasping the quarters with your fingers, the thumbs can be used to gently press on the sole. A sole that moves under this pressure is thin and there is little space between the coffin bone and the outside environment. On the other hand, if the sole does not move then the examiner knows there is at least some thickness and depth to the sole. True sole depth can be determined via radiography.

The white line (the junction between the sole and inner hoof capsule) is examined to determine its width and character. The white line is usually wider at the toe and gradually thins as it approaches the heels. It is best visualized following either light paring with the hoof knife or light rasping of the superficial portion of the sole margin. It is used as a landmark by farriers to demarcate the insensitive hoof from the sensitive hoof for the purpose of driving horseshoe nails. Everything superficial to the white line is insensitive, everything more central is considered sensitive. Widening of this area represents stress and separation of the laminar hoof wall from coronary hoof wall. The deeper the separation goes the more severe the injury. This separation can be seen anywhere on the solar surface and indicates a bending force on the wall that is pulling the wall away from the coffin bone. Most frequently this separation is seen at the toe and is referred to as 'seedy toe' because it looks like small seeds could fit between the spaces created by the separation.

Examine the bulbs of the heels to determine their relative position to one another. The strength of this tissue is assessed manually by attempting to distract the two bulbs from one another in a vertical direction. Digitally explore the heel bulbs for the presence of swelling, heat, pain, or separation at the coronet. The central sulcus of the frog needs to be examined and probed to determine its depth. Normally this should be a shallow depression of no more than a centimeter. If the sulcus goes deeper it can be due to either very serious thrush or loss of structural support in heel bulbs (the heel bulbs can be distracted in opposite vertical directions).

Lightly support the limb at the metacarpus (metatarsus) and allow the foot to drop naturally. Position your line of

Fig. 15.3
Dropped sole due to distal phalanx displacement. The sole should normally be concave.

Fig. 15.4
Solar surface of a foot prior to trimming. Lines have been drawn across the widest portion of the foot and sagittally. From this perspective the foot is in quite good balance. The dorsal and palmar portions of the foot are nearly equal. The half to the viewers right (lateral) is slightly larger than the half to the left (medial).

vision so as to appreciate foot balance and levelness of the walls (see above). Examine the entire ground surface of the foot to determine the divisions of the hoof (toe, quarters, and heels) and their proportions (Fig. 15.4). Imagine a line drawn through the axial center of the limb, which transects the ground surface of the foot, and then determine the relative proportion of medial and lateral foot to this imaginary line. For example, a given foot may demonstrate a unilateral medial heel contraction in combination with a flared lateral quarter and toe (diagonal imbalance).

Examine the foot systematically with hoof testers. Begin with the bar, move to the heel, to the quarter, and then to the toe and back toward the opposite heel. Space the sites where the hoof testers are applied at approximately 2.5-cm (1 inch) intervals. Be sure to apply hoof tester pressure at each exit point of the shoeing nails. Next, place the testers in each of the collateral sulci and across the hoof to the opposite hoof wall (progressively move the hoof tester along the hoof wall caudal to cranial to check for alterations in the pain response), then place the testers in the central sulcus to the hoof wall at the toe, and then across the heels. Finally, using the hammer gently rap the structures on the bearing surface of the sole and frog.

Repeat the palpation of the cartilages of the distal phalanx and the coronet. Bringing the limb forward and flexing the toe facilitate palpation in the region of the extensor process of the distal phalanx region and the associated distal interphalangeal joint. The thumbs can then be pressed over this area to feel for joint distension, heat, or pain. The foot also should be rotated (twisted) medial and lateral around the vertical axis of the pastern. A normal range of motion allows for 10–15° of rotation each way. Injury to the joint capsule or collateral ligaments, or chronic navicular pain, tends to reduce this motion. Likewise, distal limb flexion should reveal 30–45° of excursion. Again, injury to the joint capsule, collateral ligaments or chronic navicular pain tends to reduce this motion.

If the horse is shod, the exam should include the following additions.[1] First, determine the security of the shoe to the foot by gently rapping the shoe at 2.5-cm (1-inch) intervals with a shoeing hammer. Note the shoe type as well as the presence or absence of additions such as toe grabs, block heels, trailers, and so forth. Carefully determine if abnormal shoe wear exists. Position the hoof testers to include the hoof wall at the exit point of each nail. Record your findings because it is easy to forget subtle discoveries that may ultimately determine how the horse should be treated or shod. Remember that hoof testers are essential but certainly not foolproof. The response the examiner gets from hoof testers depends on many factors, such as the hardness of the wall, depth of the hoof, thickness of the hoof, and the stoicism of the horse.

Objective assessment of hoof balance

As part of the overall evaluation of the horse an objective assessment of hoof balance is important. The horse's weight is determined with a weight tape or scale and then 11 measurements are made of each foot:[4]

- Seven measurements are made of the hoof length with a tape measure: medial and lateral heel lengths, medial and lateral quarter lengths, dorsomedial and dorsolateral toe lengths, and sagittal toe length. These measurements are recorded on a graph to illustrate the general shape of the foot.
- The frog's length and width are measured at their longest and widest points.
- The hoof circumference immediately below the coronary band is measured.
- The hoof angle (using a hoof gauge) is also measured.

From these measurements, two additional measurements can be calculated: the frog ratio (frog width divided by length) and the body size to hoof area (horse's weight (pounds) × 12.56/square of the hoof wall circumference (inches)).

A dorsopalmar (plantar; D65PDO) and a lateromedial radiograph of the hoof can also be used to determine valuable information about hoof balance. The horse must be standing with the metacarpus (tarsus) perpendicular to the ground, which can most easily be determined by either the use of a level placed against the cannon bone or the use of a weighted string to align the leg. The radiographic beam should be horizontal and centered on the hoof. Resting the horse's foot on a block to raise the hoof off the ground facilitates these exposures (the opposite limb should be similarly elevated). A wire or radiopaque paste placed sagittally (midline) along the toe from the coronary band to the ground, a thumb tack in the apex of the frog and thumb tacks in the most caudal point of the ground contact of each heel emphasize these areas on the radiographs, making their identification much easier.

After plotting the hoof wall lengths on a graph, one should have a curve that reflects the shape of the hoof. For a hoof of average hoof angle (48–55°), flattening of the plotted curve indicates that the heels are underrun. A flat curve would also be expected for very upright hooves (≥ 60°). Generally speaking, the three measurements at the toe should be equal. The measurements at the quarter are usually 1–2 cm shorter than the toe (for the average hoof). The heel length should generally be about one-third of the toe length.

Another factor to evaluate is the size (weight) of the horse versus its foot size. Guidelines have been made relative to toe hoof length. The average toe length is a function of the horse's weight. The average pleasure horse weighing 360–400 kg (800–900 pounds) should have 7.6 cm (3 inches) of hoof length at the toe. A horse weighing 430–480 kg (950–1050 pounds) should have 8.25 cm (3.25 inches) of hoof length, and horses weighing 520–570 kg (1150–1250 pounds) should have 8.9 cm (3.5 inches) in length. Another rule of thumb that has been suggested is to add or subtract 3.3 mm (⅛ inch) of length for every 90 kg (200 pounds) using a 470 kg (1000-pound) horse carrying 8.25 cm (3.25 inches) of length. Obviously these are guidelines only. A measure that has been an excellent aid to assessment is comparing the horse's weight to the coronary band circumference using the formula of the horse's weight × 12.56 and divided by the square of the coronary

circumference to determine the weight to hoof size ratio. A ratio of 5.5 kg/cm^2 (78 lb/in^2) is seen in 99.5% of horses; horses weighing more are too heavy for their hoof size. The measurements of the frog length and width are used to determine if the hoof is contracted. Normally the frog width should be two-thirds its length. Furthermore, ideally the frog length would be two-thirds of the solar length (heel bulbs to toe).

Examination of the lateral and dorsopalmar (plantar) radiographs provides excellent pictorial evidence of imbalance. The lateral radiograph should be evaluated for P2 and P3 alignment, which may reveal the presence of a broken-hoof axis. In addition, the alignment between P3 and the hoof wall should be assessed. If the hoof wall and dorsal surface of P3 are not parallel the functional hoof angle can be determined by measuring the angle of the dorsal surface of P3 with the ground. Usually the slope of the heels can be seen on the radiograph and can also be used to determine whether the heels are underrun.

The D65P–PDO radiographic projection should be assessed for joint alignment, medial and lateral hoof wall lengths, and foot symmetry. Joint alignment is determined by examining the symmetry of the joint space. Misalignment is present if one side of the joint is narrower. This phenomenon can also be caused by poor positioning of the limb, in which case all three of the lower leg joints (fetlock, pastern, and coffin) will be affected. The hoof wall length can be measured directly from the film. The symmetry of weight bearing can be predicted in a similar manner.

Assessment of pain

The next step in developing a logical approach to the evaluation of the hoof is an accurate assessment of pain and careful evaluation of hoof structure that may predispose to or cause the pain.[5] First, examine the horse in motion; watch the foot strike for each foot. Determine if the foot lands flat, heel or toe first, medial or lateral quarter first. The landing position of the individual foot relative to the vertical axis of the respective limb should be noted. Evaluate the path the individual foot takes from foot breakover to strike. The character of motion may be a clue as to where on the foot or the limb the problem exists. Always include this examination at the walk because it is the one gait that is sufficiently slow to permit the determination of fine movement error. Repeat the same process when reviewing the horse from the left and right side. The horse is then trotted (or paced) and visualized in the same manner. Circling the horse will often exacerbate foot problems.

Four diagnostic tests should be performed: hoof tester examination, distal limb flexion, hoof extension wedge test, and palmar hoof wedge test.[5] A positive response to any of these tests is important but a negative response is equivocal and does not rule out any problem. Hoof tester examination should be performed as previously described. A positive response should be repeatable, and in the distal sesamoid region the pain response should be uniform over those areas and must be evaluated in relation to examination of the remaining foot. That is, a positive response in the heels and quarters of the sole would also be expected to cause a positive response across the distal sesamoid region in the same area of the foot. Percussion utilizing a small hammer can also provide important information regarding pain in the hoof wall or sole.

The distal limb flexion test can exacerbate lameness if any of the three distal joints of the leg are affected by synovitis or osteoarthritis. A positive response could also be expected by any condition that causes induration of the tissues of the foot. This has been shown to be positive in over 95% of horses with foot pain.[5]

The hoof extension test is performed by elevating the toe with a block, holding the opposite limb, and trotting the horse away after 60 seconds. The palmar hoof wedge test is performed by placing the block under the palmar two-thirds of the frog and forcing the horse to stand on that foot. The test can be further modified so that the wedge can be placed under either heel to determine if the pressure there causes exacerbation of the lameness.

These tests simply allow the examiner to evaluate the horse's response to a particular stress. None has been shown to be pathognomonic for any particular cause of lameness.

Diagnostic analgesia

Regional analgesia will provide the evidence to localize the region of pain. The performance of regional analgesia needs to be performed in a logical manner. Intra-articular injections anesthetize joint regions; whereas regional analgesia desensitizes skin segments.[6] Intra-articular injection is more accurate and does not interfere with regional analgesia. Regional anesthesia desensitizes local nerves that innervate areas of the limb. They provide indisputable evidence of the location of lameness. The most important point is to have some idea of what areas have been desensitized. See Chapter 14 for details on local and intra-articular diagnostic anesthesia.

Imaging of the foot

After localization of the lameness to the foot imaging will be necessary to determine what pathology is present. Radiographic examination of the hoof requires a minimum of five radiographic views of each foot.[7] The views consist of a dorso-60°-proximal to palmarodistal (D60PrPD) of the navicular bone, a dorso-45°-proximal to palmarodistal (D45PrPD) of the third phalanx, a lateral to medial projection, a horizontal dorsopalmar projection, and a palmaroproximal to palmarodistal navicular bone projection (see Chapter 10).

Furthermore, each of these views must be assessed for any significant changes in any of the bone surfaces. It is the authors' opinion that the radiographs should be assessed for change and what the change means from a pathologic sense. Most of the time, radiographs are examined for signs consistent with the tentative diagnosis. Once the basic films have been examined, it may be necessary to take additional oblique views to completely appreciate any pathologic change.

A new method of assessing navicular pathology is through the evaluation of the flexor surface of the navicular bone by contrast arthrography.[8] The distal interphalangeal (DIP) joint can be evaluated for cartilage defects or the communication of subchondral cysts with the joint. Defects or punctures into the hoof can also be examined using contrast radiography, which can give much better insight into the structures that may be involved.

Recently, it has become possible to examine the structures within the hoof sonographically.[9] The collateral ligaments of the DIP joint can be clearly outlined by ultrasonography, as can the deep flexor insertion on the third phalanx, the distal deep flexor tendon, the impar ligament, and the navicular bursa. To examine the podotrochlea, the superficial horn must be pared from the frog to expose soft, spongy frog tissue.

The metabolic activity of the foot can be evaluated through the use of nuclear scintigraphy. Scintigraphy involves the injection of a radioisotope, and its subsequent uptake into the extracellular fluid and bone. Assessment is based on the detection of radiation from the radioisotope. The technique provides information on relative vascularity and rate of tissue metabolism. This is particularly useful in studying bone pathology and can help differentiate sites of injury in the foot.

Thermography provides information regarding skin temperature.[10] This technique is 10 times more sensitive than the human hand in detecting heat. It can be an early detector of inflammation in the foot. It has also been shown to be useful in assessing the relative blood flow to the foot. This information is of particular interest when pre- and postexercise temperatures are determined. Exercise will normally cause a 0.5°C rise in skin temperature. Whenever the skin temperature does not rise to this degree, poor blood flow should be considered a factor in the disease being assessed.

Diseases of the hoof wall

Hoof wall defects

- Lameness associated with hoof wall defects is due to irritation of the sensitive lamellae due to exposure, local infection or shearing of the unstable hoof capsule.
- Treatment should clean and stabilize the defect to permit healing from the coronary band.
- Healing of defects may require 5–10 months.

Recognition

History and presenting complaint The horse is presented for evaluation of cracks, fissures or morphologic defects in the hoof wall. Lameness may or may not be a presenting complaint.

Physical examination Defects should always be examined to their depth and size. Depth can be usually determined by probing the defect. The examiner needs to determine if sensitive tissues are involved. If pain is elicited by probing the defect, then it involves sensitive tissue. A percussion hammer is useful to determine the size of defects that are not readily visible. Normal percussion of the hoof results in a crisp resonance, whereas hoof wall separated from its deeper structures has a dull resonance. Radiography is very useful in these cases in identifying gas under the hoof wall, which indicates either infection or undermined hoof wall.

Defects at or near the coronary band should have the hair clipped from the coronary band. The coronary band then should be examined for injuries, wounds, splits, or other defects that would account for the abnormal hoof growth.

Diagnostic confirmation Radiographs may be necessary to rule-out involvement of the distal phalanx or sensitive tissues of the foot.

Treatment and prognosis

Therapeutic aims The first objective and most important goal of treatment is to eliminate or correct the problem that caused the hoof defect. Adjunctive therapy will usually make it possible to return to work sooner. If the underlying problem is not corrected recurrence should be expected.

Initial treatment is done to either stabilize a defect or prevent its further extension in the hoof capsule. Debridement of the defect is necessary to remove contamination of the hoof capsule and deeper laminae. Long-term support or protection of the affected region must be made.

Therapy It must be remembered that the healing of these injuries is based on growth of new horn from the coronary band. These tissues do not heal side to side; therefore healing is slow, and may take 5 to 10 months. To prevent the defect from expanding the crack should be immobilized. This can be

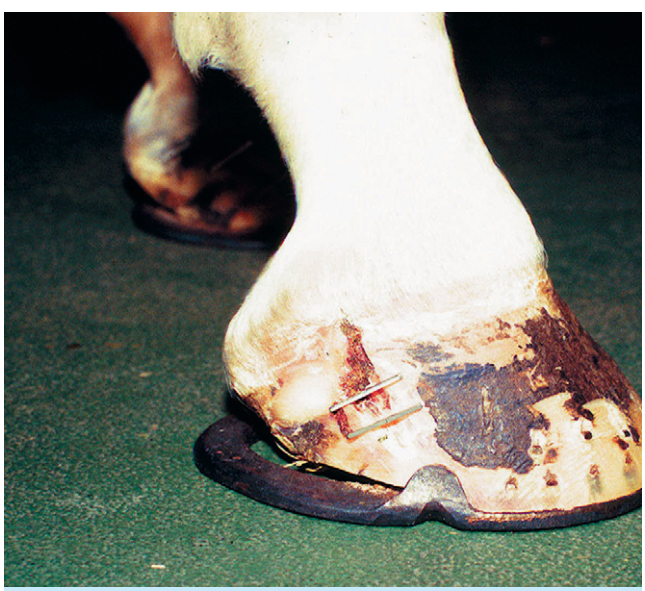


Fig. 15.5
Hoof crack with floated heel. The hoof crack has been debrided and stabilized with hoof staples. The foot has been shod with an egg bar shoe. A quarter clip is placed immediately dorsal to the hoof crack and the affected heel has been trimmed short enough to prevent contact with the shoe ('floated heel').

accomplished by application of a bar shoe that relieves pressure on the affected wall. The bar may be a full bar or a diagonal bar. Also, if the crack is near the heel, weight bearing to the heel can be reduced by 'floating' the heel (Fig. 15.5). The affected heel is trimmed short enough to prevent contact with the shoe during weight bearing. The objective is to relieve pressure, which causes movement at the area of the defect. In addition, clips placed on either side of the defect will help prevent hoof expansion and, therefore, will immobilize the crack. To further immobilize the crack it can be sutured or wired. In some cases a small metal plate can be screwed into the wall over the crack.

If the hoof crack does not extend from the ground to the coronary band changes in the hoof wall may be made to prevent crack lengthening. 'Grooving' the hoof wall perpendicular to the defect has the effect of deflecting stress away from the crack. Cracks that originate from the weight-bearing surface should be grooved at the most proximal aspect of the crack. Cracks that originate from the coronary band should be 'grooved' at their distal aspect and in the shape of a 'V'. 'Grooving' will only work if the crack does not extend into sensitive tissues, it is not cosmetic. Bonding or acrylic repair of a crack is a cosmetic and very successful method used to obliterate the crack.

Because of their horizontal orientation hoof clefts do not lengthen as do cracks. However, clefts are much more likely to involve sensitive layers and cause lameness. The horn around the cleft should be removed to the depth of the cleft. Sufficient horn should be removed so there is no undermined horn. In many cases, this may require a partial resection of the hoof wall from the cleft to the weight-bearing surface; a rotary burr (dremel tool) does an excellent job. After sufficient hoof wall is debrided, the underlying tissue should be inspected carefully.

Treatment of crumbling hoof may require wide debridement of hoof wall. As for a cleft, all undermined hoof wall should be removed. It should be removed until intact hoof wall is present around the edge of the debrided area. Again, the deep tissues must be carefully examined for necrotic tissue or contaminated debris.

Long-term support or protection of the defect is necessary to return the horse to use as soon as possible. This usually requires some type of repair to restore the integrity of the hoof wall. First, the area must be free of hemorrhage or sepsis. Controlling hemorrhage requires packing the bleeding area with gauze and wrapping the foot. Approximately 1 week is required to dry the hemorrhagic area and allow new horny growth over the area. Application of a 1% tincture of iodine to the horn in and around the defect will usually dry the area without desiccating it. If sepsis has occurred, or a foreign body has penetrated the hoof wall, it is necessary to soak the foot in a saturated solution of magnesium sulfate-tamed iodine solution to eliminate the infection. It may be necessary to soak the foot for 7 to 10 days before the septic area is healed. An alternative to soaking is to pack the affected area with a magnesium sulfate paste (ichthammol or povidone–iodine ointment mixed with magnesium sulfate). This treatment is followed by application of tincture of iodine solution. A helpful hint to determine if infection is still present is to examine the area 24 h after application of iodine. The presence of moisture or exudate in or around the defect is indicative of continued active infection. Soaking should continue until the infection is resolved.

The hoof wall can be repaired after the defect has been adequately debrided and the hemorrhage/sepsis has been controlled. The hoof should be properly trimmed and balanced. In most cases, a bar shoe with clips should be applied. The hoof should be dry. Application of either acetone or alcohol to the outer layers of the horn is an excellent method to remove debris and dry the hoof. To aid retention of the repair material, the hoof wall around the defect should be beveled inward (undermined) for 6 mm ($\frac{1}{4}$ inch) using a rotary hand burr. Some defects can be reinforced by wire laced across the gap. This not only helps immobilize the area but also adds substrate to which the repair material can bond. If the defect is not sutured, holes should be drilled from the normal hoof into the undermined area to allow penetration of repair material. The holes should be 0.5 to 1 cm apart.

There are numerous agents that are available for repair, including fiberglass, rubber, thin metal sheets, leather, and acrylic/epoxy materials. The acrylic/epoxies are the most popular materials. Modern hoof epoxies have biomechanical properties similar to normal hoof capsule, reducing the complications of hard, inflexible materials such as hoof capsule contraction. The material is mixed and applied to the defect and surrounding hoof wall. When sufficient time has elapsed to allow hardening of the material, excess acrylic is rasped away resulting in a cosmetic repair.

Two types of adhesives are used for hoof repair: acrylics and polyurethanes. Applied properly, these acrylics and urethanes have the texture, strength, and flexibility of natural hoof wall, allowing the farrier to rasp and nail to and through the bonded material, and then allowing the bonded material to 'grow down' with the hoof. Using available hoof repair composites, we can address capsular maladies such as hoof-wall cracks, avulsions, underrun heels, and thin walls. In effect, rather than having simple cosmetic repair materials, we now have materials suited for structural bonding and repair. Applied properly, the composite material alone generally provides great structural support; when combined with a reinforcing cloth, such as a fiberglass or Spectra cloth, the overall strength of the material can be increased by as much as five-fold. Subsequently, horses with hoof conditions that would have required lay-up before the advent of these new products are actively racing and competing today.

Successful application of these composite materials depends on numerous things, but manufacturers and farriers agree that the most important concern is proper hoof preparation. The farrier must thoroughly debride the hoof wall where the composite will be applied and follow this with a solvent rinse, ensuring that the hoof wall is clean, dry, and smooth. Any loose, flaky hoof wall, any moisture or oil weakens – and sometimes prevents – the bond. Indeed, improper application can result in greater disaster than a simple failed bond. Using these materials to seal moist and infected areas provides an environment conducive for bacterial and fungal proliferation, which undermines the hoof and destroys more hoof tissue.

Undoubtedly, these materials have proven themselves to be highly effective tools in the hands of the skilled farrier. However,

it is important to recognize that there is no acrylic magic wand, no composite panacea. In all cases, exercise of these animals should be minimized. Once a shoe is applied and the defect protected, work can resume. When large amounts of hoof wall have been lost, it may be necessary to complete the repair process before the horse is exercised. On occasions the entire hoof may need to be rebuilt before a shoe can even be applied.

The horse should be re-examined at 4- to 8-week intervals. The shoe will need to be reset and in many cases the repair repeated until the hoof wall grows out. If the animal is active and competitive the constant trauma may cause the repair to loosen. If the repair material loosens it should be removed and the repair repeated. Under no circumstances should new acrylic be applied over old acrylic. This can trap bacteria and cause an abscess to form.

Prognosis The prognosis for healing of hoof wall defects is usually good to excellent. Given proper hoof care, adequate time, and proper follow-up care, the defect will heal. Large defects that have resulted from an inflammatory cause may have a tendency to recur because of damage to the laminae and loss of bonding between the hoof wall layers. However, if the hoof is kept shod and protected, further problems can be avoided.

Etiology and pathophysiology

Etiology There are numerous causes of defects in the hoof. Careful examination of the hoof can often identify the probable cause, which must be eliminated before therapy will be effective. The first consideration is moisture; either excessive dryness or excessive moisture can result in defects. Dryness usually results in a brittle hoof that tends to crack when stressed. If the hoof is unprotected, large portions of hoof wall may break away at the weight-bearing edge. Conversely, excessive moisture can cause the hoof wall to crumble. This is probably due to a combination of a decay process caused by micro-organisms, a disruption of the normal horn tubules by the moisture, and stress on the hoof wall. This problem is usually characterized by hoof-wall crumbling, which starts at the weight-bearing surface. Examination of the wall reveals a hoof wall that is soft in nature at the area of crumbling. The hoof wall can easily be dislodged for several millimeters around the defect. The wall that is affected has little normal architecture and crumbles into a fine powder when pressure is applied.

The next consideration for evaluating the cause of defects is hoof conformation, balance, or improper shoe application. These problems can cause overloading of a portion of hoof wall and result in disruption of the integrity of horn. Defects resulting from speed work or work on uneven surfaces are also due to similar abnormal stresses.

Infection or foreign bodies in the hoof may also result in defects. Clefts and crumbling are the most common results of these factors. Clefts may result from either a separation of horn from the coronary band, as occurs with 'gravel', or from splitting of the hoof wall as a result of the inflammation associated with infection. Inflammation caused by infection disrupts the normal architecture of the hoof sufficiently to cause the wall to break or crumble under normal stress and usage.

Prevention

Prevention of hoof wall defects is best accomplished by regular farrier attention and early recognition and response to changes in hoof moisture (too dry, too wet). Hooves that are exposed to excessively moist conditions may benefit from application of sealing agents. Hooves that are extremely dry may be moisturized by simply allowing the paddock stock tank to overflow. The resulting muddy area will moisturize the hooves of horses that come to the water to drink. Horses that are in regular work and have a regular bath do not usually suffer from dry, cracked hooves. In fact, excessive hoof moisture remains a considerable problem in these horses.

Lacerations to the hoof and coronary band

- First aid should control hemorrhage and prevent further contamination.
- Damage to the corium may result in hoof wall defects.
- Deep wounds may affect synovial structures.
- Wounds that involve the hoof capsule will heal slowly by second intention.

Lacerations to the hoof causing loss of germinal tissue and either partial or complete avulsions of the hoof wall are not common injuries to the horse. When these injuries do occur, however, their management can be perplexing for the veterinarian.

Recognition

History and presenting complaint Horses with hoof-wall lacerations are presented for distal limb injury that usually includes considerable hemorrhage and may include varying degrees of lameness. The horse may have been caught in wire or kicked through a solid partition.

Physical examination Complete examination of the wound is necessary to determine the extent of the injury. Although the foot has as great a capacity for healing as any other tissue, the prognosis for return to full function is dependent on the severity of tissue destruction and the tissues involved. In most cases, adequate collateral circulation develops following injury. Because ischemia will impair healing and predispose the wound to infection, permanent loss of blood supply necessitates surgical removal of the ischemic portions of the wound.

Complete denervation of the foot by extensive damage to the digital nerve trunks may result in neurogenic degeneration and sloughing of the foot. Ironically, transection of the nerve, where damage has not been extensive, may aid recovery by reducing chronic pain associated with the injury.

Injuries that involve the corium of the foot should be inspected carefully. The corium is modified vascular tissue similar to the dermis, and is responsible for nutrition to the horny layers of the hoof. Damage to these structures often results in permanent defects in the coronary band and hoof. Injuries that cause avulsion or necrosis of corium will cause changes in horn production around the hoof. Many times one

must wait for the regrowth of the hoof to assess these changes and how they may affect the horse.

Deep wounds that extend to the middle or distal phalanges cause additional complications. Hoof avulsions may involve all or part of the wing of the distal phalanx. In these cases, it is usually easiest to simply remove the fractured portion of the bone. However, wounds that damage the periosteum or collateral ligaments surrounding these bones may cause permanent lameness as a result of excessive calcification of soft tissues or joint instability. Associated soft tissue injuries such as these will not be apparent on initial radiographic examination and can only be anticipated after close examination of the wound. Once soft tissue support is damaged the veterinarian may have to wait 3 to 4 months to evaluate the final consequences of this type of deep injury.

Although wounds that enter a joint may appear to have a poor prognosis, they can respond quite well if appropriate therapy is initiated immediately. Small wounds into a joint may not be readily apparent, the only sign being synovial fluid leaking into the wound. Occasionally, serum is mistaken for joint fluid or vice versa.

Other criteria that must be considered when evaluating these wounds are the horse's age, value, and function. Immature horses tend to heal more readily, and growth may help resolve some deformities. Wounds of the foot usually heal over an extended period, resulting in increased expense and residual lameness due to the injury; permanent deformity is a distinct possibility.

Special examination If any doubt exists as to whether a joint has been entered, saline is injected under pressure into the joint and the wound examined for the leakage of fluid. Another method of testing for joint involvement is to perform an arthrogram and see if leakage of contrast media from the joint is evident on a radiograph. Radiographs of the affected region should be obtained to determine if skeletal injury accompanies the hoof laceration.

Treatment and prognosis

Therapeutic aims The principal goals of surgery are to optimize conditions for wound healing and to achieve the most favorable cosmetic and functional result. The horse's hoof is not amenable to suturing and therefore wounds must heal by second intention.

Therapy Therapy consists of surgical debridement and wound apposition. The foot should be prepared for aseptic surgery. In addition, the hoof wall, sole, and frog should be trimmed, pared, and rasped to remove any contamination that may be in cracks or crevices. The hair from the fetlock distally should be clipped to allow surgical preparation of the entire foot and pastern area with an antiseptic soap. Exposed tissues should be cleansed and irrigated with a physiologic saline solution. Harsh antiseptics or irritating cleansers should not be used on exposed tissues because these chemicals may cause further damage. After thorough cleansing, the wound should be covered with a sterile, nonadherent dressing and the entire foot bandaged. The outer layer of the bandage should be impervious to water.

Surgery may be performed on either a standing or an anesthetized patient. Standing surgery should be performed with sedation and local anesthesia. However, this should be reserved for the most tractable of horses. It will also often require one person to hold the leg or to tie the leg up for surgery to be performed. General anesthesia provides optimal conditions to establish and maintain aseptic techniques, as well as optimizing the surgeon's ability to inspect the wound.

The goal of surgery is to optimize conditions for wound healing that will result in the most favorable cosmetic and functional result. The horse's hoof is not amenable to suturing and therefore wounds must heal by second intention. The most important factor in the management of these wounds is adequate debridement. Necrotic or severely damaged tissues and all foreign materials provide media for bacterial growth and impede wound healing. However, vital tissues such as nerves, arteries, and tendons should be salvaged, if possible. Complete wound excision is the simplest, most effective means of debridement. If this is not feasible, simple debridement of obviously devitalized tissue and foreign material combined with wound irrigation should be performed. Pulsating lavage is the most effective type of irrigation system.

If a synovial structure is opened or if it is suspected that a synovial cavity has been entered, the structure should be lavaged with copious amounts of physiologic saline solution so that the lavage flows out through the wound. The foot is a highly vascular structure and hemostasis is difficult. Hemostasis by ligation and electrocautery are usually not adequate. A temporary pressure bandage is usually necessary and will stop bleeding if left in place for 12 h. The initial bandage applied after surgical debridement should be moistened with sterile saline or an antimicrobial dressing over the wound and covered with an outer waterproof bandage.

Wounds of the hoof generally heal slowly, due in part to the high incidence of contamination. Subsequent wound infection can be minimized by proper cleaning, appropriate bandaging, and ensuring that enough help is available when changing the dressing (this usually requires two people). Contraction of hoof wounds is also minimal because of the inelasticity of the epithelial tissues and the fact that they are all attached to bone or rigid connective tissue. Thus, healing is the result of epithelialization and regeneration of connective tissue. All portions of corium can migrate and cover a healthy bed of granulation tissue. This process will be slow and may take 3 to 5 months.

Immobilization and protection of the wound are important considerations in the maintenance of the tissue environment achieved at surgery. A short limb cast that encases the hoof is usually the most effective method. The cast will not only immobilize the tissues and protect them from excess motion but will also serve as protection for the hoof from moisture and fecal contamination. On a long-term basis, a cast can be a much less expensive method of immobilization than daily bandage changes.

Ten to 14 days is the minimum duration suggested for cast immobilization. The cast should be maintained as long as necessary to provide a good initial healing (4 to 6 weeks if necessary). The cast needs to be monitored daily. If lameness, excessive heat, or odors develop, it should be removed.

After cast removal, bar shoes with clips can be effective in immobilizing the hoof. The glue-on shoe is also effective at immobilizing the hoof. This can also be used with less severe wounds of the foot when combined with aseptic dressings and water-impervious bandaging.

Antibiotics are indicated during the acute phase of wound healing and are indicated with traumatic wounds, when deep structures are involved, or when there has been severe tissue damage and loss. However, antibiotics should not be used in lieu of adequate surgical debridement, or without appropriate bacterial cultures and antibiotic sensitivity testing. Often the contamination in these cases involves multiple organisms, so the debrided deep tissues should be used for the culture.

Pain relief may be necessary postoperatively, particularly for 48 to 72 h. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended to reduce inflammation and to minimize the effects of unequal weight bearing on the unaffected limbs. Pain relief may also be provided by soaking the hoof in warm or hot water. This aids the wound healing by reducing surface contamination and stimulating reflex hyperemia with increased blood flow. If a wound is immersed in water, the water must be clean to prevent contaminants from contacting the wound through the water bath. Wounds involving the joints, tendon sheaths, or bursae are not soaked until healing is adequate to prevent secondary contamination.

As healing progresses, the hoof should be trimmed to remove excess horn. The hoof should have excess wall removed, the sole should be pared of scales, and the horn surrounding the wound should be kept even with the wound until complete keratinization of the wound has occurred.

The horse should not be allowed free exercise until keratinization is complete. Follow-up examination at 2- to 4-week intervals is usually adequate. Once keratinization is complete, corrective shoeing, acrylic remodeling, or simply cessation of bandaging is in order. Corrective shoeing and/or acrylic remodeling are often necessary for complete soundness. This will have to continue until the hoof completely grows out. Usually this takes about 8 to 12 months.

Prognosis The prognosis for these injuries is generally good for soundness. However, a prognosis should be withheld until after adequate inspection of the wound has been made. The prognosis should be based on the duration of injury, the structures involved, the temperament of the horse, how adequately debridement can be achieved, and the structural integrity of the hoof after debridement

Sepsis within the hoof: subsolar abscess, laminar abscess, septic navicular bursitis

- Sepsis within the hoof is a primary differential diagnosis for non-weight-bearing lameness.
- Treatment must successfully approach, open, and drain the site of sepsis.
- Deep puncture wounds must be aggressively treated with parenteral and local antibiotics. Surgical debridement may be necessary.

Sepsis within the hoof capsule may be due to defects in the sole or hoof capsule, penetrating wounds. The treatment and prognosis for successful outcome depend on the location and duration of the abscess and response to initial therapy.

Recognition

History and presenting complaint Lameness of acute onset that becomes more pronounced over several days is the primary presenting complaint for horses with sepsis within the hoof. Sole abscessation occurs more frequently when the weather changes from dry to wet conditions. The sole and white line become softer and more prone to penetration of contaminants. Penetrating wounds may cause abscessation at any site within the hoof.

Of particular concern are nails or other foreign bodies that penetrate in the caudal one-third of the foot. Contaminants that penetrate the caudal portion of the foot are readily sealed in by the elastic frog and digital cushion. Close proximity of the navicular bursa, distal interphalangeal joint, and tendon sheath make deep abscesses in the site difficult to drain and treat, with a high risk for extension of infection into these synovial spaces.

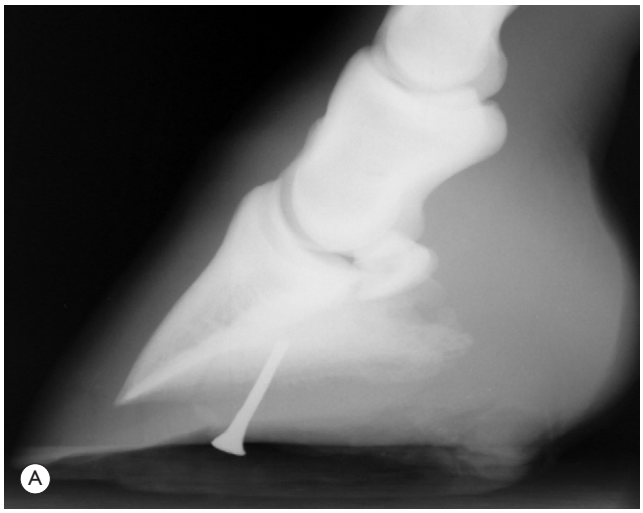
Physical examination Lameness will vary from mild (grade 2 of 5) to non-weight-bearing (grade 5 of 5). The horse will often point with the affected foot and that distal limb will usually have a pronounced digital pulse. Application of hoof testers to the affected sole usually results in a very painful response directly over the abscess site. Examination of the sole may reveal a tract, site of foreign body penetration, soft and painful spot overlying the abscess or any combination of the above. If a foreign body is found, it should be left in place, if possible, until radiographs can be taken of the foot.

Special examination Radiographs are warranted in nonresponsive cases of hoof sepsis to help identify sites of gas or fluid accumulation in the hoof or beneath the sole and to rule-out osteomyelitis or other causes of severe lameness of the distal limb. Imaging is not required for the great majority of feet suffering from routine sole abscessation.

If a foreign body is still within the foot, radiographs can be used to determine the depth of penetration and the most likely anatomical structures affected (Fig. 15.6). If a tract is suspected to be due to a foreign body that has been removed a contrast study of the foot will often provide similar information regarding location and depth of penetration.

If the foreign body penetrated the caudal one-third of the foot it is imperative to determine if synovial structures have been invaded. Arthrocentesis of the distal interphalangeal joint, navicular bursa and the distal aspect of the digital sheath may need to be done. Samples should be obtained for fluid analysis, cytology, and bacterial culture. These procedures are often accomplished most easily with the horse under general anesthesia.

Diagnostic confirmation The diagnosis is confirmed when the sole abscess is drained. Other differential diagnoses include deep penetrating wound to the foot, distal limb fracture, severe bruising of the sole, deep bruising of the sole that has become septic, laminar necrosis secondary to laminitis, keratoma, septic arthritis, and osteomyelitis.



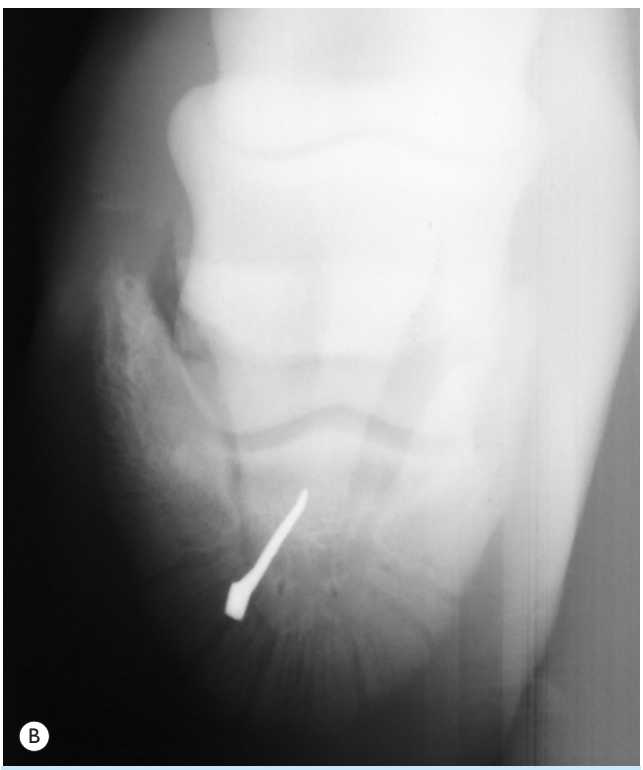


Fig. 15.6
Penetrating foreign body. (A) Lateral radiographic projection of the distal limb with a nail penetrating the sole. (B) The orthogonal view (D65Pr–PaDO) reveals that the nail has penetrated the sole overlying the distal phalanx. The position of this nail makes it unlikely that a synovial structure was penetrated.

Treatment and prognosis

Therapeutic aims Simple abscesses should be opened to allow drainage and access of antiseptic solutions. Parenteral antibiotics are not usually necessary for simple abscesses. Horses with deep penetrating wounds of the foot should be treated with broad-spectrum antibiotics, have lavage of the affected synovial spaces performed, and may require exploration and debridement of the wound tract.

Therapy The sole of the affected foot should be carefully pared to reveal clean, uniform sole. A combination of hoof tester and finger pressure may be use to localize the likely site of the abscess. If the horse is shod, the shoe must often be removed to afford evaluation of the sole margins and the white line – the most common sites for sole abscess. Tracts should be pared and followed in the painful region until the abscess is relieved or until on further paring the solar corium is revealed by a slight pink hue. A specialized hoof knife with a tightly curved tip, or a bone curette may be useful for following tracts through the sole. Most sole abscesses consist of a gray-colored, malodorous liquid that flows freely when the abscess cavity is breached during paring (Fig. 15.7). Excessive paring may result in hemorrhage from the solar corium. The size of the sole opening used to drain the abscess and permit local treatment is quite small. Excessively large defects used to drain an abscess require prolonged healing time and protection with a sole pad.

If the abscess cannot be drained on the initial visit, verify tetanus status and poultice or soak the foot. Poulticing and soaking are done to soften the foot and draw out the abscess.

Fig. 15.7
A sole abscess that has been successfully localized and opened for drainage. The characteristic gray color of the abscess material is evident.

Soaking is done by placing the foot in warm water with diluted povidone–iodine and a handful of Epsom's salts for 10 to 20 min once or twice daily. Other agents for poulticing the foot include Ichthammol and an ointment consisting of magnesium sulfate, methyl salycilate, and menthol (Magnapaste, The Butler Company, Columbus, OH). Another method of providing prolonged soaking of the foot is by using the bran mash poultice. Place a strong plastic bag that fits over the foot, add one handful of bran, a small handful of Epsom's salts. Add sufficient water to soak the bran and add povidone–iodine (approximately 1 part to 10 parts other constituents). Fit the bag with mixture over the foot and secure with gauze, elastic tape and duct tape. This poultice is changed every 24 h.

If the abscess was easily drained, apply a povidone–iodine-soaked gauze to the pared defect and protect the sole with a commercial protective boot or a bandage. Change the bandage daily for the first few days, then as needed to protect the foot. After the abscess is dry – as soon as 4–5 days or as long as 2 weeks – a shoe with a leather pad should be applied to protect the pared area. Systemic antibiotics are not administered in uncomplicated sole abscess cases. In all cases of hoof sepsis, tetanus status should be determined. If the horse has not been vaccinated within the previous 6-month period, reimmunization is indicated.

Deep sole abscesses that cannot be drained through the sole result in prolonged lameness and often break out at the coronary band of the hoof capsule or over the bulbs of the heels. If the abscess cannot be accessed from the sole or white line, radiographs may help localize the site. Radiographs will also determine if the distal phalanx has suffered osteomyelitis or osteitis due to the prolonged inflammation and infection. Rarely extensive, prolonged sole abscesses must be treated with localized, partial hoof or sole resection, and/or curettage of the distal phalanx.

More extensive treatment must be done in the case of a deep penetrating wound to the caudal one-third of the foot. At the first indication of a deep wound in this crucial location, the horse should be administered broad-spectrum parenteral antibiotics such as penicillin and gentamicin, or ceftiofur and gentamicin. Enhanced coverage for anaerobic organisms may be obtained by adding oral metronidazole to either protocol.

Because of the poor prognosis for horses that develop sepsis of the deep structures within the caudal aspect of the hoof, vigorous therapy is imperative. If the radiographic study confirms deep penetration in this critical zone the horse should be placed under general anesthesia to allow sampling and treating of the most at-risk structures: navicular bursa, distal interphalangeal joint, and the distal digital sheath.

If lameness is severe at presentation and a tract in the caudal foot is recognized surgical debridement is necessary ('street nail' procedure). This procedure requires cleansing and soaking of the foot in antiseptic solution, and progressive debridement of tissue along the foreign body tract. This usually requires cutting a 2-cm square hole through the frog and digital cushion. If the tract penetrates the deep digital flexor tendon, the debridement continues through the tendon to permit examination and debridement of the flexor surface of the navicular bone. Arthroscopic examination of the flexor surface of the navicular bone is feasible and may be appropriate (see Chapter 11).[11]

Following debridement, the foot must have sterile bandage changes to prevent contamination. This process is facilitated by applying a hospital plate shoe to the foot.

Prognosis Prognosis is usually excellent for return to complete soundness within 2 weeks for uncomplicated sole abscesses.

Deep penetrating wounds to the foot have a guarded to poor prognosis. Using the street nail procedure 32% of affected horses returned to soundness.[12] Using the arthroscopic approach 75% of treated horses returned to their intended use.[11]

Laminitis

- Bounding digital pulses, marked lameness, and postural efforts to shift weight from the affected feet characterize the signs of laminitis.
- Inciting causes include metabolic derangements, severe illness, and excessive weight bearing.
- Treatment must remove the inciting cause, reduce inflammation, maintain blood flow, and prevent distal phalanx displacement.
- Trimming using radiographic control is necessary to return the hoof to function.
- Overall prognosis for soundness in most cases is favorable.

Laminitis is defined as inflammation of the pedal laminae, which provide the support between the hoof wall and distal phalanx. Numerous causes of the disease have been defined but the leading cause remains gastrointestinal disturbances. Although the condition primarily affects the foot, the disease is actually a systemic disease, which causes disturbances in most body systems. The disease can be arbitrarily divided into four phases: developmental, acute, chronic, and postchronic.

Recognition

History and presenting complaint Horses presented with clinical signs of laminitis are always in the acute, chronic or postchronic phases of the disorder. Signs of acute laminitis include: 'bounding' digital pulses, warm feet, and 'camped in front' stance. This characteristic stance is an effort by the horse to shift weight bearing to the (usually) unaffected rear limbs. The severity of lameness relates to the severity of damage to the laminae. Pain and inflammation from ischemia to the secondary laminae is the direct cause of acute pain in laminitis. Horses with chronic laminitis are presented for misshapen hooves, seedy toe, chronic, recurring hoof abscessation, and chronic lameness.

The practitioner must be aware of potential inciting causes of laminitis. When a horse is exposed to a situation that may cause laminitis preventive measures must be taken to minimize the adverse effects. The period of time between exposure to a situation that may cause laminitis and the onset of clinical signs is called the developmental or subclinical phase. Factors that may induce laminitis should be identified in the history and include:

grain overload, colic, illness associated with endotoxemia, retained placenta, exhaustion and metabolic derangements, exposure to black walnut shavings, excessive ingestion of lush pasture grasses (grass founder), excessive concussion (road founder), Cushing's syndrome, excessive weight bearing on a limb, and excessive ingestion of cold water.[13–17]

Physical examination Horses with acute laminitis generally show varying levels of foot pain, often characterized by treading in place or a shifting limb lameness.[13,14] When severe pain is present in the forelimbs a characteristic 'walking-on-egg shells' gait is evident as the horse shifts weight to the rear limbs. Most commonly, both forelimbs are affected. All limbs may be affected in extraordinary cases. Unilateral limb involvement is usually found in the contralateral limb of horses that have non-weight-bearing lameness due to fracture or infection.[16] Digital pulses are generally increased and may be bounding in severe laminitis. Hoof tester sensitivity at the toe near the apex of the frog is usually marked. When rotation or distal displacement of the distal phalanx has occurred the sole will lose its normal concavity and a depression may be palpated at the coronary band. Imminent exposure of the distal phalanx or separation of the hoof capsule from the foot may be first recognized with serum weeping from the sole or coronary band, respectively.

Horses with chronic laminitis may have remodeling of the tip and dorsal border of the distal phalanx, solar margin fractures, and distal phalanx rotation evident on radiographic examination. Inadequate trimming may leave a dished hoof with long toes and severely underrun heels. Chronic abscessation of the hoof and coronary band associated with a wide and weakened white line is also commonly found in chronic laminitis cases.

The Obel grade classifications record the severity of gait abnormalities in horses with laminitis:[18]

- Obel grade 1: the horse exhibits constant shifting of its weight from leg to leg. The horse's gait is stiff and stilted at the trot but not the walk.
- Obel grade 2: lameness is characterized by a stiff and stilted gait at the walk and trot. The horse is reluctant to rest full weight on a leg but a leg can still be lifted off the ground readily.
- Obel grade 3: has the horse reluctant to move. Lifting a limb off the ground is very difficult. Permanent morphologic change occurs within 12 h of the onset of Obel grade 3 lameness.
- Obel grade 4: is so severe that the horse refuses to move unless forced and spends most its time recumbent.

Diagnostic confirmation Diagnosis is based on physical signs and radiographic examination. The dorsal hoof wall and dorsal distal phalanx in the normal horse should be parallel and the space should measure < 19 mm or < 30% of the length of the distal phalanx measured from its tip to its articular surface at the navicular bone (Fig. 15.8).[19] Rotation is the most common displacement and is caused by disruption of dorsal laminar attachments and the pull of the deep digital flexor tendon (DDFT). Radiographic evaluation of distal phalanx displacement may help determine a prognosis. Prognosis is good for horses with rotation < 5.5°, but poor for rotation > 11.5°.[20] Horses with distal displacement ('sinking') have a poor prognosis. Another study contradicted the aforementioned report and found no correlation between radiographically measured distal phalanx displacement and prognosis for resolution of laminitis.[14]

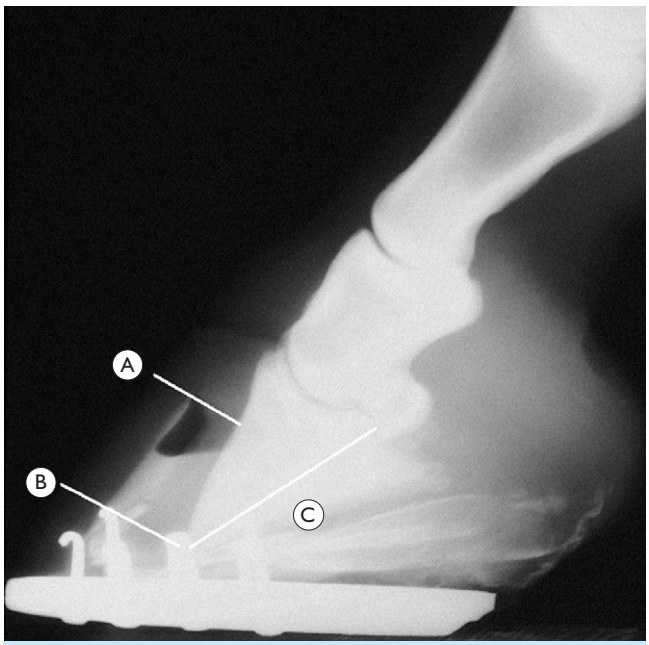


Fig. 15.8
Radiographic measurement of distal phalanx displacement. This lateral radiographic projection of the distal phalanx has been marked to demonstrate two methods for measuring distal phalanx displacement. Measured distances: A, 24 mm; B, 30 mm; C, 54 mm. Normally, A and B should measure less than or equal to 19 mm and be equal values, indicative of parallelism of the dorsal distal phalanx with the dorsal hoof capsule. A and B should also be less than 30% of the measurement taken from the tip of the distal phalanx to the articulation with navicular bone (C). In this case C/A = 44% and C/B = 55%. These values are indicative of severe distal phalanx displacement. A gas and fluid pocket indicative of lamellar necrosis is also found in the dorsal laminae.

Venograms of the distal limb have been advocated to help determine prognosis.[21] The prognosis for successful treatment is enhanced when the vasculature of the coronary corium and dorsal laminae are visible during venography.

Differential diagnoses include deep abscess, distal phalanx or navicular bone fracture, septic tenosynovitis, or deep bruising. Most of these conditions commonly occur in a single limb, but laminitis most commonly occurs bilaterally except when caused by excessive weight bearing.

Treatment and prognosis

Therapeutic aims The treatment objectives for laminitis include eliminating the inciting cause, decreasing inflammation, maintaining or re-establishing blood flow to the laminae, and preventing displacement of the distal phalanx.

Treatment during the developmental phase is done to prevent the onset of clinically apparent laminitis or to reduce the potential adverse effects of exposure to inciting causes of

laminitis. Under all circumstances the first aim of therapy is to treat and remove any potential inciting cause of laminitis.

The aims of treatment during the chronic phases of laminitis include stabilizing the distal phalanx to reduce further displacement and providing an environment where the distal phalanx, laminae and hoof capsule may re-establish a firm, stable bond. When all other significant hoof issues have been resolved, gradually returning distal phalanx to normal orientation with the ground surface is the ultimate goal.

Therapy Treatment during the developmental and acute phases of laminitis includes elimination of the inciting cause, increasing the blood flow to the laminae, antithrombotic therapy, and distal phalanx support. In the developmental phase, successful treatment should prevent the laminar damage that results in distal phalanx displacement and the untoward sequellae, while treatment in the acute phase should reduce the adverse effects and extent of the damage.

In horses that have been exposed to the inciting causes of laminitis it is prudent to exclude all grains and concentrates from the diet until the outcome is evident. Cathartics are administered in grain or pasture overload. Mineral oil or water with Epsom's salts (up to 1 kg per 4 L water) may be administered via nasogastric intubation. Gastric lavage may be performed within 2 to 6 h of overeating. Intravenous fluid and electrolyte therapy should be instituted in exhausted horses. Fractures and severe lameness should be treated to permit weight bearing in the affected limb as soon as possible.

If a severe illness, abdominal surgery, or other condition that may cause endotoxin release is present the horse should be administered hyperimmune serum and flunixin meglumine at the anti-endotoxic dose (2.5 mg/kg i.v., q 6 h).[22]

NSAIDs such as phenylbutazone (4.4–8.8 mg/kg/day), flunixin meglumine (1 mg/kg/day) or ketoprofen (2.2 mg/kg/day) should be administered in all cases of laminitis. Phenylbutazone is most commonly used, yet ketoprofen may have a slightly better effect in select cases. NSAIDs reduce prostaglandin and thromboxane production through inhibition of cyclo-oxygenase, decreasing inflammation associated with ischemia and thereby decreasing pain and promoting blood flow through small peripheral vessels by inhibiting platelet aggregation and thrombosis.

Dimethyl sulfoxide (DMSO) may be used to prevent reperfusion injury of the laminae. It acts as a free-radical scavenger and non-specific anti-inflammatory agent.[23] DMSO is administered at 0.25–1.0 g/kg i.v. in saline or 5% dextrose solution at a concentration less than 20%. In acute laminitis treatment with DMSO is usually continued for 3 days.

Blood flow to the laminae may be enhanced with peripheral vasodilators.[24] Acepromazine maleate is an α-adrenergic antagonist and is administered at 0.03–0.06 mg/kg i.m. either q 6 h or q 8 h for 3 to 5 days, or until the horse improves. This drug is readily available in all practices and should be used at the first indication of laminitis. Isoxsuprine HCl is a β- and α-adrenergic antagonist that is administered at 1.2 mg/kg p.o. q 12 h for indefinite periods. There is some controversy regarding systemic availability of this drug via the oral route and treatment effects should not be expected for days or weeks.[25]

Small vessel blood flow may also be enhanced by administering antithrombotic or anticoagulant medications. Aspirin is very effective at inhibiting platelet aggregation and may be administered at 10–20 mg/kg p.o. every other day.[14] Heparin may be administered at a dosage of 40–80 units/kg SQ q 12 h.[26]

The distal phalanx must be supported in the developmental phase to prevent displacement and in the acute phase to also prevent or limit distal phalanx displacement. Initially simple gauze rolls taped over the frogs may be helpful. Lily Pads® (Kentucky Blacksmith Supply, KY), fitted over the heel bulbs and frogs and secured with tape, may be a longer-term solution. Full sole support may be custom fitted using Scotchcast Custom Support Foam fiberglass cast padding tape (3M Orthopedic Products, St Paul, MN), dental impression material, or common foam building insulation. These pads can be frequently reset to provide the most comfort in cases with rapidly changing sole contours. Deep sand footing is a simple method to maintain good sole contact and soft bedding.

Excessive tension of the DDFT is one of the factors responsible for distal phalanx rotation and can be reduced through several methods. Special horse shoes have been developed to help reduce DDFT tension and to support the foot. The Ultimate Wedge shoe (Kentucky Blacksmith Supply, KY) raises the heel 20°, significantly reducing DDFT stress.[27] The Ovnicek shoe (Equine Digital Support System, Columbia Falls, MT) has several components that results in custom foot support and can be configured with a high heel wedge and styrofoam-like sole padding.

A surgical alternative for reducing DDFT tension also exists. Tenotomy of the DDFT at midcannon bone or at the level of the heel bulbs has been used as a salvage method for nonresponsive cases of laminitis with severe rotation and in some cases for treatment of peracute distal phalanx displacement.[28] Tenotomy at the midcannon level is a practical technique that may be performed under local anesthesia through a small stab incision. The limb is bandaged and the foot is supported with sole pads. An extended heel shoe or a shoe with a marked wedge pad is necessary to prevent subluxation of the distal interphalangeal joint. Response to tenotomy has been variable. In the successful case, the DDFT eventually heals, but scarring and adhesions may limit athletic use of the horse.

Chronic laminitis presents a variety of treatment challenges. Displacement of the distal phalanx usually occurs by rotation in the sagittal plane but may also involve complete distal phalanx displacement ('sinking'). The damaged lamellae also predispose the hoof to abscessation at both the sole and the coronary band (Fig. 15.9). The displaced distal phalanx is predisposed to solar margin fractures, especially near the toe. In the most serious cases, complete slough of the hoof may occur or the distal phalanx may penetrate the sole. Management of these conditions requires long-term treatment with NSAIDs and repeated shoeing and trimming. Follow-up treatment should always involve the veterinarian, farrier, and horse owner. Decisions regarding continued support of the sole, easing of breakover, and correct trimming of heel and toe should be made using radiographs of the affected feet taken at intervals during recuperation.

Fig. 15.9
Arrowheads identify dark tracts at the sole margin and the white line. This hoof has suffered from chronic laminitis. These tracts must be pared out at each trimming.

In most cases of mild laminitis, gradual reshaping of the hoof capsule must be performed over several months to return the distal phalanx to the proper relationship with the ground surface and the hoof. This generally requires removing excess heel and excess toe. Trimming should result in gradual changes only and should be controlled by measurements and relationships made from lateral radiographs of the distal phalanx (Fig. 15.10). In some cases more radical trimming changes may be indicated. The four-point trimming protocol as described by Ovnicek may help reduce DDFT tendon strain and the strain on the distal limb during breakover. By providing more surface area of contact with the ground surface the method may also reduce overall foot pain.

Prognosis Most mild cases of laminitis respond to treatment in several days to weeks. Those that linger, have marked displacement of the distal phalanx, display increasing levels of severe pain or suddenly 'walk out of their feet' may be candidates for euthanasia. The owner's strong desire for resolution of this devastating condition 'at all costs' because the horse is a 'best friend' must not override rational analysis of the horse's condition and humane aspects of continuing treatment. In most cases the horse should be euthanized when pain is unmanageable and the horse shows signs of anorexia, cachexia, or severe decubital ulcers. Most cases with distal phalanx penetration of the sole, sloughing of the hoof capsule, and recurrent deep abscessation of the sole or laminae should be euthanized. There are always exceptions,

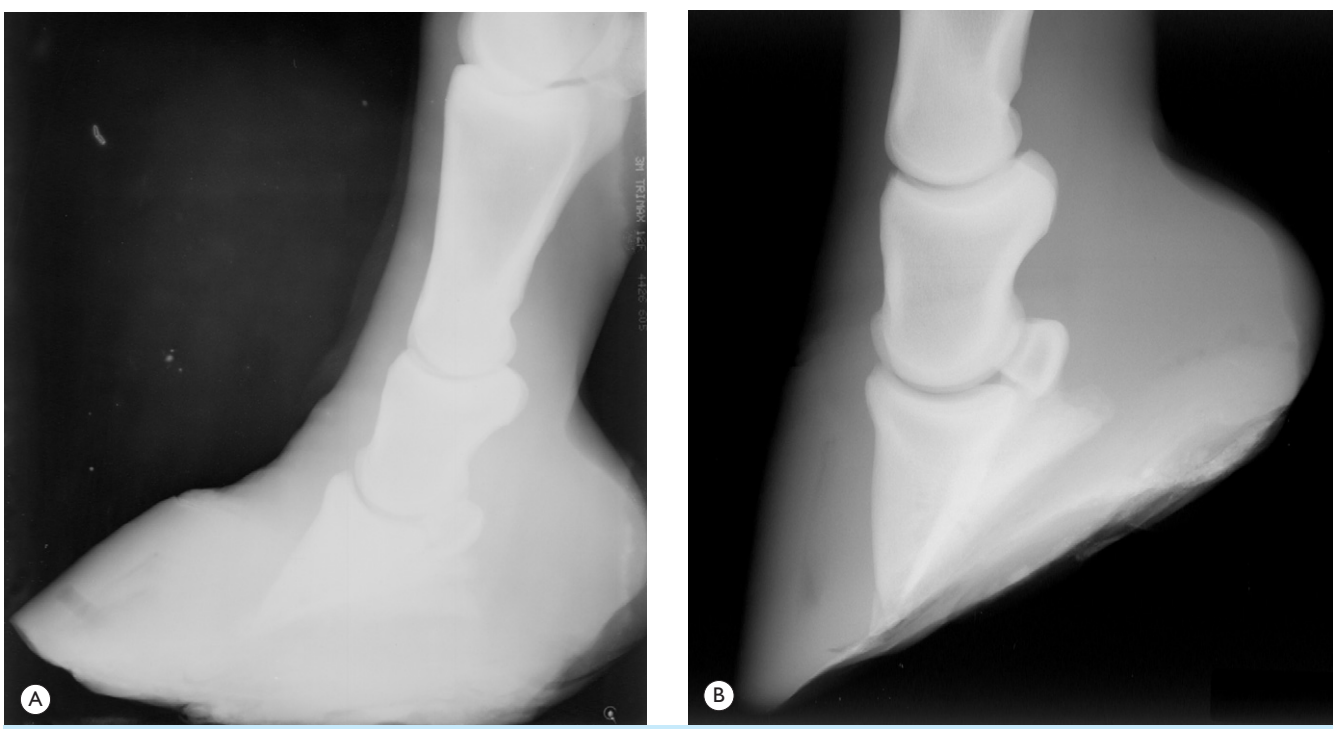


Fig. 15.10
Radiographs as an aid for trimming of chronic laminitis. (A) Lateral radiographic view of a hoof with chronic laminitis characterized by rotational distal phalanx displacement and dishing of the dorsal hoof capsule. Using this film, the farrier was able to determine the position of the distal phalanx and trim the hoof appropriately. (B) Lateral radiographic view of the foot after trimming. Following evaluation of this film even more toe was trimmed away.

and quality of life for the horse should be a primary, although at times arbitrary and qualitative, concern.

Prognosis for resolution of laminitis is usually fair to good for horses with minimal distal phalanx displacement. Prognosis is good for horses with rotation < 5.5°, but poor for rotation > 11.5°.[20] Horses with marked displacement nearly always suffer more chronic hoof problems that may limit soundness. Horses with sinking displacement have a poor prognosis for survival, as do horses that slough the entire hoof or have penetration of the sole by the distal phalanx.

Prognostic indicators for laminitis were reported in a study from the UK.[29] Of 216 horses with laminitis: 162 (77%) became sound as athletes, 7 (3%) did not become completely sound, but survived and 42 (20%) horses were euthanized or died due to laminitis. The remaining five horses were euthanized and not treated. The most significant prognostic indicator was quantification of distal phalanx displacement from radiographs. Less significant prognostic indicators were the severity of lameness, distal phalanx rotation angles, the presence of dropped sole, and the number of feet affected.[29]

Etiology and pathophysiology

Etiology The following conditions are associated with laminitis: excessive grain or lush pasture ingestion; endotoxemia associated with infectious diseases such as diarrhea, septicemia, or retained placenta; excessive metabolic stress associated with dehydration or overexertion; excessive weight bearing on a limb opposite one with a fracture or severe lameness; and management factors such as bedding with black walnut shavings, excessive obesity, and underconditioned horses worked excessively.

Pathophysiology There is general agreement that laminitis is associated with circulatory disturbances at the level of the lamellae, but the specific nature of the changes continues to be under investigation.[13,14,24,30–34] Current research suggests that there is a period of lamellar vasodilatation during the developmental phase of laminitis.[24,30,31] In experimental laminitis vasodilatation within the hoof was found from 12 to 32 h after carbohydrate overload.[30] The increased local blood flow may result in exposure of the lamellae to enzymes such as metalloproteinase-2 and metalloproteinase-9 (MMP-2 and MMP-9).[32] These enzymes are normally required to temporarily break the lamellar attachments as the keratinized hoof capsule grows and 'slides' along the dermal lamellae. In the normal hoof inhibitor enzymes are present to control MMP activity, whereas the laminitic hoof lacks these inhibitors. Vasodilatation of the vessels in the lamellae carries the activated MMP enzymes to their site of action, the cytokines and free radicals associated with reperfusion then act on the lamellae and cause their destruction. Hoof tissues from experimental horses with acute and chronic carbohydrate-induced laminitis have high expression of endothelin-1 (ET-1).[34] The presence of ET-1 causes marked vasoconstriction, which leads to ischemia of the lamellar tissues. This potential cycle of vasodilatation, followed by vasoconstriction and the attendant breakdown of lamellar attachments, necrosis, and inflammation constitutes the vicious cycle that leads to pain, distal phalanx displacement, and the other physical signs of laminitis.

Prevention

Minimizing changes in diet, particularly changes in the amount of grain fed and controlling access to lush, new pasture grasses, will decrease the incidence of laminitis. Recognize that horses that have had a previous bout of laminitis are predisposed to having the problem again. When inciting causes of laminitis are present preventive treatment should be instituted.

Diseases of the distal phalanx

Distal phalanx fractures

Distal phalangeal fractures can be classified into one of seven types (Fig. 15.11).[35–37] Type I is a non-articular fracture of the wing of the third phalanx. Type II fractures are articular wing fractures (Fig. 15.12). Type III fractures are sagittal and divide the bone nearly into equal halves. Type IV fractures comprise all extensor process fractures (Fig. 15.12). Comminuted and irregular distal phalanx fractures are type V. Fractures of the solar margin are type VI. Palmar process fractures are considered type VII (Fig. 15.13).[36]

Recognition

History and presenting complaint Acute onset of grade 3–5 of 5 lameness is the primary presenting complaint for frac-

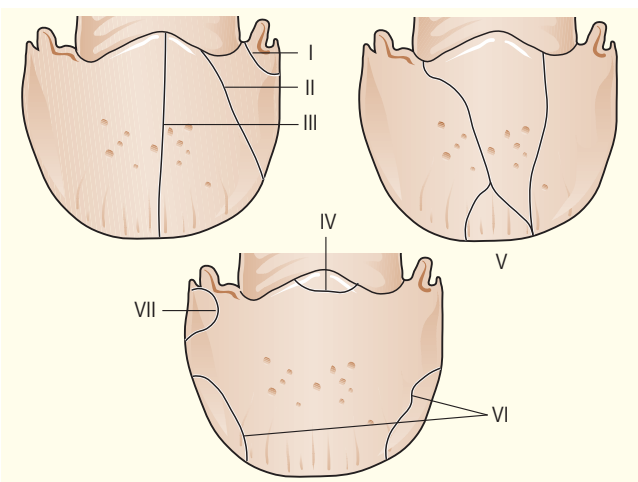


Fig. 15.11
Diagrammatic representation of distal phalanx fractures. Type I: non-articular fracture of the wing; type II: non-sagittal fracture that enters the distal interphalangeal joint; type III: midsagittal, articular fracture from the extensor process to the solar margin; type IV: extensor process fracture; type V: comminuted or irregular fractures; type VI: fractures of the solar margin; type VII: non-articular fractures of the palmar process.

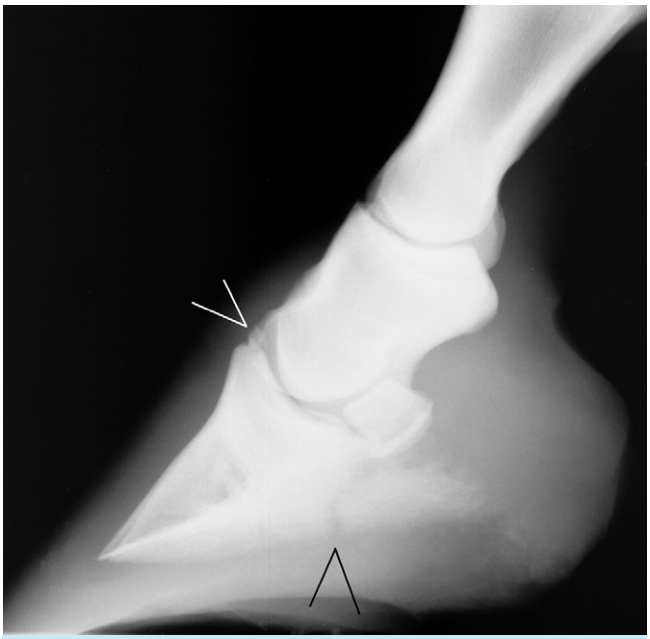


Fig. 15.12
Lateromedial radiographic view of the distal phalanx. Type II (black arrowhead) and type IV (white arrowhead) distal phalanx fractures are evident.

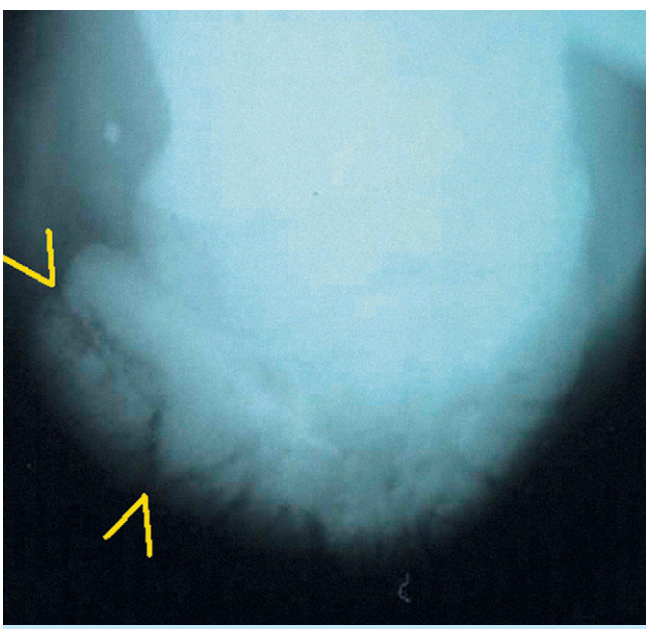


Fig. 15.13
Dorsal 65° proximal–palmarodistal oblique radiographic view of the distal phalanx. A type VII palmar process fracture is evident between the arrowheads.

tures of the distal phalanx. Often the inciting event is not seen but kicking in the stall or a miss-step followed by acute lameness may be reported. Young foals with distal phalanx palmar process fractures may be presented for evaluation of club-footed conformation that is accompanied by mild, short-term lameness.[38–40]

Physical examination Lameness is usually accompanied by an increased digital pulse. Extensor process fractures are often accompanied by swelling over the coronary band. Hoof tester examination usually reveals marked pain over the entire hoof but especially over the fracture. Hoof percussion reveals sensitivity around the entire hoof but especially over the fracture. These two techniques can usually aid the practitioner in lining up for radiography in order to center the X-ray beam on the fracture.

Diagnostic confirmation Radiographs are necessary to confirm the diagnosis. Usually at least four to five views should be made in order to examine the entire bone from several angles. The fracture may not be visible until lysis occurs along the fracture line, often for 10–14 days.[35] Nuclear scintigraphy and computed tomography are additional imaging methods to help recognize distal phalanx fractures.

Treatment and prognosis

Therapeutic aims Sufficient stability and reduced activity must be provided for the affected foot to permit healing of the fracture.

Therapy Fracture types I, II, III, and V are treated by therapeutic shoeing. A full bar shoe with quarter clips, full rim shoe, or certain glue-on shoes will immobilize the hoof capsule and effectively turn the hoof into a cast. Foals with any type of distal phalanx fracture should not be treated with a restrictive shoe because of the secondary complications that accompany hoof contracture. Foals under 1 year of age with these fractures usually respond favorably to stall or paddock confinement alone.[39,40]

Fracture types II, III, and IV may be repaired with lag screw fixation. This can be difficult because the fracture line cannot be visualized during surgery, therefore radiographic control during surgery is essential for a successful outcome. Also, the bone in the wings of the distal phalanx is porous and does not hold screws well.

Type IV fractures are best treated by surgical intervention. Small fragments are easily removed via arthroscopy. Larger fragments should be stabilized using lag screw fixation but can be removed completely via an arthrotomy. Neurectomy of the palmar digital nerve may be necessary to resolve chronic low-grade pain. Neurectomy is most effective for wing fractures but may reduce pain in all the fractures. It should not be performed if a palmar digital nerve block fails to substantially improve the lameness.

Prognosis The prognosis for soundness of fracture types I and II is fair to good.[35] Fracture types III and IV have a guarded to fair prognosis due to the likelihood of distal interphalangeal arthritis. The prognosis for type V fractures due to trauma is good, yet prognosis for this type of fracture secondary to osteomyelitis is guarded. Type VI fractures have an excellent prognosis. In adults complete healing of distal phalanx fractures may require 9 to 12 months. All fractures in foals less than 1 year of age have a very good to excellent prognosis for soundness.[39,40]

Etiology and pathophysiology

Etiology These fractures are usually caused by trauma. Pathological fractures of the distal phalanx may occur secondary to osteomyelitis. Improper shoeing, hard surfaces, stone bruises, infectious conditions, and nutritional deficiencies are all considered to be contributing factors.

Diseases of the podotrochlea

Navicular bone fractures

Navicular bone fractures are uncommon and can be classified into one of four types. These are simple sagittal fractures, comminuted fractures, avulsion fracture of the navicular suspensory ligament, and avulsion fractures of the impar ligament.

Recognition

History and presenting complaint History, presenting complaint and physical signs for avulsion fractures of the navicular bone are the same as for other causes of palmar foot pain (see below). Complete navicular fractures will present with acute onset of severe lameness that may decrease somewhat over time.[41]

Physical examination These fractures have pain referable to the navicular bone. They are usually acute and exhibit a grade III–V of V lameness. In most cases the horse is unwilling to place the heel of the affected foot on the ground. Marked pain over the navicular area is noted with hoof testers. Distal limb flexion markedly exacerbates the lameness.

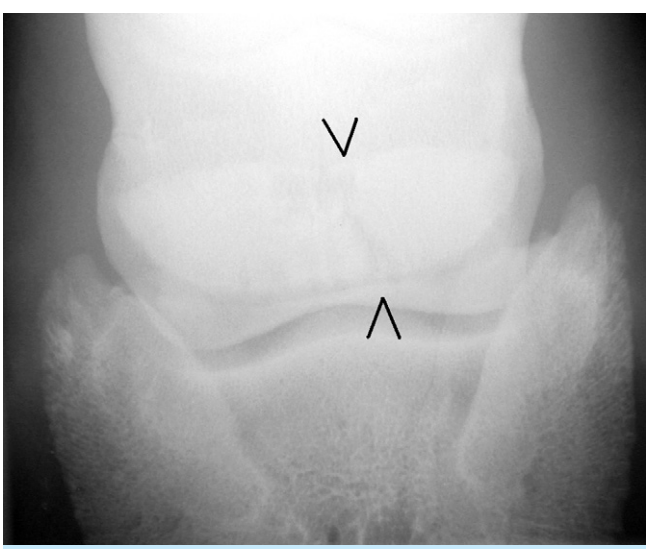


Fig. 15.14
Navicular bone fracture. The lucent line between the arrowheads is the fracture line.

Diagnostic confirmation Conformation of navicular fracture is made by localizing the foot pain to the heel region and radiographic evidence of fracture (Fig. 15.14). Recognize that occasionally the navicular bone will develop with two (bipartite) or three (tripartite) ossification centers. If these centers do not bridge with mineralized bone, the navicular bone may appear to be fractured. Localization of pain to the heel region using diagnostic local anesthesia should rule-out separate ossification centers.

Treatment and prognosis

Therapeutic aims Conventional therapy for navicular fractures is similar to that used for distal phalanx fractures. An alternative technique reduces DDFT and heel strain and is followed by a gradual exercise program to limit adhesions.

Therapy Navicular bone fractures are treated conservatively. Surgical exposure of the site and internal fixation of the fracture is exceedingly difficult. Therapy traditionally entails variable periods of rest with corrective trimming and shoeing to immobilize the hoof. Palmar digital neurectomy often is required after the fracture heals to increase soundness. However, the results of this type of therapy have been poor. The poor results are thought to be due in part to adhesion formation between the navicular bone and the deep flexor tendon.

An alternative technique may be used that reduces heel strain and returns the horse to controlled exercise sooner than conventional therapy.[42] Following the diagnosis of a navicular bone fracture, the affected hoof should be trimmed to its normal hoof pastern axis. The hoof is then shod with a flat shoe and four 3° wedge pads so as to elevate the heels 12°. The objective is to prevent the navicular bone from having weight-bearing contact with the second phalanx and to decrease the strain on the deep flexor tendon. Proper elevation of the hoof can be confirmed through the use of a lateral radiograph.

The horse should be stall rested for the first 60 days, then short periods of handwalking (15 min daily) can begin. The shoe is reset every 4 weeks. At each reset the hoof is trimmed and the horse is reshod with 3° less elevation. At the end of 4 months, when the horse is shod normally, an assessment of the degree of soundness is made. Podotrochlear bursography can be utilized at the end of the 4-month period to assess the degree of adhesion formation. Four cases have been treated utilizing this method. Three horses had simple sagittal fractures of the navicular bone involving the forelimb and one had a comminuted fracture of a rear limb navicular bone. Upon initial presentation these horses were grade 3–5 of 5 lame. Typically, the fracture was noted radiographically as a clearly demarcated fracture with well-defined margins. The fracture line became less well defined within 30 days. This was presumably due to bone resorption. Mineralization around the fracture in each of these cases occurred but complete radiographic healing of the fracture did not occur in any case. However, the horse's lameness resolved after the 4-month treatment period. Two horses returned to competition, one as a gaited horse and the other is a multipurpose Arabian show horse. The other two horses are not lame and are being ridden.[42]

Complete navicular bone fractures often heal with a fibrous, rather than an osseous, union.[41] Avulsion fractures of the proximal or distal border of the navicular bone usually respond to treatment for palmar foot pain.

Prognosis The prognosis for navicular fracture caused by trauma is guarded prognosis due to likelihood of secondary arthritis. Pathologic fractures due to infection have a grave prognosis.

Etiology and pathophysiology

Etiology The etiology of navicular fractures is always traumatic but can be predisposed by either infection or chronic demineralization from navicular disease. Repetitive trauma that predisposes the foot to palmar heel pain may lead to avulsion fractures of the proximal or distal border of the navicular bone. The navicular bone may have more than one center of ossification, resulting in either a bipartite or tripartite bone.

Palmar foot pain

- Manipulative tests and diagnostic anesthesia often do not specifically identify the site of palmar heel pain.
- Shoeing goals for palmar heel pain: correcting hoof imbalance, easing breakover, and providing concussion protection.
- There are more than 15 specific causes of palmar heel pain.
- Prognosis improves with diagnosis and treatment within 1 year of onset.

Lamenesses in this region account for more than one-third of all chronic lameness in the horse.[2] It must be understood that a palmar digital nerve block simply localizes the source of the pain the horse senses to the back of the foot. It is important to identify as specifically as one can the pathological and clinical findings. This in turn will help the clinician make their best assessment of the problem, and recommend the most specific treatment.

Recognition

History and presenting complaint Horses are presented for mild to moderate unilateral or bilateral forelimb lameness that is usually exacerbated in a circle. Quarter Horses, Thoroughbreds, Warmbloods, other Western stock-type horses and other breeds that compete over fences are predisposed to palmar heel pain. Subtle heel pain may be presented as a horse that no longer extends the forelimbs during the trot, resulting in a short, choppy or shuffling gait. Affected horses may stumble due to their preference to land toe first.

Physical examination The examination should closely follow the guidelines presented earlier in this chapter. No diagnostic test is pathognomonic for navicular or palmar foot pain.[43] Distal limb flexion has been suggested by Turner to be of importance in the differentiation of navicular disease. In that study, 87.5% of the horses responded to this test.[43] When grouped according to diagnostic analgesia response, the navicular region pain (NRP) group that blocked to a palmar digital, distal interphalangeal and podotrochlear bursa analgesic injection was positive to distal limb flexion in 88% of the cases. The palmar foot pain (PFP) group that did not respond equally to the three injections were positive to distal limb flexion in 87% of horses. This indicates that the test is good for exacerbating pain in the palmar hoof but does not help in specific differentiation of the cause.

The frog wedge test is thought to exert pressure directly on the navicular bone similar to hoof testers but is thought to be more accurate because the horse's weight exerts the pressure rather than man-made pressure. The study found that 75% of the horses responded to this test.[43] But 76% were from the NRP group and 74% from PFP group again indicating no difference.

The toe wedge test was positive in 56%. This is higher than that reported by Wright.[44] However, the test was of no help in differentiating the source of pain; 55% were positive in the NRP group and 58% were positive in the PFP group.

Hoof tester examination over the frog is considered by some clinicians as the definitive test for navicular pain. However, hoof tester examination was found not only to be less sensitive than other manipulative tests for navicular pain but that other types of palmar foot pain were more likely to respond to the hoof tester examination over the frog than horses with navicular pain.[43,44]

The first step in the treatment of palmar hoof pain is accurate assessment of the pain and careful evaluation of hoof structure that may predispose to or cause the pain. The examination of the foot has been previously described in this chapter.

Typically, all causes of lameness in the palmar foot will be improved by at least 90% after perineural anesthesia of the palmar digital nerves. Anesthesia of the distal interphalangeal (DIP) joint or the podotrochlear bursa are additional procedures that provide information about palmar hoof pain. In a study reported by Dyson and Kidd[45] 95% of the horses examined using DIP and bursa anesthesia gave significant new information about the pain the horse exhibited. The pain relief by anesthesia of any of these three regions has been shown to overlap. Further, recent identification of neuroreceptors for the navicular bone and podotrochlear region have indicated how these other diagnostic techniques may help differentiate these clinical conditions. The DIP joint and podotrochlear bursa do not communicate, and yet the response to local anesthesia injected into these synovial cavities is similar.[46] Both cavities have in common the navicular bone, the impar ligament, and the collateral sesamoidean ligament (proximal suspensory ligament of the navicular bone). The neuroreceptors for the navicular bone are in these two ligaments and they can be anesthetized from either synovial cavity.[47] Furthermore, Bowker et al. have shown that the palmar digital nerve is in very close proximity to the medial and lateral limits of the bursa and that the nerve may be anesthetized at this level whenever the bursa is injected.[48]

Special examination Podotrochlear (navicular) bursa contrast arthrography is a new method of assessing navicular pathology.[8] This technique allows evaluation of the cartilage of the flexor surface of the navicular bone. In several

cases we have been able to conclusively prove the presence of adhesions between the navicular bone and bursa.

Use of the podotrochlear bursa contrast study has provided new information regarding the flexor cartilage, the presence of adhesions between the deep flexor tendon and navicular bone, and possible tendon damage. Adhesions between the deep flexor tendon and navicular bone were seen as space-occupying lesions in the dye column across the flexor surface of the bone. In each of the cases in which this was noted the horse had navicular pain. Tendon damage was noted when the dye filled small defects in the tendon. This finding was found only in that group of horses with palmar foot pain. Flexor cartilage damage was evident by the loss of cartilage on the flexor surface. This finding was noted equally in horses with navicular pain and the group with other causes of palmar foot pain. This suggests that flexor cartilage erosion is probably of little consequence, or at least highly variable in causing navicular bone pain.

Diagnostic confirmation Radiographic examination is the imaging method most often used to assess osseous changes in the distal sesamoid bone. These changes with the exception of fractures are usually not pathognomonic but do provide insight into damage that has occurred to the foot (see Chapter 10).

Scintigraphy provides information on relative vascularity and rate of tissue metabolism. This is particularly useful in studying bone pathology and can help differentiate sites of injury in the foot. High-detail scintigraphy of the foot obtained using a skyline view can localize inflammation specifically to the navicular bone or to other structures in the palmar heel region.

Thermography has been shown to be useful in assessing the relative blood flow to regions within the foot.[10] This information is of particular interest when pre- and postexercise temperatures are determined. Exercise will normally cause a 0.5°C rise in skin temperature. Whenever the skin temperature does not rise, poor blood flow should be considered a factor in the disease being assessed.

It is clear that the diagnosis of navicular disease and palmar heel pain is facilitated by noting the response to diagnostic anesthesia. However, as discussed earlier in this chapter, none of the diagnostic anesthesia procedures employed results in specific desensitization of a single anatomic site. The diagnostician must use physical findings, response to diagnostic anesthesia, and imaging to determine the specific diagnosis.

Treatment and prognosis

Therapeutic aims Palmar heel pain is treated primarily by correcting hoof balance abnormalities, easing breakover and providing more concussion protection to the foot. Anti-inflammatory medications and peripheral vasodilating agents can also be utilized, but often play a secondary roll to corrective shoeing in the treatment of this type of lameness.

Therapy Treatment must be tailored specifically to the hoof characteristics and use of the horse. Corrective shoeing, anti-inflammatory medication, and peripheral vasodilating agents are all part of treatment protocols for palmar foot pain.

The most successful approach to shoeing is that based on individual case needs rather than a standard formula. The following principles should be followed:

1. Correct any pre-existing problems of the hoof, such as underrun heels, contracted heels, sheared heels, mismatched hoof angles, broken hoof/pastern axis.
2. Use all weight-bearing structures of the foot.
3. Allow for hoof expansion.
4. Decrease the work of moving the foot.

Shoeing is most effective when correction is made within the first 10 months of lameness, up to 96% success. This is in contrast to when shoeing changes are not made until after 1 year of lameness, where only 56% of the cases have been treated successfully.[49] The importance of a balanced foot in the treatment of equine lameness is well recognized. However, the assessment and choice of options for correction of an imbalanced foot can be quite subjective. Balance is defined as the harmonious adjustment of parts. For the hoof, balance has been defined as the equal distribution of weight, over the foot. This must be more precisely defined as equal medial to lateral distribution of weight, because more weight is normally placed on the caudal half of the foot. Caudal to cranial imbalance has been defined as deviation in the hoof alignment or as problems with heel support.

Six hoof balance abnormalities have been described: broken hoof axis, underrun heels, contracted heels, shear heels, mismatched hoof angles, and small feet. A broken hoof axis exists when the slopes of the pastern and hoof are not the same. This condition is further defined as broken-back, when the hoof angle is lower than the pastern angle, and as broken-forward when the hoof angle is steeper than the pastern angle. Underrun heels have been defined as angle of the heels of 5° less than the toe angle. Contracted heels were defined as frog width less than 67% of the frog length. Sheared heels have been defined as a disparity between the medial and lateral heel lengths of 0.5 cm or more. Small feet (small feet to body size) was defined as a weight to hoof area ratio of greater than 78 pounds per square inch. Quantification of hoof balance has been previously described in this chapter.

One of the most difficult parameters to assess is the hoof's ability to expand. Expansion of the foot is necessary for optimal concussion protection. Protection from concussion also depends on an elastic frog/digital cushion and pliable collateral cartilages.[50] Applied clinical studies have shown that the frog size influences hoof expansion. A frog in contact with the shoe or ground surface provides more hoof expansion than a frog that has no contact.[51] Identification of a narrow, recessed frog should alert the clinician that steps need to be taken to promote hoof expansion. These may vary from simply ensuring proper heel support to encouraging hoof expansion through the use of swedged or slipper heels on the shoes.

As previously discussed, shoeing parameters must be individualized for each horse. However, in most horses with

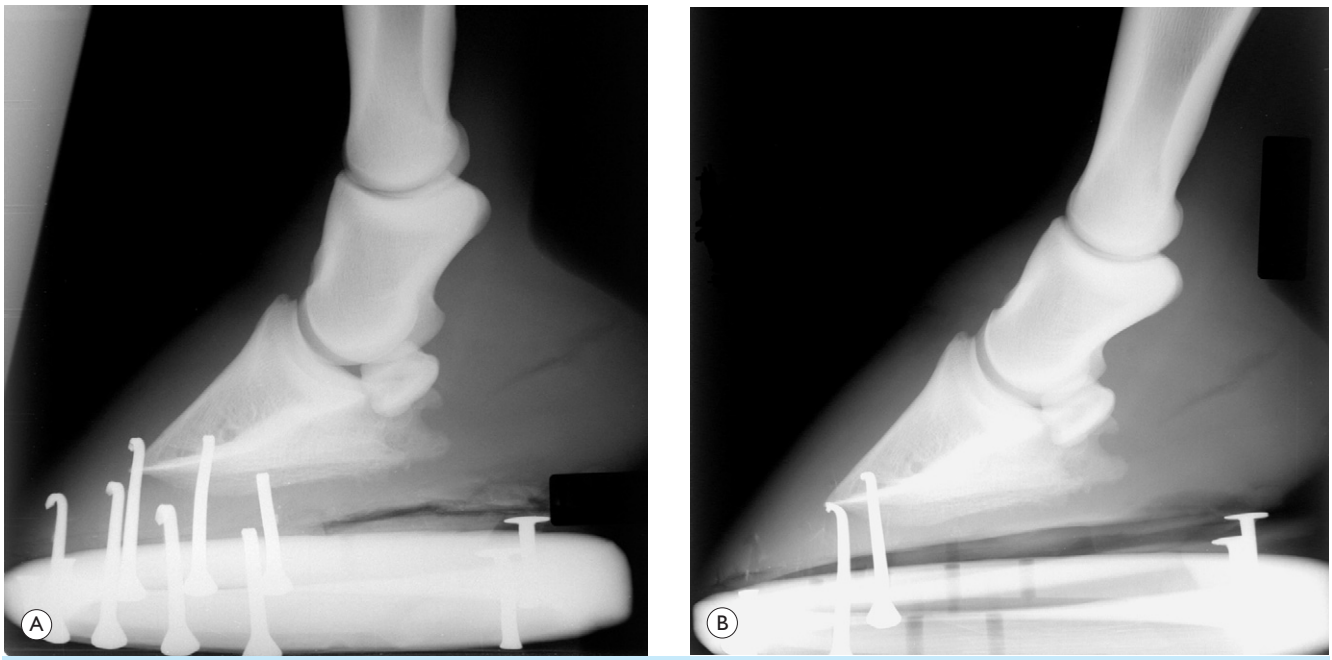


Fig. 15.15
Lateromedial radiographic projections of the distal limb. (A) Marked broken-back hoof pastern axis prior to shoe reset and trimming. This conformation results in excessive strain on the palmar aspect of the foot. (B) Improved hoof–pastern axis following trimming and placement of a larger heel wedge pad.

Fig. 15.16
Palmar view of a foot shod with an egg bar shoe. The sole is filled with resilient polyurethane packing material that provides further concussion protection and distributes weight over a larger surface area.

heel pain the following changes are made in most instances. Trim and balance the feet to eliminate hoof/pastern axis abnormalities, and underrun heels. Lateromedial radiographs may be used to determine hoof/pastern axis and to assess improvement of the axis following shoeing (Fig. 15.15). Shoe to raise the heels 2–3°, ease the breakover by rolling the toe, and provide heel support for horses with underrun heels. Decrease concussion to the foot by providing more surface area of contact (wide-web) or padding. Horses with contracted heels may benefit from shoes that encourage heel expansion during weight bearing, such as swedged heel shoes (outside rim of shoe at the heels is slightly lower than the inside rim: during weight bearing the hoof is encouraged to 'slide out'), or shoes that are not nailed caudal to the quarters. These practices will decrease stress on the DDFT and pressure of the DDFT over the navicular bone. Effective shoe types include wide-web aluminum shoes (more concussion protection than steel, less weight on distal limb), egg bar shoes (provide heel support), and 'Sneakers' (the widest-web available, with a polyurethane contact surface that provides the best concussion protection). Egg bar shoes may be filled in with resilient sole packing material to increase the surface area of weight bearing and provide further concussion protection (Fig. 15.16).

Inflammation is reduced by systemic administration of phenylbutazone (4.4–6.6 mg/kg daily) for 30 days. The DIP joint may also be medicated with triamcinolone (6 mg) and hyaluronic acid (HA; 20–40 mg). The intra-articular medication will treat coffin joint arthrosis directly, and also diffuse to navicular structures. Treatment with HA or PSGAGs is usually continued by intramuscular or intravenous routes.

Isoxsuprine HCl has also been used to treat navicular disease. It is a peripheral vasodilating agent that has been shown to improve lameness of horses with navicular syndrome.[52] The drug also may have anti-inflammatory and rheological properties that contribute to its efficacy. Treatment is continued initially for 6 weeks, if no effect is noted, discontinue its use. If a beneficial response is found treatment

may continue at once daily dosing. The drug is administered orally at 0.6–1.2 mg/kg q 12 h.

Two surgical options for treatment of navicular syndrome and palmar heel pain exist: navicular suspensory desmotomy and neurectomy. Desmotomy is indicated in horses not responding to medication and shoeing over a minimum of 20 to 30 weeks. The desmotomy procedure involves transecting the ligaments near their origin on the distal abaxial aspect of the proximal phalanx at the level of the proximal interphalangeal joint. Results may be due to reduced mechanical loading of the navicular bone associated with a slight shift in its position relative to the DDFT. There are virtually no adverse sequelae to the procedure. Horses are hand walked for 4 weeks after surgery and a gradual improvement starts in about 6 to 8 weeks. Seventy-six percent of horses treated with this technique were sound 6 months following surgery, with 43% sound at 36 months. Horses that were lame less than 10 months at the time of surgery were more likely to be sound than horses that were lame longer than 18 months.[53]

Neurectomy is the last option for treatment. Expect complications in 30% of the horses following neurectomy including incomplete denervation, regrowth of nerves, neuroma formation, unrecognized injury/abscess at desensitized heels.[54] In a follow-up study of neurectomy, 74% of horses were sound 1 year after surgery with 63% sound 2 years after the procedure.[54]

Prognosis Shoeing alone is a very effective method to treat heel pain and navicular syndrome. When correction is made within the first 10 months of lameness, up to 96% of horses are successfully treated. This is in contrast to when shoeing changes are not made until after 1 year of lameness, where only 56% of the cases have been successfully treated.[49] Addition of medications such as phenylbutazone and isoxsuprine improve the opportunity for soundness of horses with palmar foot pain.

Etiology and pathophysiology

Etiology There are numerous causes of pain in the palmar aspect of the foot of the horse. These causes can be divided arbitrarily into conditions of the hoof wall and horn-producing tissues, conditions of the third phalanx, and conditions of the podotrochlear region. Hoof problems would include hoof wall defects, such as cracks or clefts that involve the sensitive tissue; any laminar tearing, separation or inflammation; contusions of the hoof causing bruising or corn formation; abscess formation; and pododermatitis (thrush or canker). Third phalanx lamenesses blocked out by a palmar digital anesthesia would include wing fractures, marginal fractures, solar fractures, or deep digital flexor insertional tenopathy. Conditions of the podotroclear region have been reported to include distal interphalangeal synovitis, deep digital flexor tendonitis, desmitis of the impar (distal navicular ligament) or collateral sesamoidean ligaments, navicular osteitis or osteopathy, and vascular disease. The common denominator of all these conditions is that they are characterized by pain that can be localized to the palmar aspect of the hoof.

Pathophysiology Local vascular disturbances and biomechanical stresses constitute the two major hypotheses for the pathogenesis of navicular syndrome. Colles believed that thrombosis of arterioles supplying the navicular bone and consequent ischemia led to degeneration of the bone, increased size of the so-called 'vascular channels' of the distal border and the pain.[55] Agents that promoted blood flow to the distal limb such as heparin and warfarin were used successfully to treat navicular lameness based on this hypothesis, but this hypothesis has never been proven.

A unifying hypothesis for the cause of navicular disease which is based on pathologic findings has been promoted by Pool et al.[56] Changes associated with navicular syndrome are thought to be similar to degenerative joint disease found elsewhere in the horse. Repeated excessive biomechanical stresses on the flexor surface of the navicular bone result in fibrocartilage degeneration. Decreased shock absorption by the cartilage results in subchondral bone sclerosis. Defects in the cartilage may fill with granulation tissue, which can lead to adhesions between the navicular bone and DDFT. Inflammation associated with these degenerative changes causes excessive bone resorption, especially around synovial tissue attachments and may result in the increased synovial fossae of the distal border and medullary cysts seen on radiographic examinations.

Predisposing factors for lameness of the palmar heel region include faulty conformation such as long toe/ underrun heel, long sloping pastern, and small foot for large body mass. Horses used for jumping, or which are used frequently on hard footing, are also predisposed to this lameness.

Miscellaneous diseases of the distal limb

Underrun heels

Underrun heels have been defined as occurring when the angle at the heels is 5° less than the toe angle. Underrun heels are the most commonly encountered hoof abnormality (see Fig. 15.1). If left uncorrected, underrun heels can cause alterations in hoof-wall growth that can be very difficult to correct and it can predispose to lameness problems that range from bruised heels to navicular syndrome. In dealing with underrun heels it is important to assess several factors. The first is palmar hoof support. This is most easily assessed by radiography and observing where the heel ground contact is relative to the widest part of the hoof and relative to the navicular bone. It is generally accepted that at least half of the weight-bearing area of the foot should be palmar to the widest part of the foot. If this is not the case, the second assessment is of the orientation of the horn tubules in the heel region. With long-term hoof imbalance these tubules grow more horizontally. The proper position of the heels can be determined by either drawing a bisecting line through the metacarpus to the ground or by measuring the appropriate position on the radiograph. Where these lines contact the ground is the point where the heels should be. From a practical point, the heel–ground contact should be even with the base of the frog. Shoeing to achieve adequate heel support

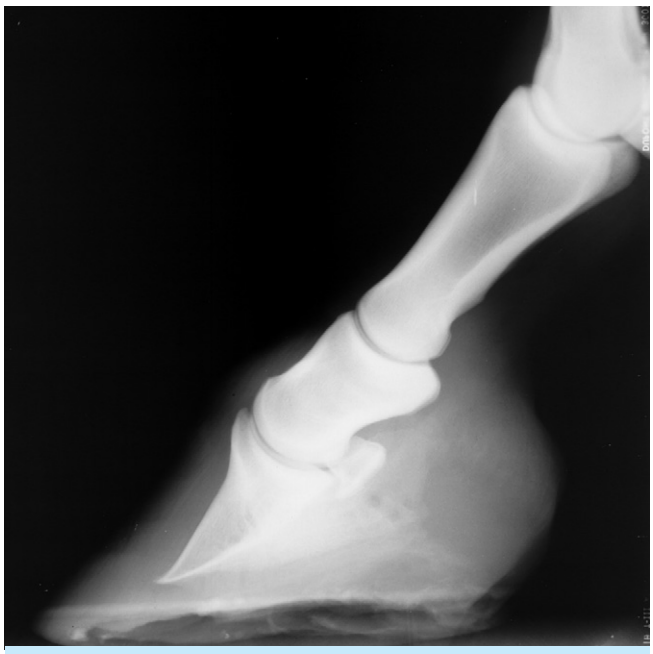


Fig. 15.17
Lateromedial radiographic projection of the distal limb with broken forward hoof pastern axis. This axis deviation is likely caused by flexural contraction of the deep digital flexor tendon.

can frequently restore the foot health. In some cases, however, it requires rebuilding the heels with acrylics or urethanes and altering the stresses on the coronary band to get the heel growth to improve. Some cases if uncorrected for too long, simply cannot be corrected.

Upright hoof

The upright or 'club' hoof is another frequently encountered problem. Most veterinarians consider this to be a problem when the hoof angle exceeds 60° (see Fig. 15.2). However, a more important consideration is the hoof–pastern axis. This axis should form a straight line when the horse is standing square. When the pastern angle is less than the hoof angle, this causes a 'broken forward' hoof axis (Fig. 15.17). The problem with this conformation is that in order to correct it, the hoof angle must be decreased. However, if the difference is more than 5° the deep flexor tendon will not allow further correction.

This can lead to several problems, such as hoof capsule separation, toe bruising, and coffin joint inflammation. A number of correction possibilities exists. In horses less than 2 years of age, extensions are placed on the toe either by shoeing or the application of acrylics or urethanes. This will cause stretching of the deep flexor tendon and muscle and slowly allow the hoof to assume a normal conformation. A problem with this method is that the stretching can actually lead to tendon injury and in some cases cause the problem to become worse.

A unique approach that has merit especially in acute cases is the use of heel wedges and rest. Raising the heel reduces deep flexor tendon stress and rest will allow the flexor muscle and tendon to relax. Wedges are continued for approximately 2 weeks. The hoof may then be trimmed or shod in a normal position. If shoeing fails to correct the axis deviation correction of this problem can always be made by inferior check (accessory ligament of the DDFT) desmotomy. Transection of the check ligament permits elongation of the flexor tendon/muscle unit. Application of a corrective shoe or acrylic toe extension is usually performed at the time of surgery. Correction of the hoof abnormality is critical to the success of club-foot confirmation due to flexor tendon contracture.

Distal interphalangeal (coffin) joint arthrosis

Distal interphalangeal (DIP) joint arthrosis is a lameness referable to the distal limb and localized to the distal interphalangeal joint with no evident radiographic abnormalities. This lameness is commonly found in many performance horses, particularly racing Quarter Horses, polo ponies, and horses that compete over fences. Horses that respond to DIP joint anesthesia should be treated for inflammation of that joint. Treatment may include parenteral NSAID therapy but intra-articular therapy or specific joint therapy should be considered. Hyaluronan and corticosteroids are commonly injected within the DIP joint for treatment.

Occasionally, horses affected with DIP joint arthrosis also have a chronic broken forward hoof–pastern axis. Many of these cases appear to be mild flexural deformities. Because of the malarticulation of the second and distal phalanges, the joint may remain inflamed despite therapy. In these cases, inferior check desmotomy to allow correction of the broken forward axis has been a very useful method to correct the hoof–pastern axis.

Keratoma

Keratoma is a rare benign tumor produced by the keratin-producing cells of the coronary band. The tumor becomes a space-occupying mass that causes pressure necrosis of the soft tissues and distal phalanx resulting in lameness, and may cause drainage from the white line or coronary band. Differential diagnoses include distal phalanx fracture, deep sole abscess, 'gravel', or corn. The diagnosis is suggested by radiographs that show smooth, circumscribed lysis of the distal phalanx. Treatment is excision via an approach through the hoof wall or sole. The mass is reminiscent of an onion: it has many layers that must be peeled away.

Collateral cartilage: side bone, quittor

Side bone is normal mineralization of the collateral cartilages and occurs in most adult horses. Mineralization may be accelerated by local trauma and is more prevalent in draft horses. Lameness is rarely associated with side bone but excessive mineralization could interfere with expansion of the heels during weight bearing.

Quittor is infection and necrosis of the collateral cartilages, usually due to trauma. The horse has localized pain and swelling at the coronary band region of the heels and may have a draining tract. Treatment is excision of the affected cartilage.

Thrush

Thrush is a degenerative condition of the frog and sulci due to excessive moisture, poor hoof hygiene, or filthy stabling conditions. It is characterized by a dark gray or black discharge around the frog, and poor-quality frog tissue. *Fusobacterium necrophorum* is frequently isolated from thrush-affected feet. Treatment consists of paring away affected tissue, cleaning the environment and providing dry bedding, and application of astringents. Simple cases respond well to daily application of povidone–iodine but formalin, phenol, strong tincture iodine, and copper sulfate have also been used alone or in varying combinations. One simple caveat: do not use Kopertox®, a liquid over-the-counter preparation consisting of copper napthanate. The liquid results in a gummy, sealed sole that traps moisture within the foot and results in accumulation of stall debris to its sticky surface.

Canker

Canker is an uncommonly encountered chronic proliferation of the keratinized tissues of the sole and/or frog and is usually associated with poor foot hygiene (Fig. 15.18). Canker may initially appear similar to proliferative granulation tissue but the tissue usually becomes white in color, bleeds easily on manipulation, and has a bad odor. Purulent exudate is often admixed with the tissue. Lameness is usually present because the proliferative tissue is very sensitive. Differential diagnosis includes severe thrush, large 'corns', and extensive underrun sole abscess.

Treatment is difficult and involves debridement of the proliferative tissue, cleaning the foot surfaces and application of topical antibiotics and astringents. The proliferative tissue may be removed with electrocautery, laser, or with cryosurgery. Astringents such as 5% picric acid or 10% neutral buffered formalin solution may be applied to the tissue. Debridement of the tissue is gradually made manually or by applying a saturated solution of benzoyl peroxide dissolved in acetone daily until the excessive keratinized tissue is all debrided. Metronidazole tablets ground into a powder and applied to the tissues are effective at controlling the bacterial infection. Prognosis for successful treatment is always guarded.

Fig. 15.18
Palmar view of a foot with severe canker affecting the frog. The white tissue now comprising the frog is very friable and bleeds easily. The horse is lame because the tissue is very sensitive to pressure.

Corns

Corns are usually found in the front feet at the angle formed by the hoof wall and bars. Shoes left on too long or shoes that overlap the bars and frog too much and irritate these tissues are implicated in the formation of corns. Corns may be dry, moist or suppurating. The tissue often appears similar to proliferative granulation tissue, but is usually only found in a localized area at the heels. The tissue is usually quite sensitive to palpation.

Treatment is similar to that used for canker, but usually does not require extensive tissue debridement.

Sole bruise

Sole bruises occur when vessels in the solar corium are traumatized and bleed. The hemorrhage is trapped with the solar tissues and causes varying degrees of lameness. Bruises are evident as discoloration of the affected sole that is painful to hoof tester application. Occasionally bruises will become contaminated and develop into a subsolar abscess.

Poor-fitting shoes, thin soles, and riding on hard terrain all are potential factors that contribute to solar bruising. Initial treatment is administration of NSAIDs, poulticing of the foot and removal of any inciting cause. Poor fitting or loose shoes should be removed. When the initial discomfort resolves the shoe should be reset. A full pad should also be used for feet with extensive bruising.

References

1. Moyer W. Clinical examination of the equine foot. Vet Clin N Am Equine Pract 1989; 5(1):29–46.
2. Balch O, White KK, Butler D. Factors involved in the balancing of equine hooves. J Am Vet Med Assoc 1991; 198(7):1980–1989.

3. Turner TA. The art and frustration of hoof balance. Am Farriers J 2002; 28(6):1A–8A.
4. Turner TA. The use of hoof measurements for the objective assessment of hoof balance. Proc Am Assoc Equine Pract 1992; 38:157–164.
5. Turner TA. Predictive value of diagnostic tests for navicular pain. Proc Am Assoc Equine Pract 1996; 42:201–204.
6. Turner TA. Intra-articular and regional anesthesia of the forelimb. Proceedings 10th Annual ACVS Symposium, 2000:255–257.
7. Butler JA, Colles CM, Dyson SJ, et al. Clinical radiology of the horse. London: Blackwell Scientific; 1993:25–99.
8. Turner TA. Use of navicular bursography in 97 horses. Proc Am Assoc Equine Pract 1998; 44:227–229.
9. Sage AM, Turner TA. Ultrasonography of the soft tissues of the equine foot. Eq Vet Educ 2002; 4:278–283.
10. Turner TA, Fessler JF, Lamp M, et al. Thermographic evaluation of horses with podotrochlosis. Am J Vet Res 1983; 44(4):535–539.
11. Wright IM, Phillips TJ, Walmsley JP. Endoscopy of the navicular bursa: a new technique for treatment of contaminated and septic bursae. Equine Vet J 1999; 31:5–11.
12. Richardson GL, O'Brien TR, Pascoe JR, et al. Puncture wounds of the navicular bursa in 38 horses: a retrospective study. Vet Surg 1986; 15:156–160.
13. Baxter GM. Acute laminitis. Vet Clin N Am Equine Pract 1994; 10(3):627–642.
14. Hunt RJ. A retrospective evaluation of laminitis. Equine Vet J 1993; 25:61–64.
15. Longland A, Cairns A. Sugars in grass – an overview of sucrose and fructan accumulation in temperate grasses. Proceedings, Dodson and Horrell International Research Conference on Laminitis, Stoneleigh, Warwickshire, England, 1998:1–3.
16. Peloso JG, Cohen ND, Walker MA, Watkins JP. Case-control study of risk factors for development of laminitis in the contralateral limb in Equidae with unilateral lameness. J Am Vet Med Assoc 1996; 209:1746–1748.
17. McCue PM. Equine Cushing's disease.Vet Clin N Am Equine Pract 2002; 18(3):533–543.
18. Obel N. Studies on the histopathology of acute laminitis. Uppsala, Sweden: Almqvist and Wiksells Boktryckteri AK, 1948.
19. Linford RL, O'Brien TR, Trout DR. Qualitative and morphometric radiographic findings in the distal phalanx and digital soft tissues of sound Thoroughbred racehorses. Am J Vet Res 1993; 54:38–51.
20. Stick JS, Jann HW, Scott EA, et al. Pedal bone rotation as a prognostic sign in laminitic horses. J Am Vet Med Assoc 1982; 180:251–253.
21. Hunt RJ. Diagnosing and treating chronic laminitis in horses. Vet Med 1996; 91:1025–1032.
22. Semrad SD, Hardee GE, Hardee MM, Moore JN. Low dose flunixin meglumine: effects on eicosanoid production and clinical signs induced by experimental endotoxemia in horses. Equine Vet J 1987; 19:201–206.
23. Blythe LL, Craig AM, Christensen JM, et al. Pharmacokinetic disposition of dimethyl sulfoxide administered intravenously to horses. Am J Vet Med Assoc 1986; 47:1739–1743.
24. Adair HS, Goble DO, Shires GM, Sanders WL. Evaluation of laser Doppler flowmetry for measuring coronary band and laminar microcirculatory blood flow in clinically normal horses. Am J Vet Res 1994; 55:445–449.
25. Deumer J, deHaan F, Tulp MTM, et al. Effect of an isoxsuprine-resin preparation on blood flow in the equine thoracic limb. Vet Rec 1991; 129:427–429.
26. Cohen ND, Parson EM, Seahorn TL, et al. Prevalence and factors associated with laminitic horses with duodenitis/proximal jejunitis: 116 cases (1985–1991). J Am Vet Med Assoc 1994; 204:250–254.
27. Redden RF. 18° elevation of the heel as an aid to treating acute and chronic laminitis in the equine. Proc Am Assoc Equine Pract 1992; 37:375–379.
28. Hunt RJ, Allen D, Baxter GM, et al. Mid-metacarpal deep digital flexor tenotomy in the management of refractory laminitis in horses. Vet Surg 1991; 20:15–20.
29. Cripps PJ, Eustace RA. Factors involved in the prognosis of equine laminitis in the UK. Equine Vet J 1999; 31(5):433–442.
30. Pollitt CC, Davies CT. Equine laminitis: its development coincides with increased sublamellar blood flow. Equine Vet J (Suppl.) 1998; 26:125–132.
31. Trout DR, Hornof WJ, Linford RL, O'Brien TR. Scintigraphic evaluation of digital circulation during the developmental and acute phases of equine laminitis. Equine Vet J 1990; 22(6):416–421.
32. Pollitt CC. Equine laminitis: a revised pathophysiology. Proc Am Assoc Equine Pract 1999; 45:188–192.
33. Molyneux GS, Haller CJ, Mogg K, Pollitt CC. The structure, innervation and location of arteriovenous anastomoses in the equine foot. Equine Vet J 1994; 26(4):305–312.
34. Katwa LC, Johnson PJ, Ganjam VK, et al. Expression of endothelin in equine laminitis. Equine Vet J 1999; 31(3):243–247.
35. Honnas CM, O'Brien TR, Linford RL. Distal phalanx fractures in horses: a survey of 274 horses with radiographic assessment of healing in 36 horses. Vet Radiol 1988; 29:98–100.
36. Honnas CM, O'Brien TR, Linford RL. Solar margin fractures of the equine distal phalanx. Proc Am Assoc Equine Pract 1987; 33:399–410.
37. Yovich JV. Fractures of the distal phalanx in the horse. Vet Clin N Am Equine Pract 1989; 5(1):145–160.
38. Kaneps AJ, O'Brien TR, Redden RF, et al. Characterisation of osseous bodies of the distal phalanx of foals. Equine Vet J 1993; 25:285–292.
39. Kaneps AJ, O'Brien TR, Willits NH, et al. Effect of hoof trimming on the occurrence of distal phalangeal palmar process fractures in foals. Equine Vet J (Suppl.) 1998; 26:36–45.
40. Yovich JV, Stashak TS, DeBowes RM, Ducharme NG. Fractures of the distal phalanx of the forelimb in eight foals. J Am Vet Med Assoc 1986; 189(5):550–554.
41. Lillich JD, Ruggles AJ, Gabel AA, et al. Fracture of the distal sesamoid bone in horses: 17 cases (1982–1992). J Am Vet Med Assoc 1995; 207:924–927.
42. Turner TA. How to treat navicular bone fractures. Proc Am Assoc Equine Pract 1997; 43:370–371.
43. Turner TA. Predictive value of diagnostic tests for navicular pain. Proc Am Assoc Equine Pract 1996; 42:201–204.
44. Wright IM. A study of 118 cases of navicular disease: clinical features. Equine Vet J 1993; 25:488–492.
45. Dyson SJ, Kidd L. A comparison of responses to analgesia of the navicular bursa and intra-articular analgesia of the distal interphalangeal joint in 59 horses. Equine Vet J 1993; 25:93–98.
46. Bowker RM, Linder K, VanWulfen KK et al. Distribution of local anesthetic injected into the distal interphalangeal joint and podotrochlear bursa: an experimental study. Pferdeheilkunde 1996; 12:609–612.
47. Van Wulfen KK, Bowker RM. Evaluation of tachykinins and their receptors to determine sensory innervation in the dorsal

hoof wall and insertion of the distal sesamoidean impar ligament and deep digital flexor tendon on the distal phalanx in healthy feet of horses. Am J Vet Res 2002; 63(2):222–228.
48. Bowker RM, Linder K, Van Wulfen KK, Sonea IM. Anatomy of the distal interphalangeal joint of the mature horse: relationships with navicular suspensory ligaments, sensory nerves and neurovascular bundle. Equine Vet J 1997; 29(2):126–135.
49. Turner TA. Diagnosis and treatment of navicular disease in horses. Vet Clin N Am Equine Pract 1989; 5:131–143.
50. Bowker RM, Van Wulfen KK, Springer SE, Linder KE. Functional anatomy of the cartilage of the distal phalanx and digital cushion in the equine foot and a hemodynamic flow hypothesis of energy dissipation. Am J Vet Res 1998; 59(8):961–968.
51. Roepstorff L, Johnston C, Drevemo S. In vivo and in vitro heel expansion in relation to shoeing and frog pressure. Equine Vet J (Suppl.) 2001; 33:54–57.
52. Turner AS, Tucker CM. The evaluation of isoxsuprine hydrochloride for treatment of navicular disease: a double-blind study. Equine Vet J 1989; 21:338–341.
53. Wright IM. A study of 118 cases of navicular disease: treatment by navicular suspensory desmotomy. Equine Vet J 1993; 25:501–509.
54. Jackman BR, Baxter GM, Doran RF, et al. Palmar digital neurectomy in horses: 57 cases 1984–1990. Vet Surg 1993; 22:285–288.
55. Coles CM, Hickman J. The arterial supply of the navicular bone and its variations in navicular disease. Equine Vet J 1977; 9:150–154.
56. Pool RR, Meagher DM, Stover SM. Pathophysiology of navicular disease. Vet Clin N Am Equine Pract 1989; 5:109–129.

CHAPTER 16

Distal limb: fetlock and pastern

Alicia L. Bertone

The fetlock joint is a rotary joint that can exhibit the greatest range of motion of any equine joint, ranging from 120° of extension to 120° of flexion, particularly during athletic events such as racing or jumping (Fig. 16.1). This high degree of activity makes this joint particularly susceptible to exercise-induced wear and indeed, the fetlocks are commonly associated with injury and signs of degenerative joint disease. The pastern joint, by contrast, is a low range of motion joint exhibiting ~30° range of motion in the normal horse (Fig. 16.2). The pastern is less frequently afflicted with injury or degenerative wear than the fetlock, although its location just above the hoof and at the termination of the suspensory apparatus makes it vulnerable to high-impact, traumatic injury. Degenerative joint disease (high ringbone) frequently follows pastern joint injury. The combination of high-impact loading during sport performance and the distal location of these joints puts them at higher risk for fractures and breakdown.

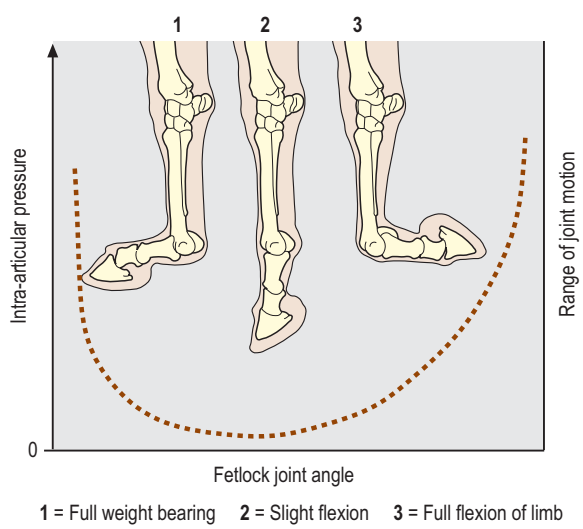


Fig. 16.1
The wide range of joint motion and intra-articular pressures associated with the fetlock joint.

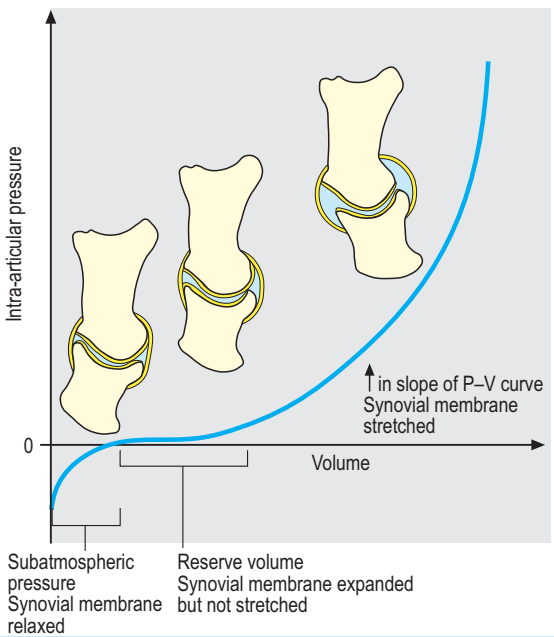


Fig. 16.2
The low range of joint motion and intra-articular pressures associated with the pastern joint.

Fractures of the fetlock joint

- Signs include acute lameness that often resolves in days, joint effusion and pain on flexion.
- Radiography confirms the diagnosis.
- Treatment is arthroscopic removal or internal fixation based on size and location of fragment.

Osteochondral (chip) fractures

Recognition

History and presenting complaint Most articular chip fractures of the fetlock are of the eminences of the proximal

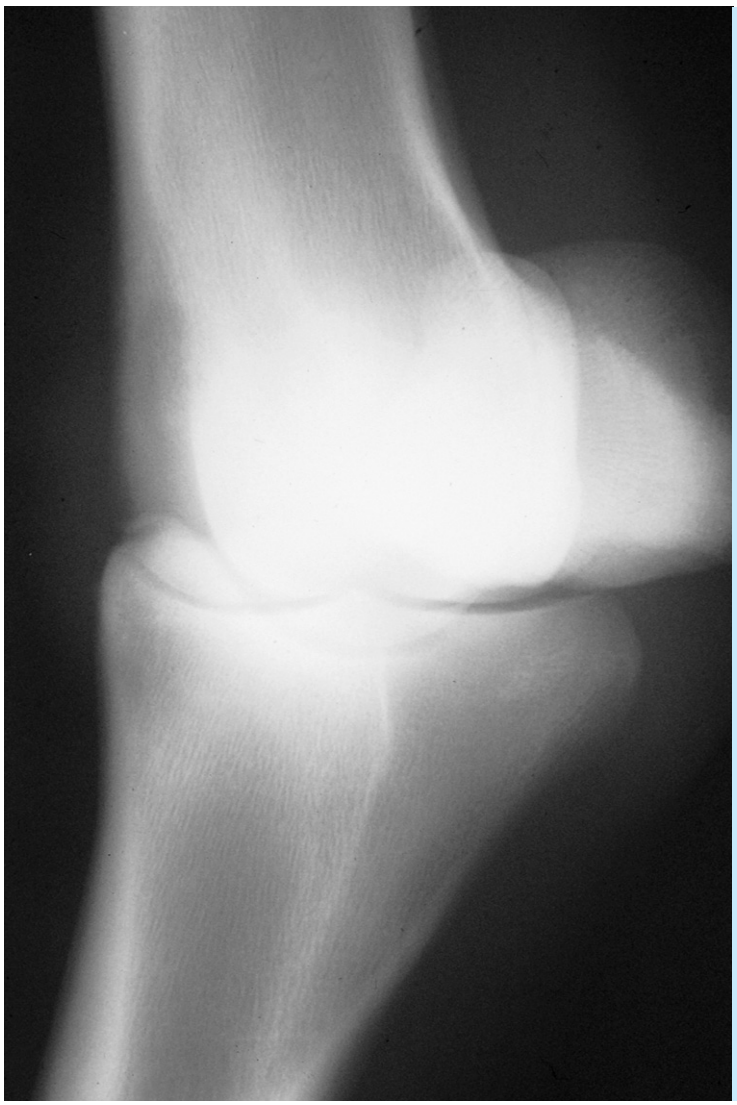


Fig. 16.3
Dorsolateral to palmaromedial oblique radiograph of the fetlock joint demonstrating a typical dorsomedial eminence first phalanx osteochondral 'chip' fracture.

phalanx (P1) and are relatively common in the forelimb of the horse, particularly the sport horse (Fig. 16.3). In race horses, the left forelimb and medial eminence are affected more often. Other less frequently occurring fractures of the fetlock include fractures of the palmar/plantar eminences which, if articular and small, can be successfully removed arthroscopically with a good prognosis (~ 70%) for return to performance. These fractures, however, may be associated with subluxation of the fetlock joint and/or disruption of a palmar/plantar osteochondrosis lesion.[1–3] Careful evaluation of the joint is indicated to identify this more complex injury which can include injury to the collateral ligaments and distal sesmoidean ligaments.

Palmar/plantar fractures of the proximal phalanx are uncommon and should not be confused with osteochondral fragmentation of this site in young growing horses.[3] Developmental osteochondral fragmentation of the caudal eminences of the proximal phalanx occurs in ~5% of Standardbreds and Thoroughbreds without clinical signs in most horses. Clinical signs can occur as a high-performance lameness in which case fragments can be arthroscopically removed. True fractures of the caudal eminences of the proximal phalanx usually cause lameness and soreness to direct pressure over the eminence. Developmental osteochondral fragmentation in this location should not induce pain to pressure.

Physical examination Horses that sustain fetlock chip fractures develop clinical signs within hours after the injury. Clinical signs include fetlock joint effusion, pain on fetlock flexion and lameness at the trot. Soreness resolves within weeks with stall rest and anti-inflammatory medication. Chronic chip fractures are usually associated with generalized fetlock joint disease and may have capsular fibrosis, dorsal enlargement and reduced range of joint motion. Joint effusion, however, may or may not be present. Lameness may resolve with rest and return with athletic use.

Special examination In chronic fractures of unknown contribution to a lameness, direct intra-articular fetlock anesthesia may be indicated to localize the soreness to the intra-articular structures. Resolution of the lameness with a fetlock block would support arthroscopic exploration and fragment removal.

Diagnostic confirmation Diagnosis is confirmed with radiography, to include four views of the affected fetlock joint and the contralateral fetlock if surgery is to be considered. Osteochondral fragments are readily visible on the oblique radiographic views (see Fig. 16.3).

Nuclear scintigraphy can be used to distinguish fractures from incidental caudal eminence fragments.

Treatment and prognosis

Therapeutic aims Osteochondral fragments are removed, usually with arthroscopy, to decrease painful synovitis and to prevent further degenerative joint disease.

Therapy In horses with continued athletic expectations, acute fractures are preferably removed arthroscopically unless they are completely non-displaced. In non-displaced fractures a follow-up radiograph at 30 days is indicated as many of these fragments go on to displace and result in a non-union. In chronic chip fractures, other lesions commonly seen include proliferative synovitis of the dorsal metacarpal synovial pad (32% of which have chip fracture) and cartilage erosion of the metacarpal condyle.[4] Two to four months' rest is recommended before training is resumed depending on the degree of joint damage and cartilage debridement.

Fractures that continue to be a source of pain or are large enough to secure with a bone screw can be treated surgically. Injury to the collateral ligaments in conjunction with palmar/plantar fractures of the proximal phalanx should be supported by cast or support boot for 4–8 weeks to minimize joint laxity and osteoarthritis. Reconstruction of the ligament has been reported but is generally felt not to be necessary to regain use of the joint. Palmar/plantar eminence fracture healing is poor due to distraction by the distal sesmoidean ligament insertions and usually requires 4–6 months' rest.

Prognosis The prognosis for return to athletic performance, including elite performance, is ~80% with arthroscopic surgery to remove fragments. Concomitant injuries to the fetlock lower the prognosis.[5–8]

Etiology and pathogenesis

Etiology Concussion and overextension of the joint, exacerbated by fatigue, are factors in the production of these fractures and suspensory apparatus injury (Fig. 16.4). The overextension causes pinching of the dorsal eminences and dorsal metacarpal synovial pad.

Prevention

Incidence of fracture may be reduced by use of elastic bandages placed over the fetlock in a snug figure-of-eight configuration during hard workouts. The bandage absorbs some of the kinetic energy in the limb, thereby reducing the kinetic energy absorbed by the tissues supporting the fetlock.

Proximal sesamoid bone fractures

- Sesamoid fractures are most common in race horses.
- Apical fractures occur most commonly, followed by basilar and midbody fractures.
- Treatment is excision for fragments less than one-third the size of the entire bone and internal fixation for larger fractures.
- Prognosis may be affected by suspensory branch desmitis.

Fractures of the proximal sesamoid bones are a common fracture of the fetlock joint. Most are articular although non-articular (suspensory avulsion) fractures occur and can be distinguished by lack of joint effusion and firm swelling over the caudal aspect of the bone. Fetlock breakdown, including sesamoid fractures, is the most common fatal fracture in racing Thoroughbreds and Quarter Horses.[9] Sesamoid fractures are categorized as apical, abaxial (articular and

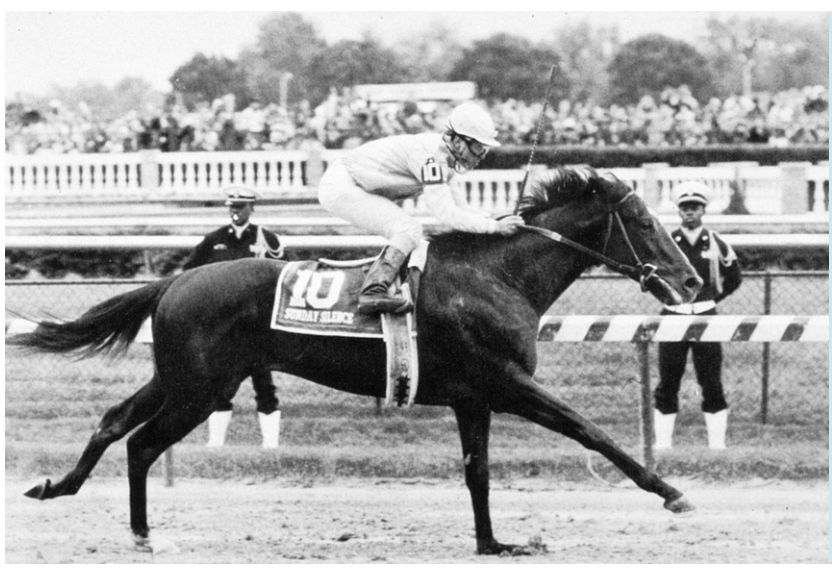


Fig. 16.4
Finish-line photograph demonstrating the extreme dorsiflexion of the fetlock joint at the finish of the race with fatigue and maximal loading.

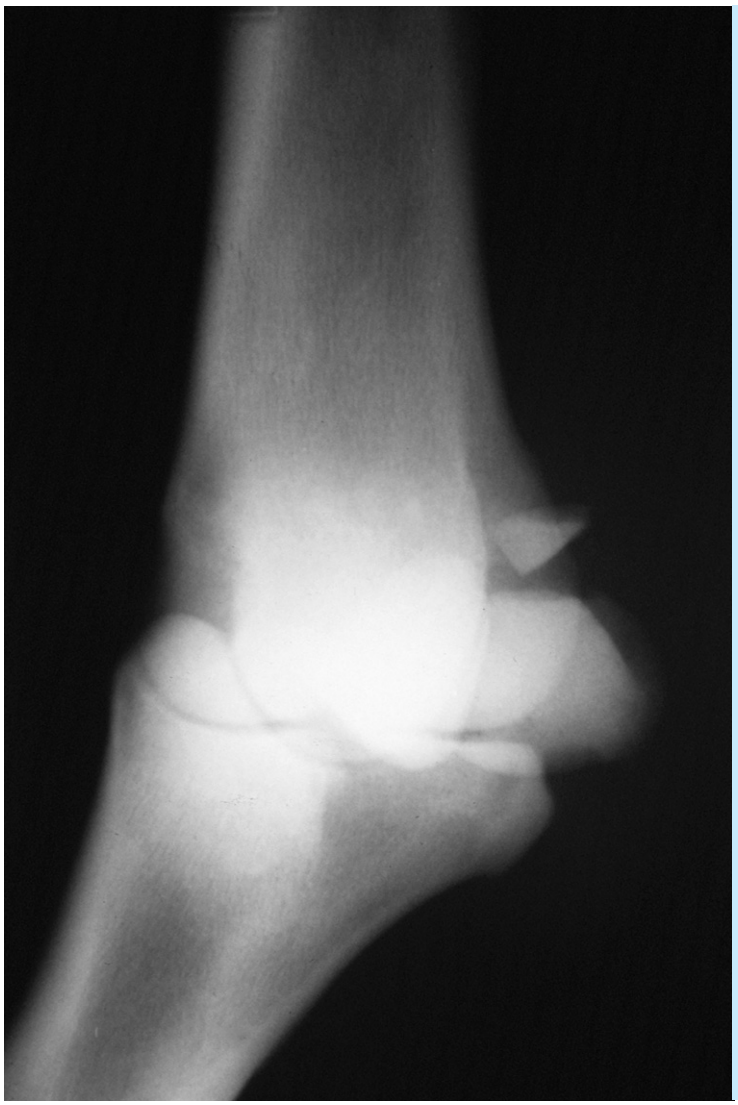


Fig. 16.5
Oblique radiograph of a typical displaced apical sesamoid fracture. Recommended treatment is arthroscopic removal.

non-articular), midbody, basilar (articular and non-articular), sagittal and comminuted.[10]

Sesamoid fractures are most common (53.4%) in 2-year-old and then 3-year-old (23%) race horses. Apical sesamoid fractures are the most common, comprising over 88% of sesamoid fractures with an approximately equal distribution between the right and left limbs (Fig. 16.5). Apical fractures are frequently articular and singular, rarely comminuted and usually involve less than one-third of the bone.

Basilar fractures are more common in the Thoroughbred than the Standardbred, comprise 6% of sesamoid fractures in Standardbreds and represent an avulsion fracture associated with the distal sesamoidean ligaments. Basilar fractures are often comminuted into two pieces through a sagittal separation. These fractures can vary in size, from the smaller, triangular articular pieces to the larger fragments with a significant non-articular component.

Abaxial fractures appear to be more common in Thoroughbreds and Quarter Horses than in Standardbreds (3% of sesamoid fractures).[11,12] These can be difficult to diagnose and may require an additional tangential projection on the radiographic examination to identify their exact location or can be identified on the craniocaudal view.[13] Articular abaxial fractures will have joint effusion.

The midbody transverse fracture is seen most frequently in the Thoroughbred, older Standardbreds (mean age 6.5 years) and in young foals under 2 months of age. Most have a several millimeter gap and are distracted at the caudal surface. Fracture of both sesamoids usually results in complete loss of suspensory support and a 'dropped' fetlock (hyperextended during loading).[10]

Recognition

History and presenting complaint As with other fetlock fractures, horses become lame with joint effusion within hours of injury. Non-articular sesamoid fractures may not have joint effusion and swelling may be directly over the abaxial surface of the sesamoid.

Physical examination Clinical signs include lameness which is very pronounced in acute stages. Associated suspensory desmitis may confuse the diagnosis if radiographs are not taken. The horse evidences pain when pressure is applied to the affected bone. After 1–2 weeks' rest, lameness at the walk and trot may not be obvious but joint effusion persists.

Diagnostic confirmation Diagnosis is confirmed with radiography (see Fig. 16.5). Non-displaced fractures may be hard to see with plain radiography. The addition of the skyline projection of the abaxial surface of the sesamoid bone may help identify the exact location of fractures on the abaxial surface.[13] Suspicious but unconfirmed fractures should have a repeat radiograph taken after 2–4 weeks of stall rest or nuclear scintigraphy can be performed.

Treatment and prognosis

Therapeutic aims Most fractures should be surgically removed, usually arthroscopically, for the fastest return to athletic function and soundness. Large fractures may be best treated with internal fixation. Stall rest may be satisfactory for incomplete sesamoid bone fractures.

Therapy Preferred treatment for articular sesamoid fractures (apical, basilar or abaxial) of less than one-third of the bone is arthroscopic removal to provide the most rapid return to athletic use and least risk of degenerative joint disease and sesamoid reinjury. Stall rest (with or without soft cast or external coaptation) for 3–4 months may achieve fibrous or partial bony union, but management is prolonged, weakening of the bone is anticipated and continued soreness or refracture can occur due to failure of complete bony union.[12–17] Non-articular fractures can be removed, but conservative treatment is considered to produce similar outcomes and is generally recommended. Midbody transverse fractures affecting the middle third of the proximal sesamoid bones can be treated successfully with lag screw fixation or circumferential wiring to provide postoperative bone compression and immobilization.[13,18–21]

Fractures involving disruption of both sesamoid bones are a common cause of breakdown in speed horses.[9] Many of these horses are humanely euthanized due to compounding of the injury (disruption of the skin) or loss of vascular supply. Horses without an open injury and with immediate support to the limb with a support splint can be salvaged for breeding or retirement. The preferred management is appropriately timed surgical arthrodesis for the fastest return to comfort and to reduce the risk of contralateral laminitis from overloading[22] (see Fetlock luxation below). Fractures of the sesamoid can occur in conjunction with a condylar fracture of the metacarpus or metatarsus. This concomitant injury significantly reduces the prognosis for returning to sport athletics even with repair of the condylar fracture.[23] These sesamoid fractures are usually sagittal and axial from avulsion of the intersesmoidean ligament that occurs when the condylar fracture displaces. The fractures indicate significant soft tissue injury to the fetlock joint and degenerative joint disease is likely to develop.

Prognosis The prognosis for most simple sesamoid fractures ranges from fair to excellent. Eighty-eight percent of Standardbreds with apical fractures,[24] 71% of Thoroughbred or Quarter Horse race horses with abaxial fractures,[12] 50–60% of Thoroughbreds with basilar fractures[14,17] and 50–60% of Standardbreds with midbody fractures repaired by either lag screw fixation or circumferential wiring can return to racing.[18,19] Conservatively managed basilar or midbody fractures are most likely to develop significant degenerative joint disease and restricted range of joint motion. If both sesamoids are fractured, the prognosis is less favorable.

Etiology and pathogenesis

Etiology Sesamoid fractures are a result of excessive forces within the bone, generated by the tension of the suspensory apparatus during loading and occasionally contributed by direct concussion with the ground during fatigue–fetlock 'rundown'[11,13,14,23] (see Fig. 16.4). The forelimbs are most frequently affected in flat racing, whereas the hindlimbs are more frequently affected in Standardbreds. Displaced fractures are common due to the pull of the suspensory ligament proximally and the distal sesamoidean ligaments distally.

Severe blunt trauma to the sesamoid bone can cause highly comminuted fractures. The fetlock can contact the ground in an athletic event or at the time of a uniaxial sesamoid fracture. Fractures caused by 'running down' or interference are most likely to also contain a wound.

Pathophysiology Although the vascular pattern of sesamoid bones may be implicated in site selection of fractures as the orientation and distribution of vessels correspond to the configuration of apical fracture patterns,[25] the sesamoid fracture or the predisposition for sesamoid fracture has not been associated with the presence of sesamoiditis. Sesamoiditis describes a condition of sesamoid pain that demonstrates radiographic lucencies which parallel vascular channels seen radiographically.[25]

Prevention

Protective and support bandages for the fetlock can be worn during hard workouts to help prevent direct injury to the sesamoid and to reduce strain in the suspensory apparatus during loading. Appropriate training can result in strengthening and conditioning of the bone which is important to help prevent sesamoid fractures. Smooth racing surfaces may help prevent missteps.

Longitudinal fractures of the first phalanx

- Fractures may be complete or incomplete.
- Most fractures are treated with internal fixation.
- Some proximal incomplete fractures will heal with stall rest.

The first phalanx is prone to sagittal and, less commonly, frontal plane longitudinal fractures that occur during heavy exercise (Fig. 16.6). Almost all of these fractures are initiated at the articular surface of the fetlock joint and propagate distally.[26] Patterns of propagation for sagittal fractures include

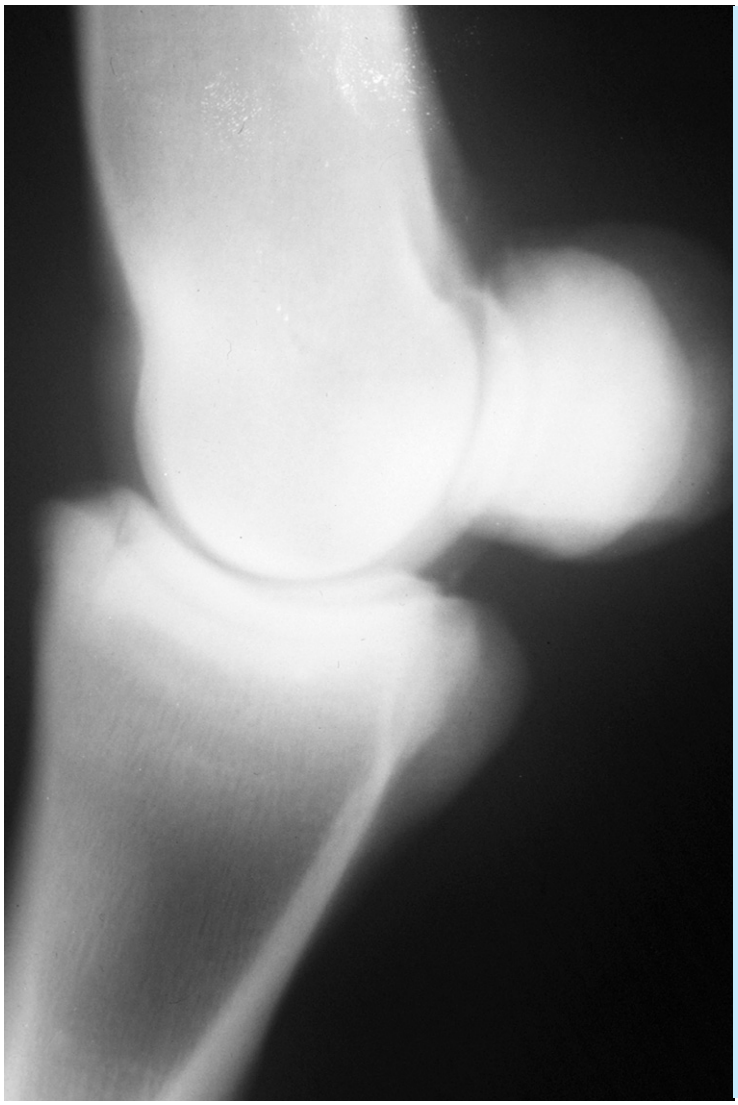


Fig. 16.6
Lateral radiograph of a typical frontal plane dorsal first phalanx fracture.

spiral fractures toward the pastern joint and/or lateral deviation toward the cortex (Fig. 16.7). If fractures extend into the pastern joint or exit the lateral cortex, they are considered complete. Many sagittal fractures are incomplete and propagate distally for varying distances, ranging from < 1 cm (short incomplete) to 5–6 cm (long incomplete) and ending just above the pastern joint.[27,28] Complete fractures can be displaced or non-displaced. Incomplete fractures are non-displaced or minimally displaced. A small proportion of sagittal fractures can also contain frontal plane fractures (Fig. 16.8). If this combination of fractures occurs it is highly predisposed to displacement (comminution) since the sagittal ridge of the metacarpus/tarsus acts as a pile driver upon loading, even with the limb in a cast or splint. Securely positioning the limb vertically on the toe minimizes this effect.

A portion of these fractures will also have a third fracture plane (transverse or coronal) which commonly results in complete instability and displacement of the fragments (comminution). Displaced, comminuted fractures are categorized by the presence or absence of an intact strut of bone from the proximal metacarpal/tarsophalangeal joint to the proximal interphalangeal joint. Prognosis for successful surgical reconstruction is greater if an intact strut of bone is present due to the longitudinal support to prevent collapse and providing a secure anchor for reconstruction of fragments.[26]

Frontal single plane longitudinal fractures can occur in the first phalanx, but are much less common than sagittal fractures (see Fig. 16.6). Clinical signs, treatment and outcome are as for sagittal fractures.[29] If a frontal plane fracture is identified on a lateral radiograph, an additional sagittal plane fracture should be suspected and ruled out.

Recognition

History and presenting complaint Most first phalanx fractures occur at racing speeds and therefore are closely associated with heavy workouts or competitive events. More severe fractures are associated with immediate lameness and rapid swelling (within minutes to hours).

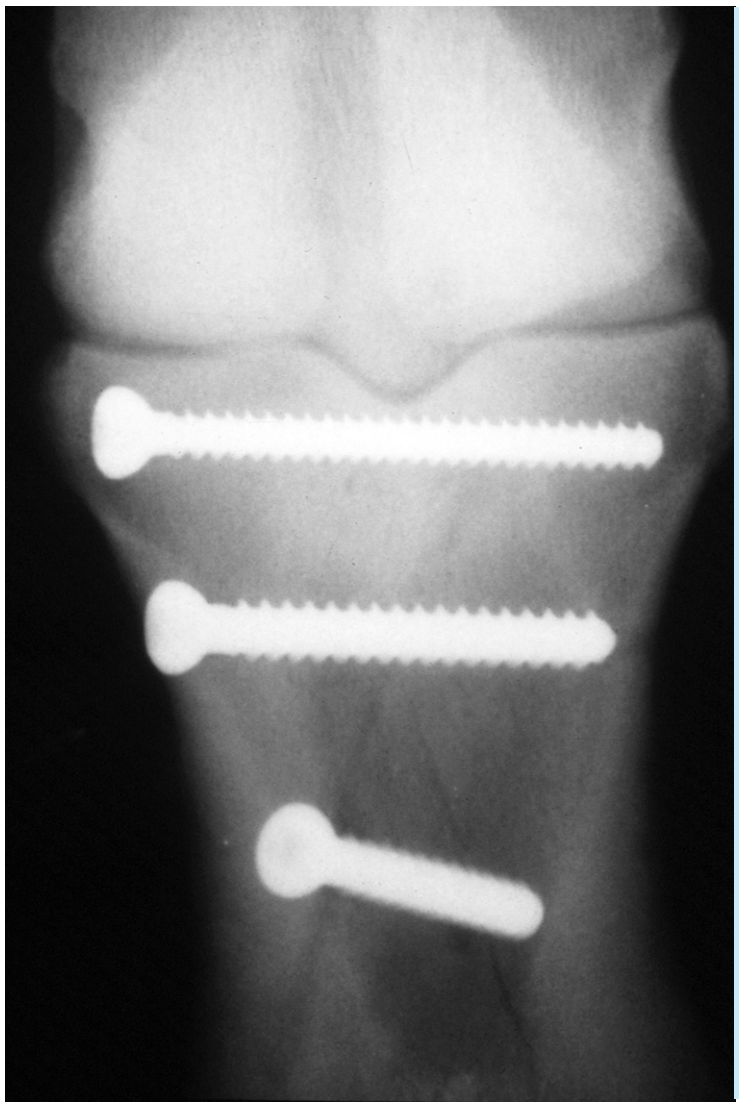


Fig. 16.7
Craniocaudal radiograph of a recently repaired typical complete sagittal first phalanx fracture. The fracture originates near the sagittal groove and exits the lateral cortex.

Physical examination Clinical signs of longitudinal fractures include lameness, which is immediate for all but the short incomplete fractures, fetlock joint effusion and pain on joint manipulation early after injury. Pain can be elicited by squeezing the P1 bone, particularly proximally. Lameness can resolve with stall rest within days to weeks with incomplete fractures, particularly short fractures, and local swelling may be imperceptible. Complete fractures usually result in a non-weight bearing lameness that persists and swelling in the pastern is present.

Special examination A first phalanx fracture should be suspected in any competitive horse, particularly a race horse, that is lame the day after the race and has fetlock joint effusion. The horse should not be jogged excessively or jogged following a nerve block to the distal limb as complete bone failure may occur.

Diagnostic confirmation The diagnosis can usually be confirmed with a complete series of radiographs. Most fractures are evident on the craniocaudal view (sagittal fractures) or lateral view (frontal plane fractures). Acute non-displaced first phalanx fractures can be undetectable by radiography. If a high degree of suspicion for a first phalanx fracture persists due to clinical signs and history, the radiographs should be repeated in 2–4 weeks or a nuclear scan performed. Horses with a confirmed fracture should remain on stall rest with appropriate coaptation for the fracture configuration until surgery, if elected.

Treatment and prognosis

Therapeutic aims The goals of therapy are to prevent worsening or displacement of an existing fracture with stall rest and coaptation and surgical treatment to provide immediate reduction and compression of the fracture. Internal fixation provides the most rapid healing and best joint alignment.

Therapy Most sagittal and frontal plane first phalanx fractures are best treated with surgical lag screw compression if the fracture length on radiograph is > 1 cm[26–29] (see Figs 16.7, 16.8). In non-displaced fractures, screws can be placed in lag fashion through small stab incisions. In displaced fractures an incision can improve exposure to ensure anatomic

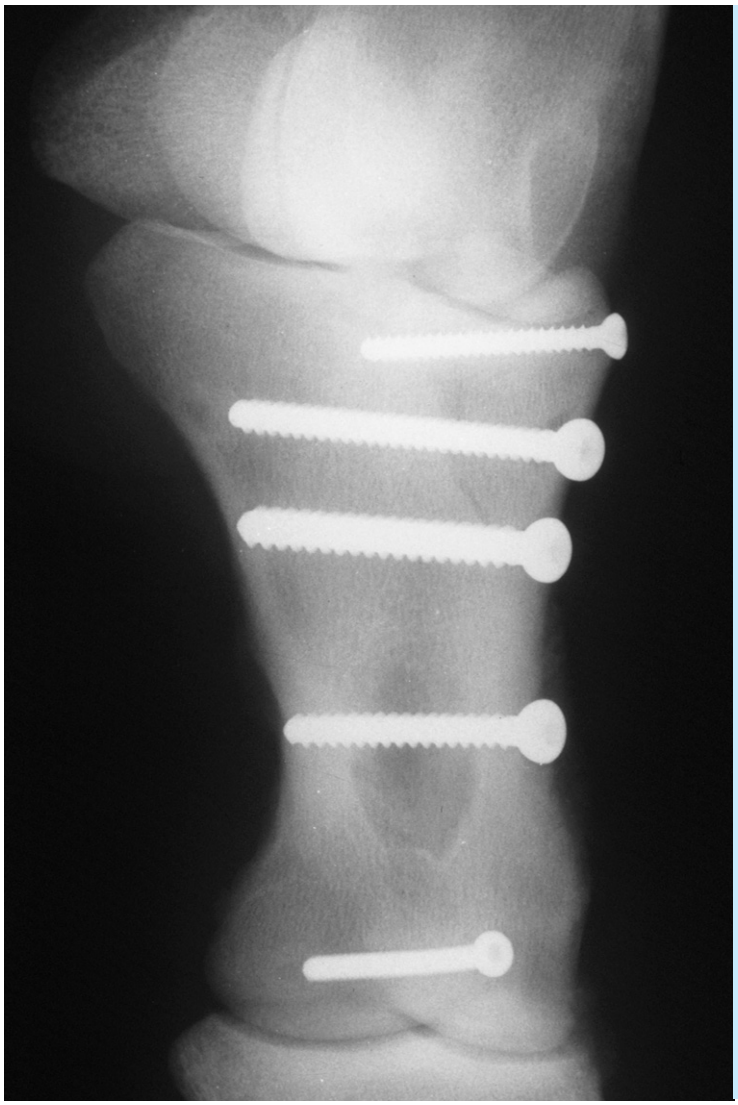


Fig. 16.8
Lag screw repair of a comminuted first phalanx fracture. Frontal and sagittal fracture planes required fixation in multiple planes. The fracture was complete into the pastern joint.

reduction prior to screw placement. Comminuted fractures that have lost an intact strut of bone support from the fetlock to the pastern joint are best treated ideally for several weeks with diverted loading through coaptative devices.[30] Positive profile transfixation pins in the metacarpus/tarsus supported with a cast or use of an external fixator apparatus have been successful in managing these fractures and can be used in the presence of open wounds.

Prognosis The prognosis for return to athletic use following repair is good to excellent (> 70%) for non-comminuted, incomplete, non-displaced fractures and complete fractures that exit the lateral cortex.[26–28] The prognosis following repair for complete fractures that enter the pastern joint is lower (49%).[27] The prognosis for complete fractures is also good if surgical repair effectively compresses the fracture with minimal displacement in the pastern joint. Repair of displaced complete fractures or comminuted fractures can achieve pasture soundness and breeding soundness, but athletic soundness is usually compromised.

Etiology and pathogenesis

Etiology Sagittal first phalanx fractures occur as the sagittal ridge of the metacarpal/tarsal condyle is loaded rapidly into the first phalanx during galloping (see Fig. 16.1). The shape of the bones and the rotation during movement create torsional forces within the bone, resulting in the classic spiraling fracture.

Pathophysiology Preceding bone pathology is not necessary for this fracture to occur and it is considered a high-speed casualty.

Proximal sesamoiditis

- Lameness localized to the fetlock and suspensory branches.
- Radiographically apparent widened vascular channels in the sesamoid confirms the diagnosis.
- Reduced exercise level and time for bone remodeling are necessary.

Fig. 16.9
Typical radiographic appearance of sesamoiditis with wide and prominent vascular channels.

Recognition

History and presenting complaint Sesamoiditis is a condition characterized by pain and associated lameness located to the proximal sesamoid bones and attachment of the suspensory branches.

Physical examination Pain, heat and inflammation are detected at the insertion of the suspensory ligament early in the disease, but usually marked lameness and limitations on performance occur without any clinically detectable signs.[31,32]

Lameness is usually obvious, particularly after exercise. Pain on pressure over the abaxial surface of the sesamoid bone and on fetlock flexion is typical. A distal metacarpal nerve block, but not an intra-articular fetlock block, will locate the lameness to the extra-articular structures of the fetlock. Additional diagnostic tests would include radiographs and ultrasound examination of the suspensory ligament.

Special examination Primary disease of the suspensory ligament or distal sesamoidean ligament can accompany the bone pain and should be evaluated with diagnostic ultrasound.

Radiographs can reveal a range of changes from accelerated early remodeling response in the bones (increased size and number of vascular channels) to marked proliferation of bone along the abaxial margin of the sesamoid and increased bone density of the sesamoid (Fig. 16.9). Some radiographic changes associated with chronic sesamoiditis are persistent and present in sound performing horses.

Nuclear scintigraphy usually demonstrates increased radiopharmaceutical uptake in the sesamoids of greater degree than bone remodeling associated with training and of lesser degree than sesamoid bone fracture.

Diagnostic confirmation The diagnosis is confirmed with a combination of radiographic changes indicated above, lameness that locates to the fetlock area and fetlock lameness that does not locate intra-articularly with a fetlock joint block. Ultrasound examination of the suspensory ligament is often normal.

Treatment and prognosis

Therapeutic aims The goal of therapy is to reduce bone pain so that a convalescent training program can be initiated to strengthen the bone. Bone remodeling will need to occur to permit the sesamoids to accommodate to the high-tensile strains of competitive sport without reinjury.

Therapy Initial therapy is stall rest, anti-inflammatory and pain medication to eliminate lameness. With a convalescent exercise program, bone remodeling can conclude, heal the injury and suspensory strength be regained.[31]

Treatment is palliative, including anti-inflammatory medications, physical and adjunctive therapy and supportive wraps in the acute phases. X-ray and γ-ray radiation, laser heat application, shock wave therapy and a balanced mineral diet are considered by some to be valuable in this condition. Rest from athletic activities is necessary until soundness is achieved. A convalescent exercise program would include lower levels of exercise that would stimulate bone strengthening, but not induce pain or bone damage. Typical pro-grams are prolonged, similar to suspensory ligament injuries (7–9 months). Pain can recur upon return to original levels of performance and may force retirement or a reduction in level of athletic competition.

Prognosis The specific prognosis is case dependent and can range from poor for severe cases with concomitant suspensory ligament injury to good for cases with mild lameness and minimal radiographic changes.

Etiology and pathogenesis

Etiology The etiology is considered to be excessive strain to the suspensory apparatus around the fetlock, including the sesamoid bones and the insertion of the suspensory ligament branches.

Pathophysiology The intraosseous blood supply to the sesamoid bone enters through a series of abaxial vascular channels that correspond to the enlarged channels seen

radiographically in sesamoiditis, indicating bone resorption. This may represent the initiation of the remodeling response to bone stress of training or may reflect an increase in blood flow due to inflammation and injury to the suspensory ligament, or both.[25] Sesamoid bone remodeling is a normal response to training and only if stresses exceed the capability to strengthen bone would microfracture and bone damage occur. Although radiographic vascular changes of bone remodeling were not associated with sesamoid fracture, the vascular structures course along known lines of fracture in adult racehorses. The sesamoid bones have an extensive sensory nerve supply that may explain bone pain associated with trabecular bone injury.[33]

Epidemiology

Sesamoiditis is observed frequently in racing horses and hunters and jumpers.[10]

Prevention

Appropriate training schedules to permit time for bone strengthening are helpful. A dietary cause has not been identified.

A separate condition of the axial border of the sesamoid bones, an osteomyelitis, has also been called sesamoiditis. Horses with axial sesamoid osteomyelitis are quite lame at the walk and radiographs reveal surface bone lysis at the attachment of the intersesamoidean ligament. The lesions and clinical signs suggest a septic condition in some animals but on histology infarction and necrosis predominate. Presumably an injury to the attachment of the intersesamoidean ligament and possibly seeding with bacteria from intra-articular injections may be associated with the condition. The prognosis for soundness with or without surgical debridement is poor.[34]

Rupture of the suspensory apparatus

- Injury unique to the race horse.
- Fractures of the sesamoid bones and/or suspensory ligament disruption occur.
- First aid splinting should be done to preserve soft tissues and the local blood supply.
- Surgery is done to stabilize the joint for salvage as a breeding animal.

Disruption of the suspensory apparatus is a common cause of acute breakdown in the racing Thoroughbred and frequently results in humane destruction of the animal.[9,22] Disruption can occur because of rupture of the suspensory ligament, fracture of both proximal sesamoid bones or avulsion of the distal sesamoidean ligaments. Due to the violent nature of these injuries, open fractures, fetlock joint luxation and loss of the vascular supply to the distal limb are associated complications. Successful treatment of these injuries requires immediate and appropriate emergency management of the horse, including sedation, possibly general anesthesia, ambulance service and limb stabilization. Commercial splints such as the Kimzey Leg Saver Splint (Kimzey Welding Works, Woodland, CA) have been designed for this purpose. Euthanasia may be chosen due to the extent of the injuries, risk of treatment failure, lack of sentimental or breeding value of the horse and cost of treatment.[22]

Recognition

History and presenting complaint These injuries occur during maximal exercise and are immediately recognized by distortion of the distal limb and the inability of the horse to bear weight without collapse of the distal limb.

Physical examination Immediate sedation or general anesthesia is recommended to gain control of the panicked horse for examination by palpation, radiography, ultrasound and Doppler ultrasound.

Special examination and diagnostic confirmation The diagnosis is confirmed by observation (the fetlock drops to the ground upon loading), palpation and radiograph. Ultrasound evaluation can locate the sites of suspensory ligament failure and, with Doppler, assesses blood flow to the distal limb. The vascular supply is best evaluated after the horse has been treated for shock and the limb has been stabilized to over-ride initial vasoconstriction. Radiographic examination most often reveals the proximal displacement of the intact sesamoid bone (rupture of the distal sesamoidean ligaments) or proximal displacement of the apical portions of the fractured sesamoid bones (sesamoid fracture).

Treatment and prognosis

Therapeutic aims The goal of treatment is to salvage the horse's life for breeding or as a retired pasture com-panion. Surgical fusion of the fetlock joint can be successful if limb blood supply is intact and infection can be prevented.

Therapy If treatment is chosen, a splint should be maintained for 4–5 days prior to the selection of the final treatment to permit recovery from the shock and trauma and to define the extent of skin necrosis and loss of vascular supply accompanying the injury. The arthrodesis procedure should be undertaken at the optimal time and evaluation of the soft tissue injury and permanent deficit and risk of infection must be ascertained to properly predict the outcome with surgery.[22] Surgical treatment options include fetlock ankylosis supported by use of an external fixator placed on the foot and metacarpus to fix the position of the joint during healing[35] or arthrodesis with implants and bone graft to achieve a pain-free stable fusion of the fetlock joint.[10,22] For implants, the soft tissues should be intact and the risk of infection minimal. Treatment by surgical means is preferable to relieve extended loading on the contralateral limb. In conservative management, supporting limb laminitis and erosion of the sesamoid bones by casts and splints is a significant cause of failure.

Prognosis The prognosis is grave for horses that also have open joint luxation, significant skin loss, loss of vascularity and open wounds. With the preselection and appropriate management of cases, the prognosis is good for pasture and breeding soundness. In one report, 60% of horses with fetlock arthrodesis fused the joint, survived and eventually had unrestricted activity.[22]

Etiology and pathogenesis

Etiology Fetlock disruption occurs during racing or maximal exercise as a traumatic event.
Pathophysiology Disruption of the suspensory apparatus is due to extreme overextension of the fetlock at high speeds and forces of loading. Pre-existing pathology of the bones or suspensory ligament is not a prerequisite for this injury to occur.

Epidemiology

Risk factors have been identified and include an abnormal finding in the suspensory ligament on pre-race inspection by a regulatory veterinarian[36] and racing with toe grabs.[37]

Prevention

Pulling horses with abnormal suspensory ligament findings from racing and maintenance of optimal track conditions will reduce the number of these catastrophic failures.

Fetlock luxation

Recognition

History and presenting complaint Luxation of the fetlock is usually in the frontal plane and occurs during a high-impact injury, such as slipping, running into an object or catching the hoof under a board or in a hole. A collateral ligament ruptures, resulting in an obvious varus or valgus deformity of the limb.[38] The dislocation of the joint may be temporary and often replaces spontaneously or is reduced by an attendant.
Physical examination After reduction, lameness may be minimal. Articular fractures of palmar/plantar eminence of the first phalanx may accompany the luxation[39] and can be avulsed several inches proximally. Medial to lateral laxity is present and the joint may be subluxated upon flexion. Swelling of the joint and torn soft tissues will locate over the injured side of the joint within hours. Persistent laxity can be palpated and presumably contributes to the chronic osteoarthritis that is often the sequela to this injury.[40]
Special examination Reluxation can occur at any moment if the joint is not stabilized until the swelling and pain begin to protect the joint, so it is critical to restrict the horse's activity.
Diagnostic confirmation The diagnosis is often made by the historical description of the limb deformity and manipulation of the fetlock. Radiographs should be taken to identify an avulsion fracture, intra-articular fractures or damage to the articular surface that has entered into the subchondral bone. Craniocaudal stress radiographs displacing the distal limb medially or laterally will identify more laxity to the fetlock joint than the contralateral joint, but is not necessary for a diagnosis (Fig. 16.10).

Treatment and prognosis

Therapeutic aims The goal of therapy is to reduce the luxation and stabilize the limb to prevent reluxation and decrease the risk of osteoarthritis.
Therapy Arthroscopic removal of articular fragments can be undertaken if the chances for athletic soundness are to be optimized. Reduction and immobilization for 4–6 weeks will result in fibrous restabilization of the joint and a good prognosis for light riding soundness. Surgical repair of the ligament is reported,[38,41] but is not universally accepted as an improvement over conservative coaptation. If osteoarthritis and permanent lameness occur as sequelae, a surgical arthrodesis can result in pasture soundness. In open fractures/luxations, external fixation may be necessary followed by bone grafting and stimulated joint fusion.
Prognosis Closed luxations without fracture that are quickly reduced can result in soundness, although competitive athletic soundness is less likely. Most luxations result in some degree of osteoarthritis and lameness with exercise. Luxations with associated injuries, such as an open joint, additional fractures or disrupted vascular supply, would carry a less favorable prognosis.

Etiology and pathogenesis

Etiology This injury is a sporadic, relatively random traumatic event.
Pathophysiology Lateral and medial luxation of the fetlock joint is a recognized syndrome, affects all ages and breeds of horses and usually occurs during high-speed falls or collisions. Pre-existing joint disease or collateral ligament disease is not associated with injury.

Traumatic synovitis and capsulitis

- Definitive diagnosis is via intra-articular anesthesia.
- Rule out osteochondral fractures.
- Treatment reduces joint inflammation to prevent deterioration of cartilage.

Traumatic synovitis/arthritis of the fetlock joint is one of the most common conditions in the equine athlete. The high range of rotary motion predisposes this joint to injury and wear.

Recognition

History and presenting complaint Most horses present with the onset of lameness of one limb initially which may be intermittent and worse after exercise. A specific injury may have been noted.
Physical examination Joint effusion, soreness to joint flexion and joint heat (detected by palpation or thermography) are the classic clinical signs.
Special examination Radiographs are normal until the condition becomes chronic and degenerative joint disease (osteoarthritis) develops. Arthrocentesis and fluid cytology are often not performed as the clinical signs are not severe enough to warrant them; however, intra-articular and systemic joint medication is commonly used. If training is continued with the use of aggressive medical therapy, a proportion of these horses will develop proliferative synovitis

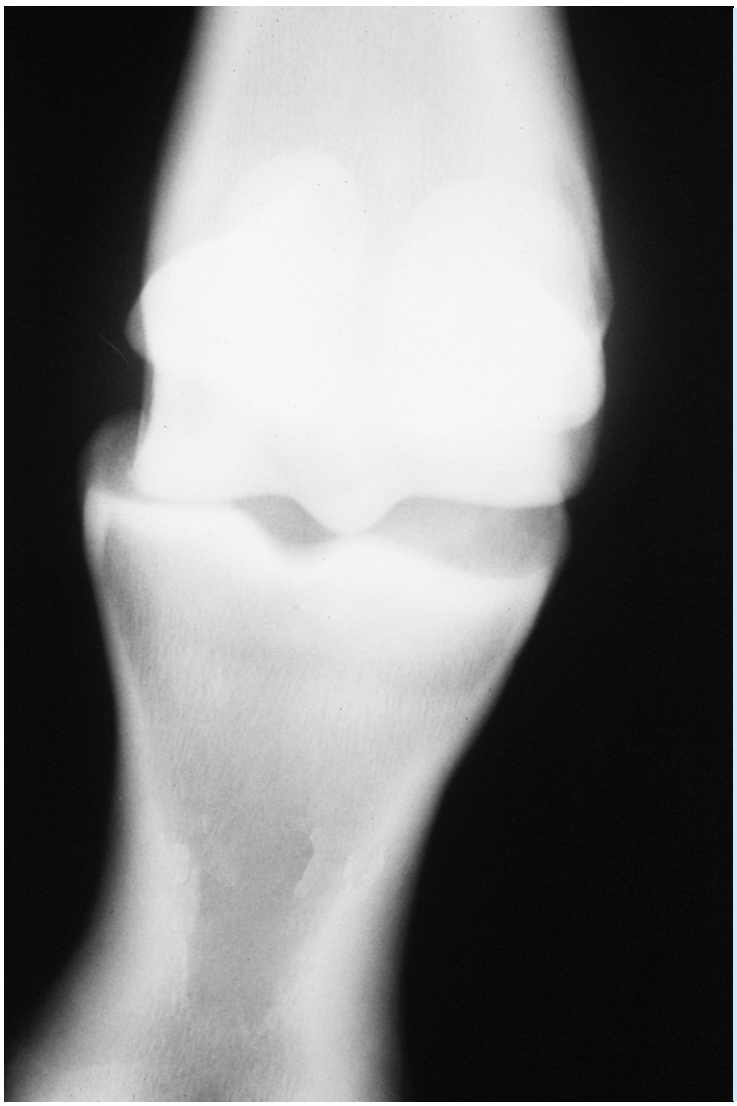


Fig. 16.10
Stress radiograph demonstrating excessive joint laxity in the frontal plane, indicating rupture of the medial collateral ligament.

(see next section), chip fractures and articular cartilage damage (erosion and scoring). Intermittent hemarthrosis may be detected with primary traumatic synovitis but often indicates injury to subchondral bone, such as chip fracture or cartilage elevation.

Laboratory examination Synovial fluid analysis may be normal or reveal a mild increase in white blood cell count or protein concentration.

Diagnostic confirmation The diagnosis is definitive if the lameness resolves with an intra-articular fetlock joint block, radiographs are normal and a synovitis or hemarthrosis is present on synovial fluid analysis.

Treatment and prognosis

Therapeutic aims Most primary traumatic synovitis is mild, permitting continued training with medical management. Medical management is aimed at reducing joint pain and inflammation.

Therapy Early medical intervention and appropriate joint rest and physiotherapy are critical to prevent loss of glycosaminoglycan from articular cartilage and permanent joint wear. Early loss of articular cartilage proteoglycan is reversible with medication and joint rest. Systemic hyaluronan and polysulfated glycosaminoglycans may be used to reduce joint inflammation and assist with protection of articular cartilage. Topical dimethylsulfoxide (DMSO) and hyperosmotic agents under plastic and supportive wraps assist with removal of joint edema and fluid accumulation. Non-steroidal anti-inflammatory medication can reduce joint inflammation and should be used if close monitoring of the lameness is not critical. Long-term use of non-steroidal anti-inflammatory drugs would require continued evaluation of the patient.

Prognosis The prognosis for traumatic arthritis ranges from good for minor and first-time injuries to poor for severe or recurrent injuries. Early and less severe disease that is permitted joint rest to resolve the inflammation can often be

managed. Traumatic arthritis can be progressive or result in degenerative joint disease.

Etiology and pathogenesis

Etiology Traumatic arthritis usually begins as a strain to the joint during exercise that results in a joint bleed, pinching of the synovium and/or a cartilage erosion and secondary joint inflammation. Horses with high action and high-impact loading are the most susceptible.

Pathophysiology Joint inflammation (synovitis) induced by a traumatic injury results in immediate swelling of the synovium and possible joint hemorrhage. Capillary leakage introduces fluid and white blood cells into the area of injury and increases blood flow locally. These cells release inflammatory mediators, such as interleukins, eicosanoids and nitric oxide that perpetuate the inflammation until healing occurs. The result is joint effusion, synovial hemorrhage and edema, an increased joint fluid white blood cell count and protein content and activation of joint pain (see Chapter 9).

Epidemiology

Horses at risk for traumatic synovitis are in active training with maximal performances on a regular schedule. This includes all racing breeds (Thoroughbred, Standardbred, Quarter Horse, Warmbloods) and types of racing competition (flat racing, barrel racing, cross-country, steeple chase); dressage horses; Western performance horses; hunters; jumpers; three-day competition; and show horses.

Prevention

Regular exercise, appropriate warm-up, conservative competitive schedules and judicious use of joint medications, particularly steroids and non-steroidal anti-inflammatory drugs, will reduce the risk of joint trauma and prolong joint health.

Proliferative (villonodular) synovitis

- Result of chronic joint inflammation.
- Radiographically evident as supracondylar lysis.
- Treatment is surgical resection of proliferative tissue if medical therapy fails.

Proliferative synovitis is a clinical condition in which chronic traumatic synovitis and continued exercise result in a painful thickening of the synovium, particularly in areas of compression trauma.[8,42–46]

Recognition

History and presenting complaint Classic clinical presentation for chronic proliferative villonodular synovitis is joint effusion, decreased range of joint motion and soreness on joint flexion.

Physical examination Enlargement at the dorsal fetlock is often visible and disproportionately large for the amount of palmar effusion. The joints may appear and palpate normally, however.

Special examination Confirmation of enlargement of the pad is most easily obtained with dorsal metacarpophalangeal joint ultrasound. Normal dorsal fetlock pads measure < 4 mm dorsal to palmar in a plane perpendicular to the mass surface. A typical enlarged pad in clinical disease measured 11 mm.[8] Proliferative synovitis is often bilateral and therefore comparative measurements of one limb to another may not be helpful. Diagnosis can also be made with contrast arthrography and at arthroscopy (Fig. 16.11). Joints should be radiographed prior to surgery to identify presence and extent of bone erosion, mineralization in the masses, degenerative joint disease and concomitant proximal phalanx chip fractures. In a recent report of 63 horses, 93% of joints demonstrated a concavity at the distal dorsal metacarpus and 32% had a first phalanx chip fracture[8] but these findings are not conclusively diagnostic for an enlarged dorsal pad. In severe cases, these masses can become locally invasive of bone and joint capsule, continuing expansion beyond normal joint structures, similar to benign tumors.

Laboratory examination Synovial fluid analysis may be normal or indicative of mild to moderate synovitis.

Diagnostic confirmation The presence of clinical signs, pain located to the fetlock joint and a measurably enlarged synovial pad confirm the diagnosis. Radiographic changes are supportive, but not always present, particularly in early disease.

Treatment and prognosis

Therapeutic aims The goal of therapy is to reduce joint pain and inflammation and reduce the size of the dorsal synovial pad to prevent immediate recurrence on resuming exercise.

Therapy Upon identification of an enlarged dorsal fetlock proliferative mass, initial therapy would include joint rest, all forms of adjunctive joint synovitis therapy and consideration of a short-acting intra-articular steroid. Intra-articular steroids are potent suppressors of angiogenesis and fibrosis and will reduce active inflammation. Short-acting steroids, such as soluble dexamethasone and hydrocortisone, may minimize the long-term corticosteroid influence on chondrocyte metabolism. Arthroscopic surgical mechanical or laser removal of the enlarged masses is indicated if any associated fractures are identified, if pain persists or at planned lay-off periods.[47] Surgery should be undertaken before signs are associated with bone changes, articular cartilage damage or degenerative joint disease.

Prognosis Successful return to racing is reported in Thoroughbreds[8] and trotters[43] after surgical removal of the dorsal pad and intra-articular chip fractures. Proliferation of the pad can return despite surgical and medical management, but most horses are clinically improved with a longer performance career with surgical treatment.

Diffuse proliferative synovitis and capsulitis is also common in the fetlock joint and can be associated with chronic joint injection, joint damage and joint wear. Palpable

Fig. 16.11
Contrast arthrogram of the fetlock joint demonstrating a space-occupying soft tissue mass in the dorsal and palmar joint recesses typical of proliferative synovitis.

joint soft tissue thickening and loss of joint range of motion are classic clinical findings and are commonly noted in retired jumpers and race horses. Fibrosis of the joint capsule and loss of fine villous architecture are notable at arthroscopy. Diffuse synovectomy in these cases is probably of minimal benefit as restoration of normal villi is unlikely and loss of remaining villous architecture may be permanent. The loss of joint motion is permanent and may not be associated with lameness in retired horses.

Etiology and pathogenesis

Etiology This condition is most commonly seen in Thoroughbred race horses. High-impact joint use with extreme dorsiflexion causes direct mechanical trauma to the dorsal fetlock synovial pad between the metacarpal/tarsal condyle and the first phalanx.

Pathophysiology Proliferative synovitis is a clinical condition in which chronic traumatic synovitis and continued exercise result in a painful thickening of the synovium, particularly in areas of compression trauma.[8,42–46] The most common location in the horse for this condition is the dorsal fibrous pad of the metacarpophalangeal joint. This pad is normally present at the dorsal reflection of the metacarpophalangeal joint directly under the broad, flat extensor tendon and associated joint capsule.[8] At hyperextension and maximal flexion, this pad is compressed and can result in intrasynovial hemorrhage, granulation tissue formation, fibrosis and mineralization. Pigment in the pad is often hemosiderin, but melanin has also been noted.

Epidemiology

The condition is typically progressive as joint trauma is continued with use.

Prevention

Early treatment and adequate rest early in the disease process may arrest the development or progression of this condition.

Osteoarthritis of the fetlock (osselets)

Osteoarthritis is a chronic degenerative joint condition with the hallmark criteria of joint pain, articular cartilage degeneration, subchondral bone change, osteophyte production and loss of joint motion.[48] The fore fetlocks in athletic horses are probably the most commonly affected joint with this condition and therefore it is common bilaterally in geriatric horses, retired horses and exceptional athletes.

Recognition

History and presenting complaint Lameness is insidious in onset, often bilateral with one limb less and later affected.

Physical examination The gait is classically a stiff and shortened stride with an asymmetrical lameness. Lameness worsens on turns and after exercise. Joints are stiff, but may be minimally sore to forced flexion.

Laboratory examination Standard synovial fluid analysis is often normal.

Diagnostic confirmation The diagnosis is confirmed by the combination of clinical signs and radiographic evidence of osteophytes, subchondral bone sclerosis and narrowed joint space (Fig. 16.12). Extent of cartilage degeneration can only be assessed by direct visualization arthroscopically or by magnetic resonance imaging.

Treatment and prognosis

Therapeutic aims The goal of therapy is to relieve joint pain and improve joint use.

Therapy Treatment of osteoarthritis includes medical therapy and regular joint motion exercises, both passive and active. Surgical debridement of frayed cartilage and exposed bone as well as copious joint lavage have been described to alleviate pain in people, but are palliative only. Use of hyaluronan and glycosamine products systemically and intra-articularly is advised as needed. Intra-articular steroids can be used on a limited basis to provide comfort or short durations of athletic use. Non-steroidal anti-inflammatory medication, such as phenylbutazone, is commonly needed in these horses to permit their turnout or restricted athletic use. Chronic use of non-steroidal anti-inflammatory medication is common for osteoarthritis and can alleviate pain and permit activity. Chronic use can be associated with complications such as oral and gastrointestinal ulcers so it should be titrated to the lowest dose possible and used intermittently. Regular exercise on a limited basis is critical to maintain joint comfort and improve quality of life.

Many other adjunctive therapies, such as heat application, passive joint flexion, swimming, etc. have been anecdotally described as effective.

Prognosis The prognosis for resolution of osteoarthritis is poor because the cartilage degeneration is permanent. Disease-modifying drugs, such as interleukin-1 antagonists, are available for use in humans, but are costly and species specific.

Etiology and pathogenesis

Etiology Chronic joint 'wear and tear' associated with athletic careers is typical in the sport horse.

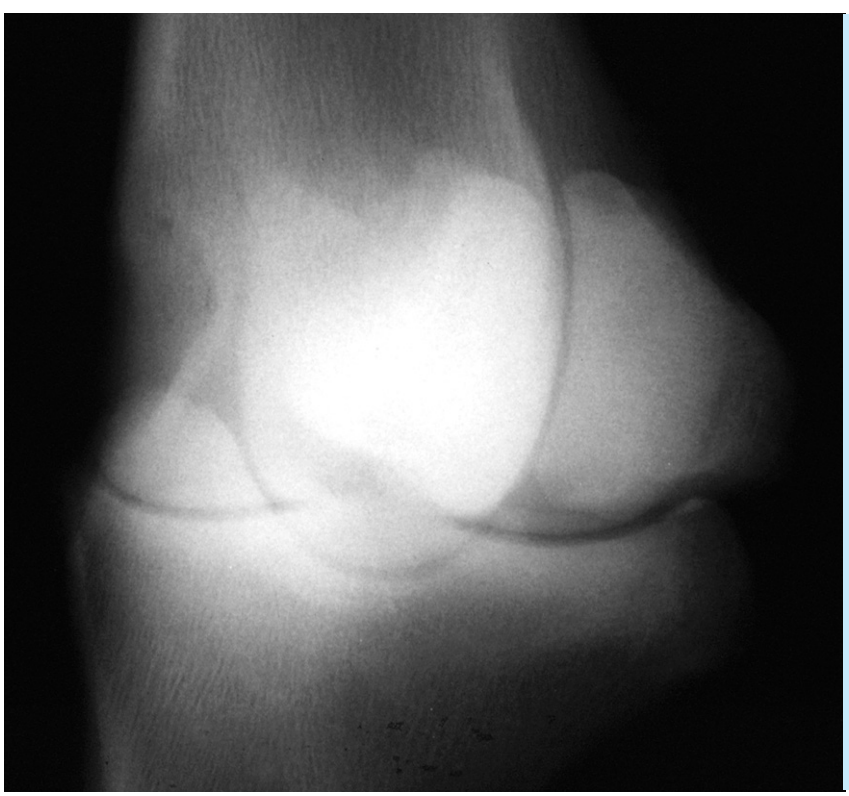


Fig. 16.12
Radiograph of a fetlock joint with osteoarthritis demonstrating osteophyte formation on the dorsal eminence of the first phalanx and proximal sesamoid bones and dorsomedial joint space narrowing.

Pathophysiology Healthy joints can develop osteoarthritis with time and use. A predisposition to earlier and more severe osteoarthritis may exist and be related to prior joint injury, conformation and use.

Epidemiology Osteoarthritis is seen more commonly in geriatric and career horses.

Prevention

Care of the joints during a horse's athletic career may help maintain joint health. Joint support wraps, judicious use of joint medications and immediate veterinary attention to joint injury are critical to containing the development and progression of osteoarthritis.

Fetlock annular ligament constriction

- Annular ligament constriction is usually secondary to chronic digital sheath synovitis or tendinitis.
- Treatment of the primary cause is often insufficient.
- Annular ligament resection may be done using arthroscopy.

The fetlock annular ligament is a ~3 cm wide fascial band spanning the abaxial ridges of the sesamoid bones and strategically located to support the superficial and deep flexor tendons as they course around the back of the fetlock joint. Synovia from the digital sheath reflects on the deep surface of the ligament. Damage to the flexor tendons can result in swelling and pressure within the sheath.

Recognition

History and presenting complaint The primary complaint is 'windpuffs' or swelling of the digital sheath. Lameness may or may not be evident initially.

Physical examination The clinical signs include pain, restricted range of fetlock motion and ischemia to the tissues within the fetlock canal (tunnel syndrome). Once present,

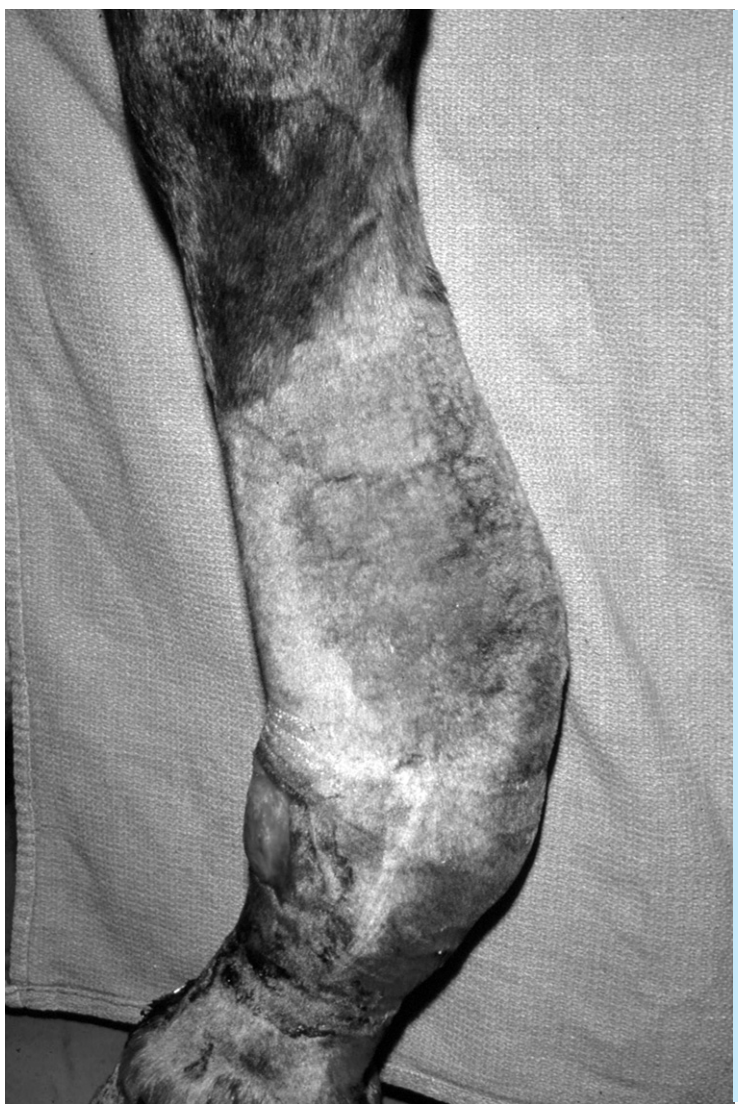


Fig. 16.13
Chronic low superficial digital flexor tendinitis with interference at the annular ligament.

lameness is persistent and worsens with exercise. Lameness is characterized by a decreased extension of the fetlock during weight bearing and a shortened caudal phase to the stride. In the most severe cases the horse will be reluctant to place the heel on the ground.

The pathognomonic clinical sign of fetlock annular ligament constriction is swelling of the palmar/plantar soft tissues of the distal limb around the fetlock and a characteristic observable proximal border of the annular ligament ('notching') caused by annular ligament constriction. Typically, there will be distension of the digital sheath of the superficial and deep flexor tendons proximal to the annular ligament and thickening of the superficial flexor tendon (tendinitis) (Fig. 16.13).

In Warmblood horses with fetlock annular ligament constriction, nine had thickening of the annular ligament and tenosynovitis, three were dominated by distension of the sheath, three had superficial digital flexor tendon injury and one had marked synovial sheath proliferation.[49] In race horses, superficial digital flexor tendinitis may be more commonly associated with fetlock annular ligament constriction.[50]

Special examination Regional diagnostic anesthesia usually results in improvement after a metacarpal block. Direct anesthesia of the digital sheath incompletely alleviates pain. Radiographic evaluation should be performed but is often normal unless infection is a cause. In 38 cases of annular ligament constriction, six horses had proximal sesamoid bone abnormality and 12 had bone enthesiophytes at the attachment of the annular ligament (insertion desmopathy).[51]

Laboratory examination Synovial fluid analysis of the sheath fluid and contrast radiography can be of value, but are usually limited in diagnostic value.

Diagnostic confirmation Diagnostic ultrasound confirms the diagnosis and permits the differentiation of structures involved, including thickening of the annual ligament (> 2 mm thick), tears of the deep flexor tendon, sheath adhesions and proliferative tenosynovitis.

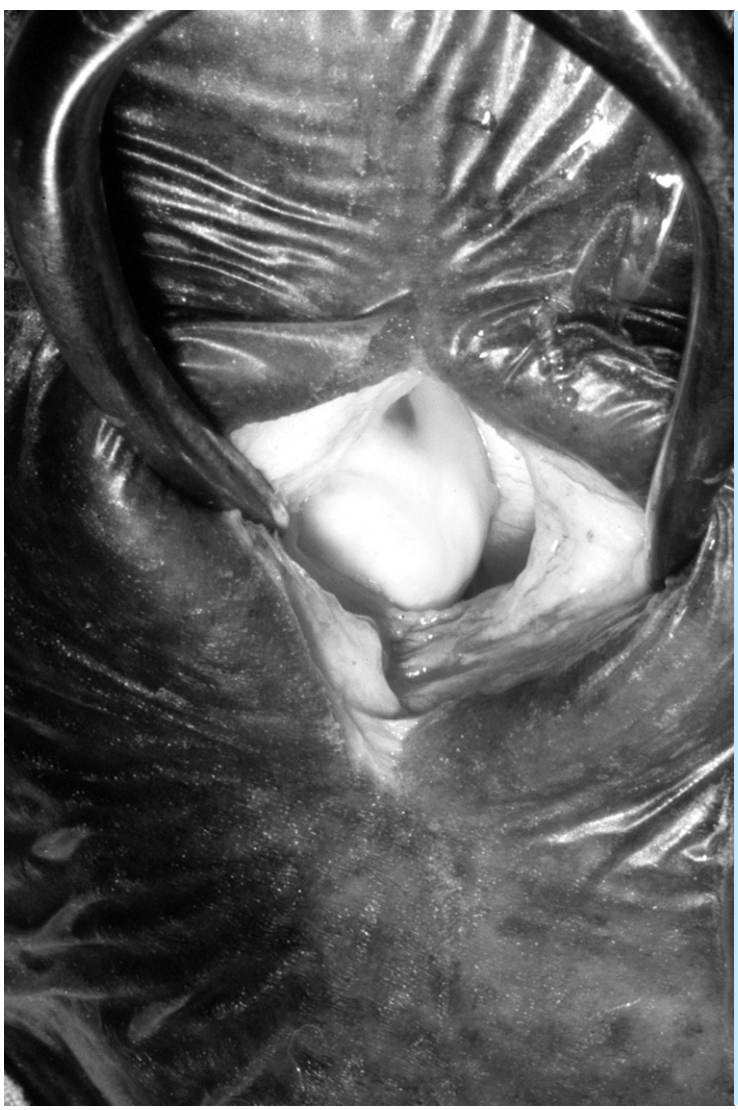


Fig. 16.14
Open annular ligament transection revealing a chronic blunt end of the deep digital flexor tendon.

Treatment and prognosis

Therapeutic aims The goal of therapy is to reduce the constriction of the annular ligament by either decreasing sheath effusion or releasing the ligament or both.

Therapy Initial conservative treatment often includes an intrathecal injection of steroid to decrease sheath effusion. This is typically palliative and may further weaken or slow healing of injured tendinous structures. To relieve the constriction, the annular ligament is transected either percutaneously or endoscopically. Accessory ligament desmotomy of the superficial digital flexor tendon, tendon splitting, adhesiolysis and synovial resection to simultaneously treat tendinitis, tendon core lesions, adhesions and synovial proliferation, respectively, are indicated.[52–54] Limitations of open transection include incisional drainage and dehiscence, limited visibility as compared to tenoscopy, and greater soft tissue morbidity. Open transection may be necessary for tendon repair (Fig. 16.14).

Prognosis If the primary etiology is desmitis of the palmar or plantar annular ligament and is not accompanied by extensive changes in the tendon (bowed tendon), the prognosis is good (84% returned to performance).[55,56] The Standardbreds in which annular ligament desmotomy was performed in addition to other surgical procedures for tendinitis improved and were able to race.[50] In horses with synovial masses or adhesions that were resected endoscopically at the time of annular ligament resection, the prognosis for athletic soundness was 72%.[53]

Etiology and pathogenesis

Etiology Specific causes are usually trauma and/or infection (Fig. 16.15) and are associated with distal superficial digital flexor tendinitis (low bow) (see Fig. 16.14), fibrosis from wounds and tenosynovial adhesions and inflammation. The annular ligament may also be directly injured and thickened

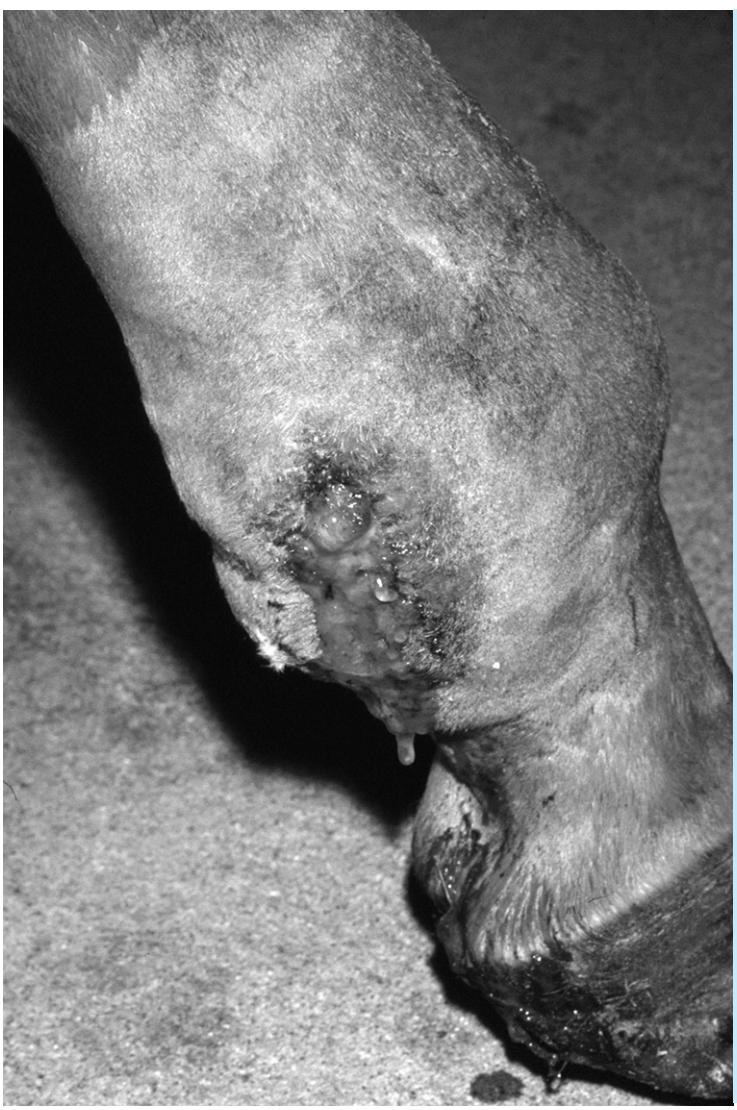


Fig. 16.15
Infectious tenosynovitis and digital sheath swelling associated with annular ligament constriction.

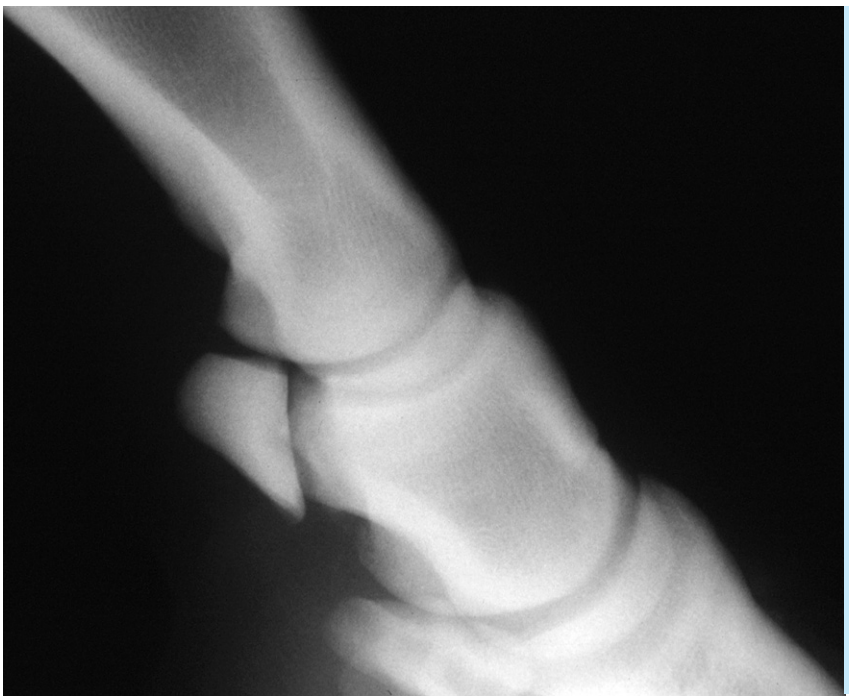


Fig. 16.16
Typical biaxial palmar second phalanx eminence fracture.

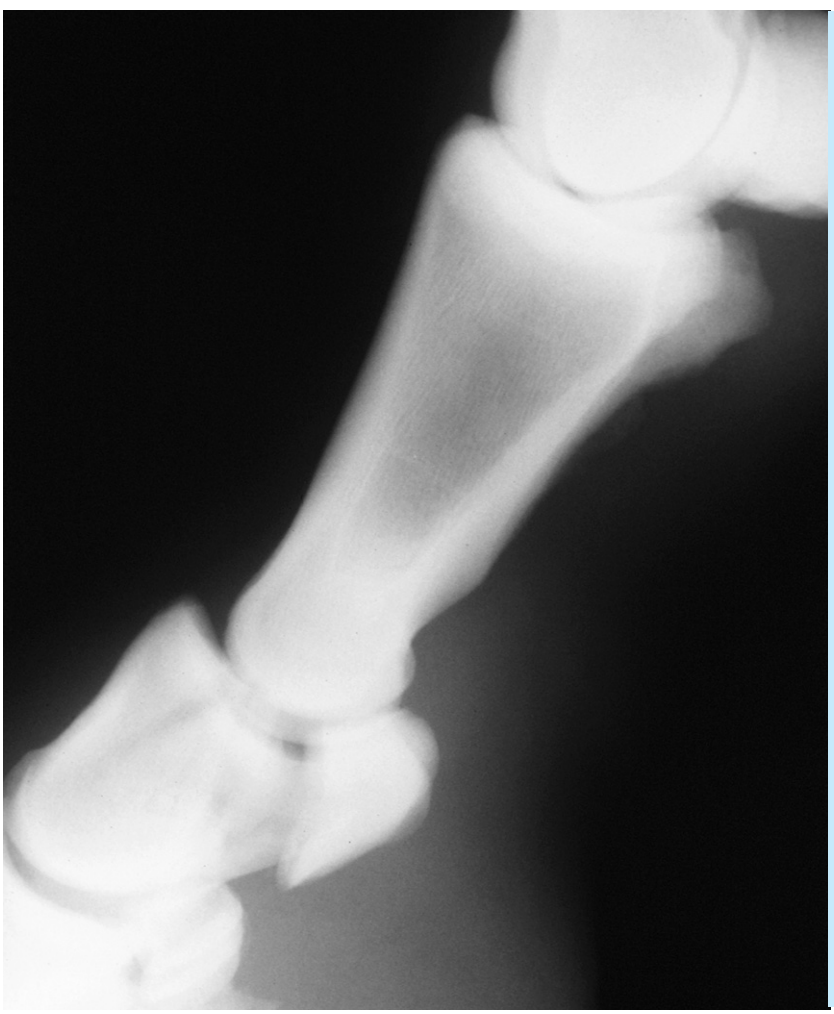


Fig. 16.17
Typical comminuted second phalanx fracture.

(desmitis) with the same constricting result. The fetlock annular ligament constriction syndrome is reduction in pain-free movement of the fetlock due to the movement of the structures within the fetlock canal. The result is persistent lameness.

Pathophysiology Thickening of the ligament occurs through the process of fiber tearing and fibrosis.

Epidemiology

Desmitis of the fetlock annular ligament is diagnosed mainly in sport horses and less frequently in race horses and histologic changes suggest it is traumatic in origin.[55,57] Excessive use of the hindlimbs, such as in jumpers and cross-country competitors, puts horses at increased risk.

Prevention

Protection of fetlock support structures, such as with support wraps and heel extension shoes, particularly in the hindlimbs, may decrease risk of injury.

Pastern joint injuries

Intra-articular fractures

The pastern joint is uncommonly involved in articular fractures, in comparison to other joints. Articular chip fractures can occur from the proximal dorsal eminences of the second phalanx (P2) and the palmar/plantar intereminence of P2 (Fig. 16.16).

Recognition

History and presenting complaint These injuries are associated with acute onset of lameness and swelling at the pastern.

Physical examination Lameness located to the distal limb with regional nerve blocks and visible pastern swelling are often present.

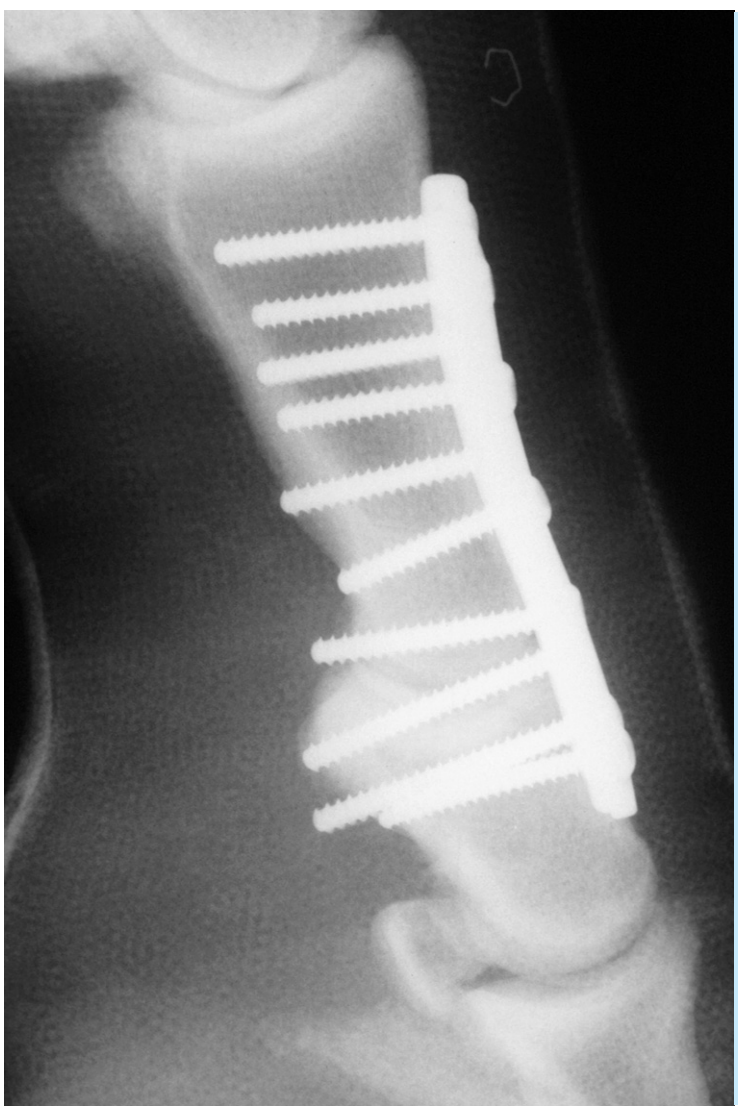


Fig. 16.18
Surgical repair of a comminuted second phalanx fracture at 2 months postoperatively. Pastern arthrodesis and fracture fragment stabilization were performed simultaneously.

Diagnostic confirmation Source of the lameness can be confirmed with direct pastern joint block but this is often not necessary in acute cases. Fractures are confirmed on radiographs.

Treatment and prognosis

Therapeutic aims The goal of therapy is to eliminate or reduce the lameness due to the fracture. In many cases a pastern arthrodesis may ultimately be necessary for soundness.
Therapy The smaller articular fragments are retrievable surgically by direct arthrotomy (dorsally) or arthroscopy (palmar/plantar pouch). Unfortunately, degenerative joint disease is often a sequela because significant soft tissue injury is necessary to induce a fracture in such a stable joint. Disruption of the joint capsule frequently results in persistent thickening of the joint and chronic lameness due to osteoarthritis (high ringbone).

Immediate stabilization of the distal limb in splints or preferably casts is recommended to prevent collapse or displacement for comminuted fractures of the second phalanx (Fig. 16.17). Prognosis is dependent on the degree of displacement, particularly at the coffin joint. Surgical exposure of the coffin joint is not possible to aid in reduction, so prevention of distraction or displacement is strongly advised. Preferable treatment is surgical reduction, lag screw fixation and simultaneous plate arthrodesis of the pastern joint[58,59] (Fig. 16.18).

Caudal eminence traction fractures usually heal with a fibrous union. For athletic soundness, pastern arthrodesis is recommended either at the time of fracture or if soundness does not result with time. Reduction and direct lag screw fixation of the fragment is described, but osteoarthritis is often the sequela. Pastern arthrodesis is recommended (Fig. 16.19).
Prognosis With surgery, prognosis for pasture or breeding soundness is good to excellent (Fig. 16.20). Athletic soundness can be achieved with pastern arthrodesis if fractures did

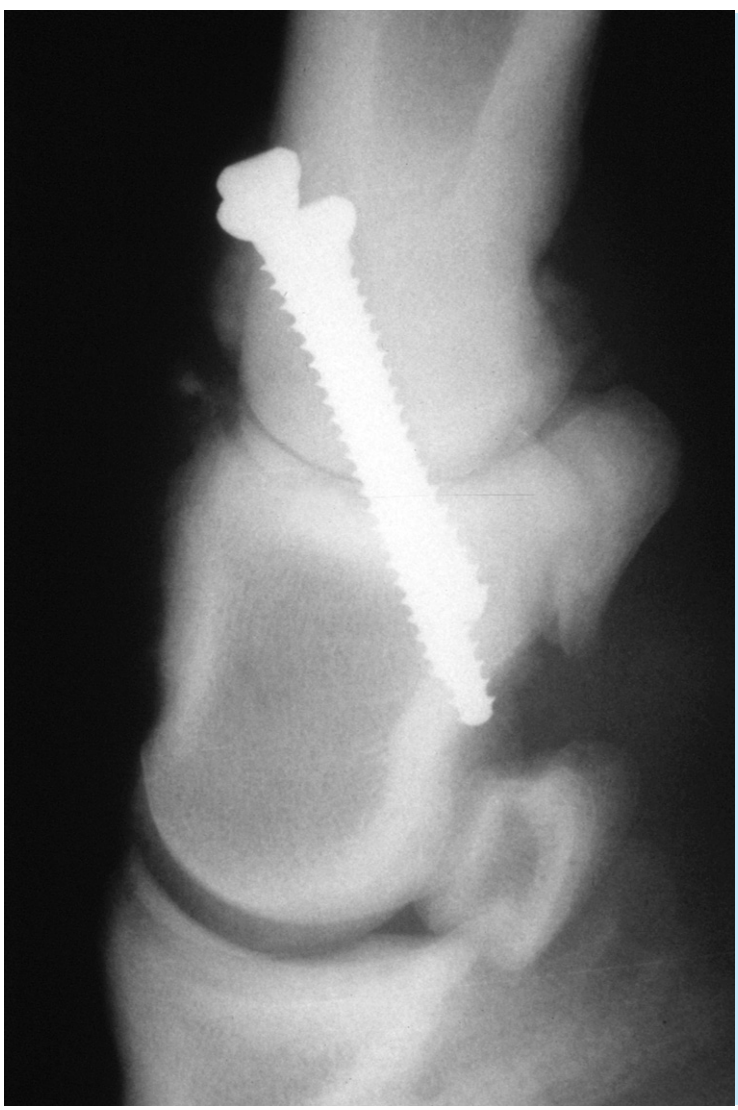


Fig. 16.19
Triple lag screw pastern arthrodesis as treatment for a caudal eminence fracture.

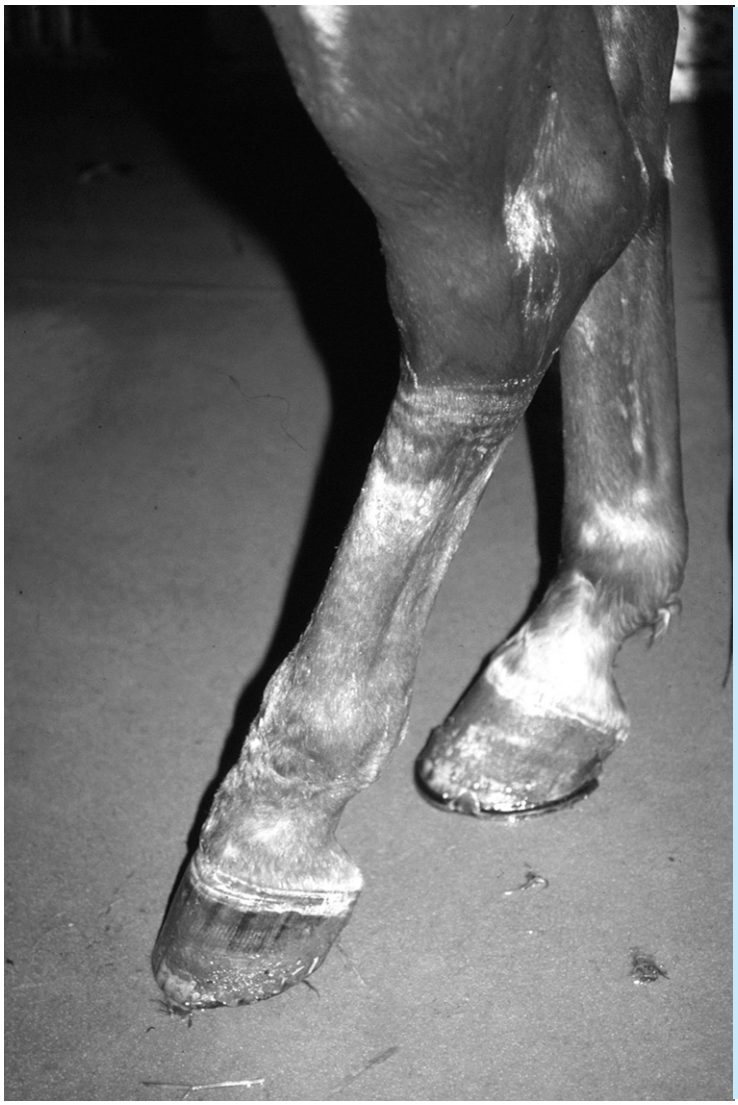


Fig. 16.20
Comminuted second phalanx surgical repair at 2 months postoperatively, demonstrating excellent healing and early use of the limb.

not enter the coffin joint. Prognosis for athletic soundness is guarded if the fracture entered the coffin joint. The prognosis for pasture or breeding soundness with conservative treatment is guarded to fair as horses remain lame for extended periods of time and healing is usually asymmetrical.

Etiology and pathogenesis

Etiology Fractures of the second phalanx can occur at exercise, typically when the horse is turning on a supporting limb.

Pathophysiology Pathophysiology is dependent on the type of second phalanx fracture. Larger caudal eminence fractures usually occur on the second phalanx, are often articular and can be biaxial. These fractures are distracted due to pull of the insertion of the collateral ligaments, flexor tendons and palmar annular ligaments.

Longitudinal and comminuted fractures of the second pastern bone are probably the most common fracture involving the pastern joint and can be catastrophic. Fractures of this short bone are high-energy injuries, usually from high-speed twists and turns with the foot planted. It is often reported that a loud 'pop' sound, like a gun going off, was heard and the horse was immediately non-weight bearing in the limb. Palpation can confirm the immediate pain, swelling and instability. Most P2 fractures are initiated at the pastern joint surface and spiral toward (incomplete) or into (complete) the distal interphalangeal joint (coffin joint). Fractures are often displaced and comminuted into five pieces in a classic pattern.[58]

Epidemiology

This injury may occur more commonly in Quarter Horses and jumpers, during slides, landings and turns.

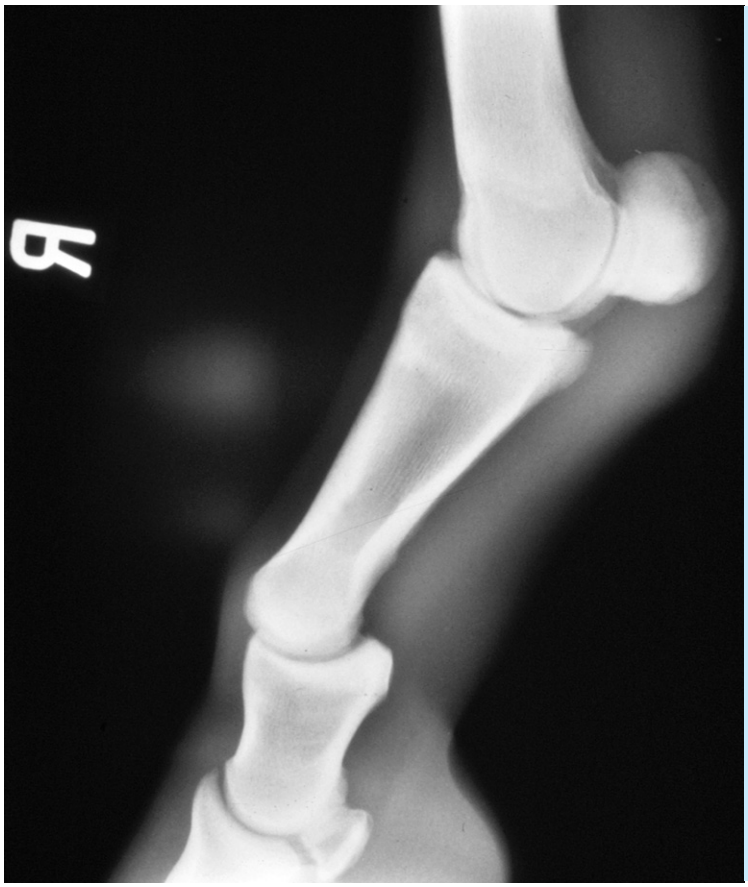


Fig. 16.21
Pastern luxation with typical dorsal displacement.

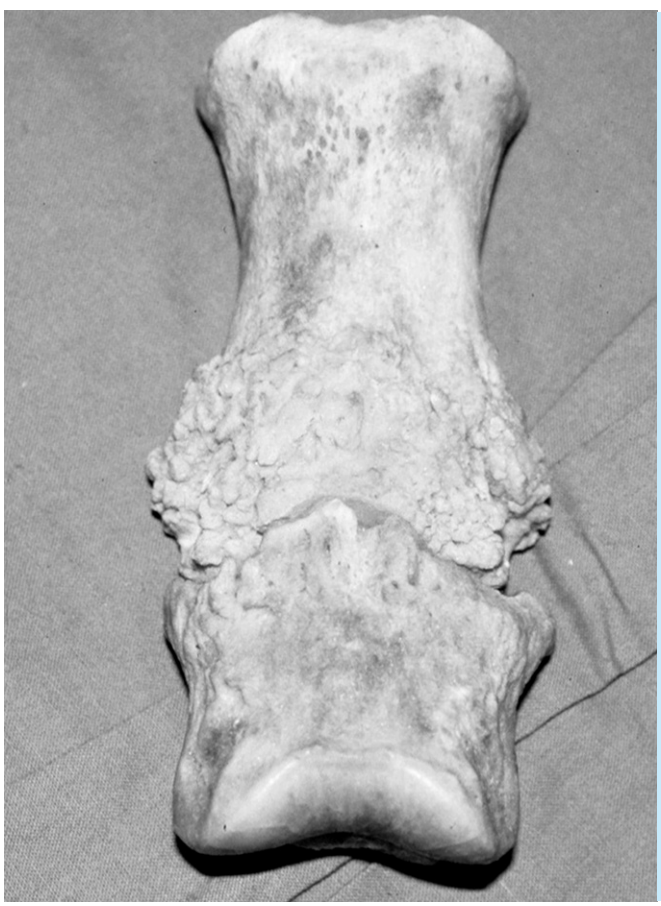


Fig. 16.22
Degenerative joint disease of the pastern joint demonstrating bony proliferation and joint destruction typical of ringbone.

Prevention

This injury is considered a sporadic and relatively random event that cannot be prevented.

Traumatic luxation/subluxation of the pastern joint

Traumatic luxation of the pastern joint usually occurs in front limbs with dorsal displacement of the first phalanx and is considered secondary to disruption of the insertion of the superficial digital flexor tendon and superficial distal sesamoidean ligament and palmar joint capsule[60] (Fig. 16.21). In the author's experience it is seen most commonly in event horses. This injury can appear similar to a fetlock breakdown injury in that the fetlock area drops upon weight bearing. However, closer observation reveals the distortion to the pastern with loading. The fetlock drops as the first phalanx moves dorsally. In complete luxations, similar complications can occur as with fetlock luxations. In subluxations, the pastern joint retains some stability although dorsal subluxation of the first phalanx is evident on palpation and radiograph.

Lameness depends on the degree of subluxation and disruption of the support structures of the pastern. Pastern arthrodesis is the treatment of choice as the outcome can be pasture and breeding soundness and possibly athletic soundness, depending on the extent of soft tissue injury to the flexor tendons. Use of strong implants and consideration of caudal joint wiring is recommended as the normal caudal support structures to the joint are disrupted. Repair should be approached in a similar manner to a fetlock luxation with loss of the caudal support structures.[22]

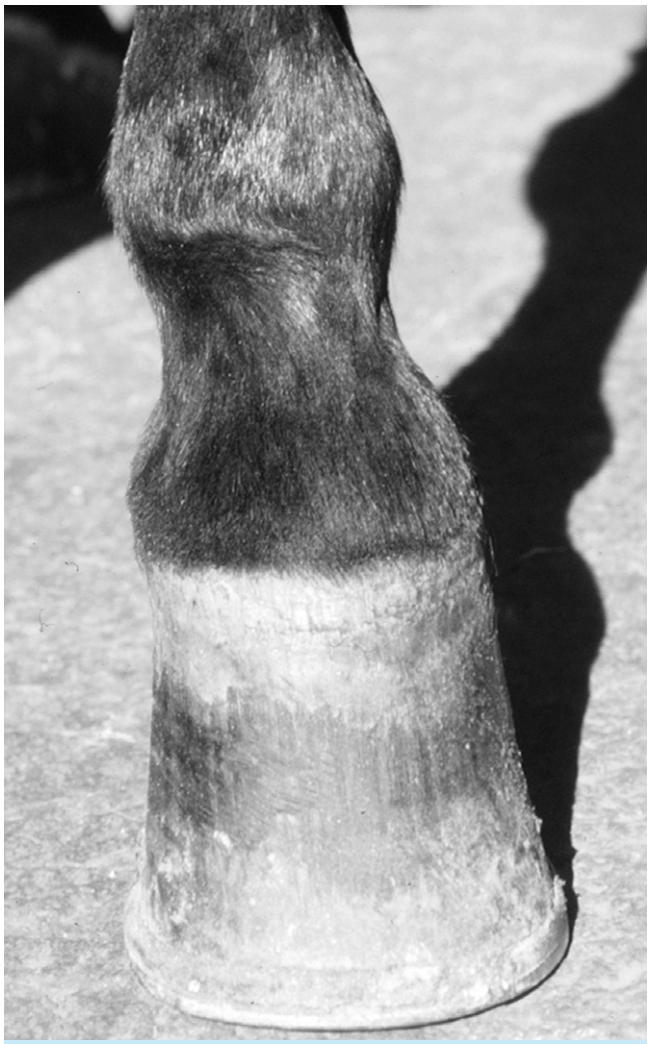


Fig. 16.23
Typical pastern joint appearance with high ringbone or pastern arthritis.

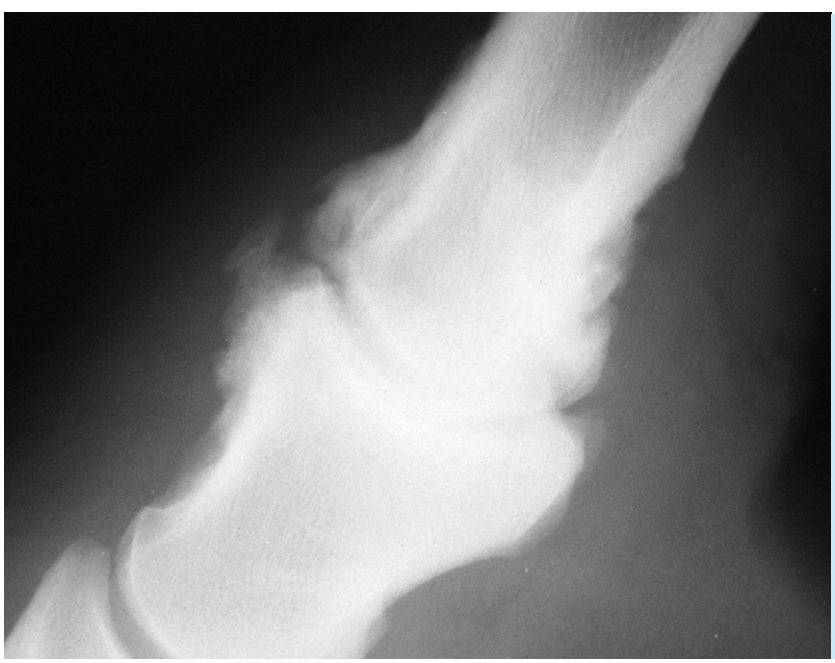


Fig. 16.24
Lateral radiograph of a pastern joint with arthritis demonstrating joint space narrowing and severe osteophytosis.

Pastern arthritis

Degenerative joint disease of the pastern joint is commonly called high ringbone or ringbone (Fig. 16.22).

Recognition

History and presenting complaint Horses are typically lame in one limb with a spontaneous onset. A traumatic etiology is often inferred. The lameness persists and pastern joint enlargement, although often overlooked, may be noted by the owner.

Physical examination Pastern arthritis has a classic outward appearance of an enlarged, thickened pastern joint (Fig. 16.23). Horses are lame often at the walk and are sore to flexion of the limb or joint.

Diagnostic confirmation The diagnosis is confirmed by radiography demonstrating osteophytes, narrowing of the joint space and subchondral bone sclerosis (Fig. 16.24).

Treatment and prognosis

Therapeutic aims The goal of therapy is to reduce pain and inflammation. To achieve athletic soundness, the joint must fuse.

Therapy Treatment with joint therapies is less successful in the pastern due to the greater degree of lameness, but non-steroidal anti-inflammatory medication improves movement and gait. Intra-articular steroids may improve comfort but often do not result in athletic soundness. Rest does not result in joint fusion. Resolution of lameness can be achieved with surgical pastern arthrodesis. Current procedures with plates and screws usually produce fusion within 6 months, even in older horses (Fig. 16.25). Assuming the pastern was the sole source of lameness, complete athletic soundness can be expected in > 80% of horses treated with surgical arthrodesis (Fig. 16.26). Current technique employs a combination of plates and screws for transarticular compression and stabilization.[61–64]

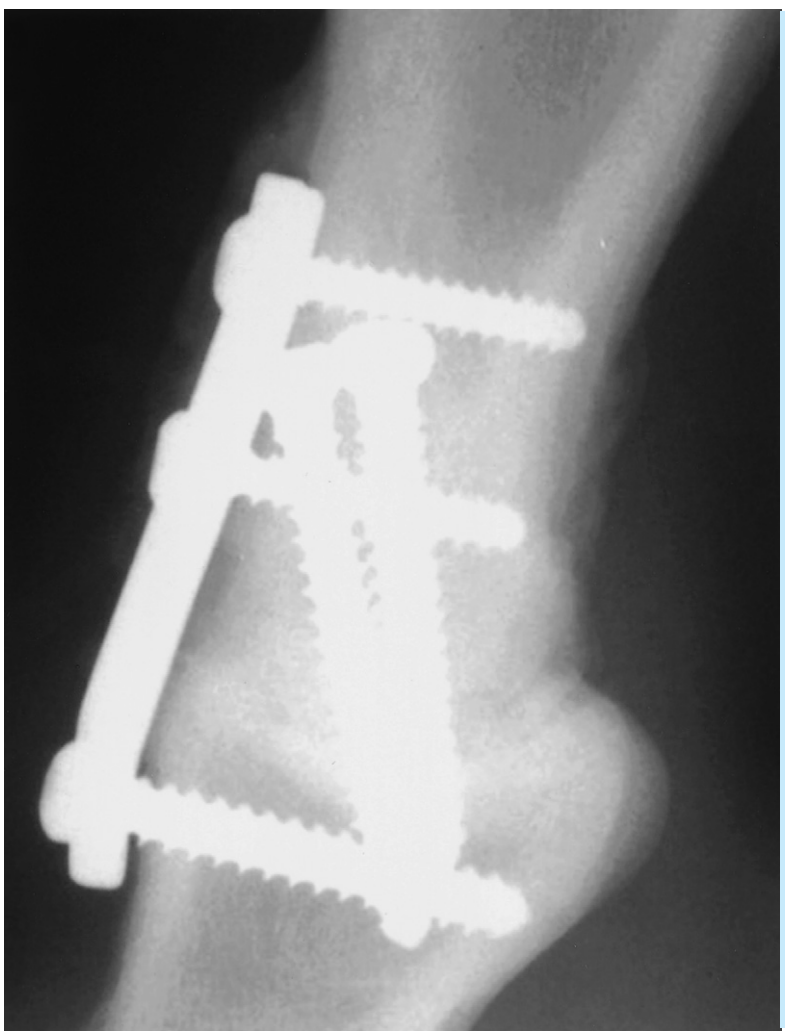


Fig. 16.25
Recommended surgical technique for pastern arthrodesis for adult horses is a single plate and two transarticular compression screws.

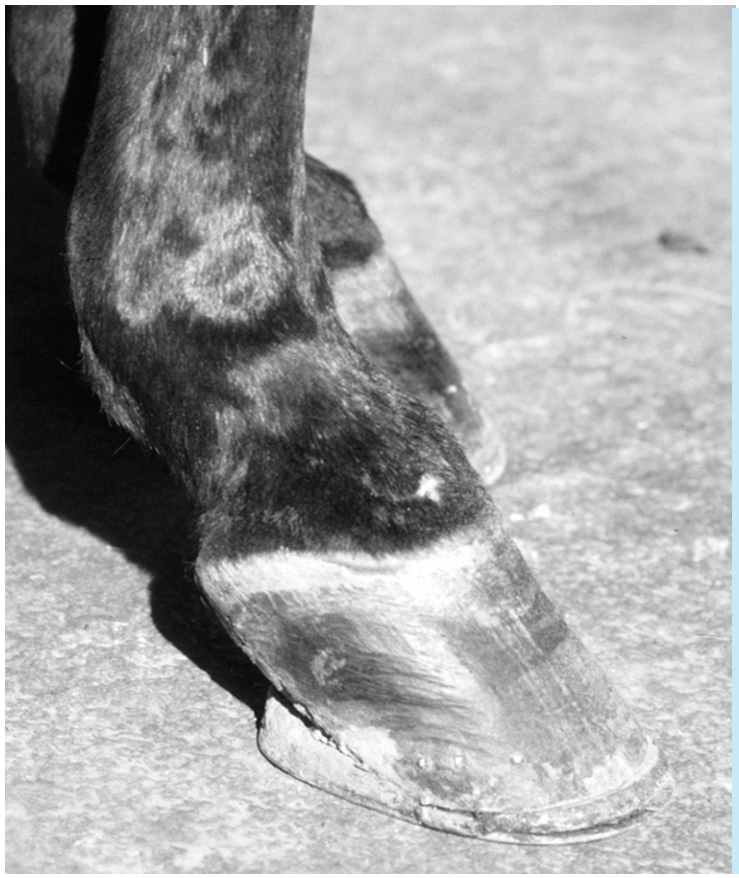


Fig. 16.26
Tennessee walking horse in full competition
2 years post-pastern arthrodesis of the right front. Pastern enlargement is minimal.

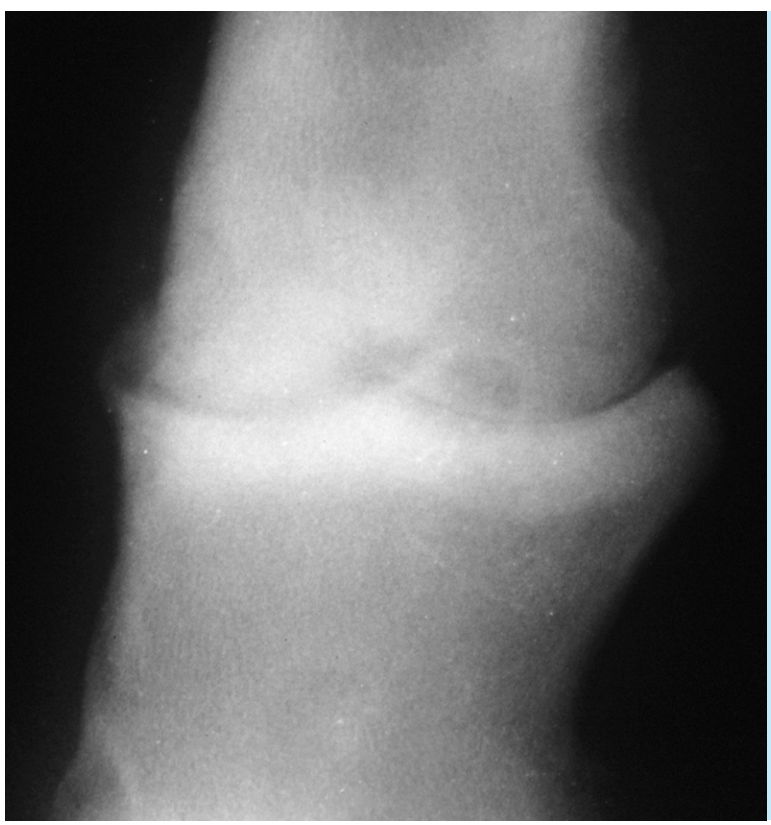


Fig. 16.27
Radiograph of pastern osteochondrosis demonstrating articular cysts and joint destruction.

Prognosis The prognosis is poor for soundness or fusion of the joint without surgical intervention. The pastern joint does not fuse on its own, even with extended time, in the author's experience.

Etiology and pathogenesis

Etiology Trauma and/or repetitive use are common inciting causes.
Pathophysiology Initial joint injury (fracture or sprain) results in joint inflammation and capsulitis. The process of persistent inflammation results in chronic joint destruction and degeneration.

Epidemiology

Although osteoarthritis of the pastern may not be as common as osteoarthritis of the fetlock, it is progressive and produces a greater degree of lameness in almost 100% of affected horses. Many horses with ringbone are lame at the walk and do not want to move around in pasture. Severe osteopenia of the affected limb and contralateral limb laminitis are complications of chronic ringbone.

Pastern osteochondrosis

Articular developmental orthopedic disease (osteochondrosis) occurs in the pastern joint.

Recognition

History and presenting complaint Lameness may be acute in onset and associated with heavy exercise or an incident, such as a fall, suggesting a traumatic etiology.

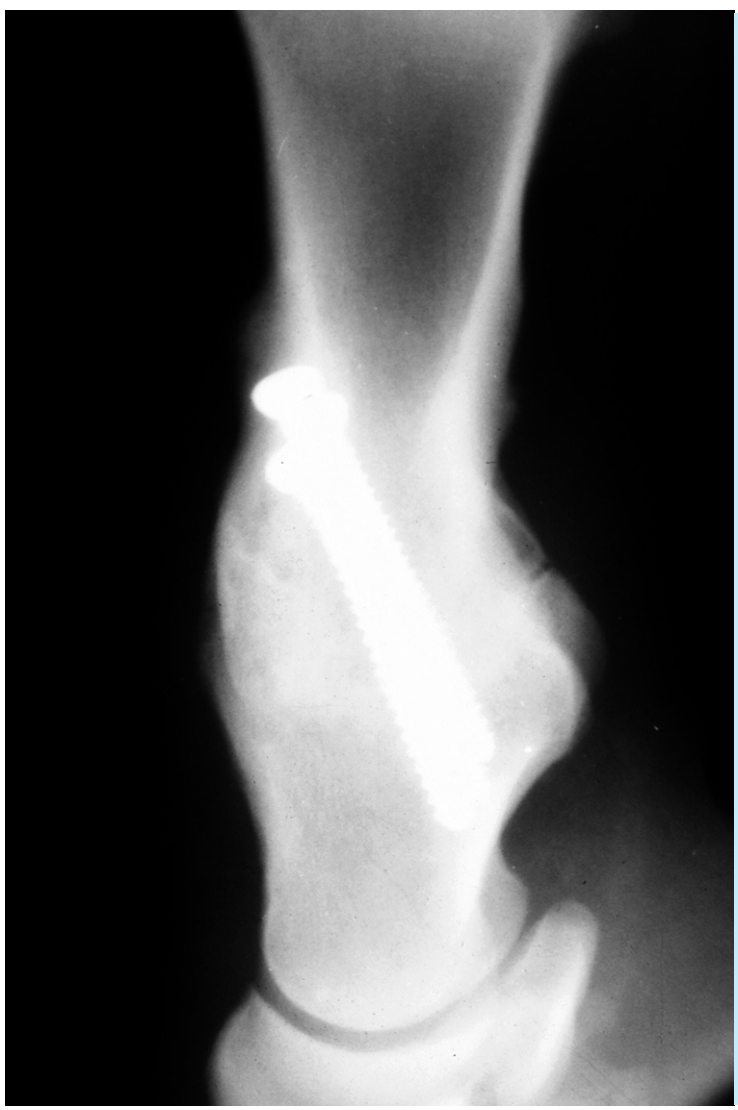


Fig. 16.28
Same horse as in Fig. 16.27 1 year after triple lag screw pastern arthrodesis, demonstrating complete bony fusion. The horse was sound for athletic use.

Physical examination Lameness and an enlarged pastern joint are the hallmark signs. Clinical signs occur most commonly in yearlings and become identical to osteoarthritis of the pastern (ringbone).

Diagnostic confirmation Radiographs demonstrate cysts on the articular surface and irregularity to the articular surface (Fig. 16.27). Osteophytes may not be present early on in the disease. The condition is often bilateral and contralateral radiographs are indicated before surgical treatment is considered.

Treatment and prognosis

Therapeutic aims The goal of therapy is to eliminate the lameness with joint fusion.

Therapy Preferable treatment is surgical arthrodesis[65] as has been described for pastern arthritis.

Prognosis In young horses, the possibility of full athletic soundness is excellent and fusion is relatively rapid (3–4 months) (Fig. 16.28). Left untreated, the joint will progress into osteoarthritis and lameness will persist.

Etiology and pathogenesis

Etiology Osteochondrosis is part of a developmental orthopedic disease complex.

Pathophysiology Endochondral ossification of articular cartilage is delayed or arrested, such that it forms abnormally. Articular cartilage flaps and cysts develop during growth, and joint pain and ultimately arthritis are a consequence.

Prevention

Although osteochondrosis has multifactorial risk factors, including high-energy diets, rapid growth and male gender, it is not possible to control the onset of clinical disease by controlling these factors. This is an active area of research.

References

1. Pettersson H, Ryden G. Avulsion fractures of the caudoproximal extremity of the first phalanx. Equine Vet J 1982; 14(4):333–335.
2. Hubert J, Williams J, Moore RM. What is your diagnosis? Avulsion fracture of the medial plantar eminence of the first phalanx; subluxation of the metatarsophalangeal joint resulting from avulsion of the insertion of the medial collateral ligament. J Am Vet Med Assoc 1998; 213(2):203–204.
3. Grondahl AM. Incidence and development of ununited proximoplantar tuberosity of the proximal phalanx in Standardbred trotters. Vet Rad Ultra 1992; 33(1):18–26.
4. Dabareiner RM, White NA, Sullins KE. Metacarpophalangeal joint synovial pad fibrotic proliferation in 63 horses. Vet Surg 1996; 25(3):199–206.
5. Yovich JV, McIlwraith CW. Arthroscopic surgery for osteochondral fractures of the proximal phalanx of the metacarpophalangeal and metatarsophalangeal (fetlock) joints in horses. J Am Vet Med Assoc 1986; 188(3):273–279.
6. Kawcak CE, McIlwraith CW. Proximodorsal first phalanx osteochondral chip fragmentation in 336 horses. Equine Vet J 1994; 26(5):392–396.
7. Colon JL, Bramlage LR, Hance SR, Embertson RM. Qualitative and quantitative documentation of the racing performance of 461 Thoroughbred racehorses after arthroscopic removal of dorsoproximal first phalanx osteochondral fractures (1986–1995). Equine Vet J 2000; 32(6):475–481.
8. Elce YA, Richardson DW. Arthroscopic removal of dorsoproximal chip fractures of the proximal phalanx in standing horses. Vet Surg 2002; 31(3):195–200.
9. Johnson BJ, Stover SM, Daft BM, et al. Causes of death in racehorses over a 2 year period. Equine Vet J 1994; 26(4):327–330.
10. Bertone AL. The fetlock. In: Stashak TS, ed. Adams' lameness in horses, 5th edn. Philadelphia, PA Lippincott, Williams and Wilkins; 2002; 8:768–796.
11. Torre K, Motta M. Incidence and distribution of 369 proximal sesamoid bone fractures in 354 Standardbred horses (1984–1995). Equine Pract 1999; 21(8):6–12.
12. Southwood LL, Trotter GW, McIlwraith CW. Arthroscopic removal of abaxial fracture fragments of the proximal sesamoid bones in horses: 47 cases (1989–1997). JAVMA 1998; 213(7):1016–1021.
13. Bertone AL. Fractures of the proximal sesamoid bones. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 16:163–171.
14. Parente EJ, Richardson DW, Spencer P. Basal sesamoidean fractures in horses: 57 cases (1989–1991). JAVMA 1993; 202(8):1293–1297.
15. Boure L, Marcoux M, Laverty S, Lepage OM. Use of electrocautery probes in arthroscopic removal of apical sesamoid fracture fragments in 18 Standardbred horses. Vet Surg 1999; 28:226–232.
16. Malone ED, Anderson BH, Turner TA. Proximal sesamoid bone fracture following cast removal in two horses. Equine Vet J 1997; 9:185–189.
17. Southwood LL, McIlwraith CW. Arthroscopic removal of fracture fragments involving a portion of the base of the proximal sesamoid bone in horses: 26 cases (1984–1997). JAVMA 2000; 217(2):236–240.
18. Henninger RW, Bramlage LR, Schneider RK, Gabel AA. Lag screw and cancellous bone graft fixation of transverse proximal sesamoid bone fractures in horses: 25 cases (1983–1989). JAVMA 1991; 199(5):606–612.
19. Martin BB, Nunamaker DM, Evans LH, et al. Circumferential wiring of mid-body and large basilar fractures of the proximal sesamoid bone in 15 horses. Vet Surg 1991; 20(1):9–14.
20. Woodie JB, Ruggles AJ, Litsky AS. In vitro biomechanical properties of 2 compression fixation methods for midbody proximal sesamoid bone fractures in horses. Vet Surg 2000; 29(4):358–363.
21. Rothaug PG, Boston BC, Richardson DW, Nunamaker DM. A comparison of ultra-high-molecular weight polyethylene cable and stainless steel wire using two fixation techniques for repair of equine midbody sesamoid fractures: an in vitro biomechanical study. Vet Surg 2002; 31(5):445–454.
22. Bramlage LR. Fetlock arthrodesis. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, Saunders; 1996; 17:172–178.
23. Bassage LH, Richardson DW. Longitudinal fractures of the condyles of the third metacarpal and metatarsal bones in racehorses: 224 cases (1986–1995). JAVMA 1998; 212:1757–1764.
24. Woodie JB, Ruggles AJ, Bertone AL, et al. Apical fracture of the proximal sesamoid bone in standardbred horses: 43 cases (1990–1996). JAVMA 1999; 214(11):1653–1656.

25. Trumble TN, Arnoczky SP, Stick JA, Stickle RL. Clinical relevance of the microvasculature of the equine proximal sesamoid bone. Am J Vet Res 1995; 56(6):720–724.
26. Markel MD, Richardson DW. Noncomminuted fractures of the proximal phalanx in 69 horses. J Am Vet Med Assoc 1985; 186(6):573–579.
27. Holcombe SJ, Schneider RK, Bramlage LR, et al. Lag screw fixation of noncomminuted sagittal fractures of the proximal phalanx in racehorses: 59 cases (1973–1991). J Am Vet Med Assoc 1995; 206(8):1195–1199.
28. Tetens J, Ross MW, Lloyd JW. Comparison of racing performance before and after treatment of incomplete, midsagittal fractures of the proximal phalanx in standardbreds: 49 cases (1986–1992). J Am Vet Med Assoc 1997; 210(1):82–86.
29. Dechant JE, MacDonald DG, Crawford WH. Repair of complete dorsal fracture of the proximal phalanx in two horses. Vet Surg 1998; 27(5):445–449.
30. Schneider RK, Ratzlaff MC, White KK, Hopper SA. Effect of three types of half-limb casts on in vitro bone strain recorded from the third metacarpal bone and proximal phalanx in equine cadaver limbs. Am J Vet Res 1998; 59(9):1188–1193.
31. Grondahl AM, Gaustad G, Engeland A. Progression and association with lameness and racing performance of radiographic changes in the proximal sesamoid bones of young standardbred trotters. Equine Vet J 1994; 26(2):152–155.
32. Clayton HM. Cinematographic analysis of the gait of lame horses II: chronic sesamoiditis. Equine Vet Sci 1986; 6:310–312.
33. Cornelissen BP. The proximal sesamoid bone of the horse; vascular and neurologic characteristics. Tijdschr Diergeneeskd 1998; 123(12):375–380.
34. Wisner ER, O'Brien TR, Pool RR, et al. Osteomyelitis of the axial border of the proximal sesamoid bones in seven horses. Equine Vet J 1991; 23(5):383–389.
35. Richardson DW, Nunamaker DM, Sigafoos RD. Use of an external skeletal fixation device and bone graft for arthrodesis of the metacarpophalangeal joint in horses. J Am Vet Med Assoc 1987; 191(3):316–321.
36. Cohen ND, Peloso JG, Mundy GD, et al. Racing-related factors and results of prerace physical inspection and their association with musculoskeletal injuries incurred in thoroughbreds during races. J Am Vet Med Assoc 1997; 211(4):454–463.
37. Kane AJ, Stover SM, Gardner IA, et al. Horseshoe characteristics as possible risk factors for fatal musculoskeletal injury of Thoroughbred racehorses. Am J Vet Res 1996; 57(8):1147–1152.
38. Yovich JV, Turner AS, Stashak TS, McIlwraith CW. Luxation of the metacarpophalangeal and metatarsophalangeal joints in horses. Equine Vet J 1987; 19(4):295–298.
39. Hubert J, Williams J, Moore RM. What is your diagnosis? Avulsion fracture of the medial plantar eminence of the first phalanx; subluxation of the metatarsophalangeal joint resulting from avulsion of the insertion of the medial collateral ligament. J Am Vet Med Assoc 1998; 213(2):203–204.
40. Simmon EJ, Bertone AL, Weisbrode SE. Instability-induced osteoarthritis in the metacarpophalangeal joint of horses. Am J Vet Res 1999; 60(1):7–13.
41. van der Harst MR, Rijkenhuizen AB. The use of polypropylene mesh for treatment of ruptured collateral ligaments of the equine metatarsophalangeal joint: a report of 2 cases. Vet Q 2000; 22(1):57–60.
42. Vickers KL, Ross MW. Atypical villonodular synovitis in a horse. J Am Vet Med Assoc 1996;209(9):1602–1603.
43. Roneus B, Andersson AM, Ekman S. Racing performance in standardbred trotters with chronic synovitis after partial arthroscopic synovectomy in the metacarpophalangeal, metatarsophalangeal and intercarpal (midcarpal) joints. Acta Vet Scand 1997; 38(1):87–95.
44. Kannegieter NJ. Chronic proliferative synovitis of the equine metacarpophalangeal joint. Vet Rec 1990; 127(1): 8–10.
45. van Veenendaal JC, Moffatt RE. Soft tissue masses in the fetlock joint of horses. Aust Vet J 1980;56(11):533–536.
46. Murphy DJ, Nixon AJ. Arthroscopic laser extirpation of metacarpophalangeal synovial pad proliferation in eleven horses. Equine Vet J 2001; 33(3):296–301.
47. McIlwraith CW. Diseases of joints, ligaments and related structures. In: Stashak TS, ed. Adams' lameness in horses, 5th edn. Philadelphia, PA: Lippincott Williams and Wilkins; 2002; 7:533–543.
48. Verschooten F, Picavet TM. Desmitis of the fetlock annular ligament in the horse. Equine Vet J 1986; 18(2):138–142.
49. Hawkins JF, Ross MW. Transection of the accessory ligament of the superficial digital flexor muscle for the treatment of superficial digital flexor tendinitis in standardbreds: 40 cases (1988–1992). J Am Vet Med Assoc 1995; 206(5):674–678.
50. Stanek C, Edinger H. Radiographic diagnosis of stricture of, or constriction by, the annular ligament of the equine fetlock. Pferdeheilkunde 1990; 6(3):125–128.
51. Bertone AL. Septic tenosynovitis. In: Dyson S, ed. Equine tendon injuries. Philadelphia, PA: Saunders; 1995; 163–177.
52. Fortier LA, Nixon AJ, Ducharme NG, et al. Tenoscopic examination and proximal annular ligament desmotomy for treatment of equine 'complex' digital sheath tenosynovitis. Vet Surg 1999; 28(6):429–435.
53. Honnas CM, Schumacher J, Cohen ND, et al. Septic tenosynovitis in horses: 25 cases (1983–1989). J Am Vet Med Assoc 1991; 199(11):1616–1622.
54. Gerring EL, Webbon PM. Fetlock annular ligament desmotomy: a report of 24 cases. Equine Vet J 1984; 16(2):113–116.
55. van den Berg MJ, Rijkenhuizen AB, Nemeth F, Gruys E. The fetlock tunnel syndrome: a macroscopic and microscopic study. Vet Q 1995; 17(4):138–142.
56. Rose PL, Seeherman H, O'Callaghan M. Computed tomographic evaluation of comminuted middle phalangeal fractures in the horse. Vet Radiol Ultrasound 1997; 38(6):424–429.
57. Dik KJ, van den Belt JM, Keg PR. Ultrasonographic evaluation of the fetlock annular ligament constriction in the horse. Equine Vet J 1991; 23(4):285–288.
58. Galuppo LD, Stover SM, Willits NH. A biomechanical comparison of double-plate and Y-plate fixation for comminuted equine second phalangeal fractures. Vet Surg 2000; 29(2):152–162.
59. Crabill MR, Watkins JP, Schneider RK, Auer JA. Double-plate fixation of comminuted fractures of the second phalanx in horses: 10 cases (1985–1993). J Am Vet Med Assoc 1995; 207(11):1458–1461.
60. Harrison LJ, May SA. Bilateral subluxation of the pastern joint in the forelimbs of a foal. Vet Rec 1992; 131(4):68–70.
61. Schaer TP, Bramlage LR, Embertson RM, Hance S. Proximal interphalangeal arthrodesis in 22 horses. Equine Vet J 2001; 33(4):360–365.
62. MacLellan KN, Crawford WH, MacDonald DG. Proximal interphalangeal joint arthrodesis in 34 horses using two parallel 5.5-mm cortical bone screws. Vet Surg 2001; 30(5):454–459.

63. Watt BC, Edwards RB 3rd, Markel MD, et al. Arthrodesis of the equine proximal interphalangeal joint: a biomechanical comparison of three 4.5-mm and two 5.5-mm cortical screws. Vet Surg 2001; 30(3):287–294.
64. Watt BC, Edwards RB 3rd, Markel MD, et al. Arthrodesis of the equine proximal interphalangeal joint: a biomechanical comparison of two 7-hole 3.5-mm broad and two 5-hole 4.5-mm narrow dynamic compression plates. Vet Surg 2002; 31(1):85–93.
65. Yovich JV, Stashak TS, Sullins KE. Bilateral pastern arthrodesis in a horse. Equine Vet J 1986; 18(1):79–81.

CHAPTER 17

Metacarpus/metatarsus

Lance H. Bassage II

Dorsal metacarpal disease (the 'bucked shins' complex)

'Bucked shins' or dorsal metacarpal periostitis and dorsal cortical stress fractures of the third metacarpus (MC-III) are the two components of dorsal metacarpal disease (DMD). Over the last 2–3 decades, extensive investigation into the etiopathogenesis of the condition – including the role of the training regimen, track surface and shoeing techniques – has led to a far greater understanding of the syndrome of DMD and how to prevent it. However, despite these advances, 'bucked shins' and dorsal cortical stress fractures remain important problems in the racing industry.

- Common in young Thoroughbreds and Quarter Horses in early race training.
- Bilateral dorsal metacarpal swelling, heat and pain, with stiffness/soreness or 'choppy-gaited' lameness.
- Acute onset following a high-speed workout ('breeze') or first race.
- Treatment involves anti-inflammatory therapy, rest and controlled exercise, and modified training.
- Prevention involves modification of the training regimen.
- Prognosis is generally very good to excellent and recurrence is rare in skeletally mature horses.
- Horses that develop clinical 'bucked shins' are at risk for dorsal cortical stress fractures in the future.

Recognition

History and presenting complaint

Horses with 'bucked shins' present with an acute onset of bilateral soft tissue swelling, heat and sensitivity over the dorsal aspect of the metacarpus, with an associated lameness or 'stiffness' immediately after a high-speed workout ('breeze') or race. Very often this is the first race or first speed work for the horse at near-racing distances. In some horses there may be a more gradual onset of these signs, with a marked exacerbation following the first race or a longer 'breeze'. If training continues the lameness typically worsens considerably, as opposed to the horse 'warming out of it'. The signs of 'bucked shins' are generally so specific that most experienced trainers can make a reliable diagnosis.

Physical examination

Horses with 'bucked shins' exhibit variable degrees of soft tissue swelling, heat and sensitivity on palpation over the dorsal diaphyses of MC-III. When viewing the metacarpi from the lateral aspect there is often a distinct dorsal convexity. Firm digital pressure in this location will elicit a painful response. These signs are particularly pronounced in the acute stages, but after a period of rest and anti-inflammatory treatment there is generally considerable improvement. The exceptions are horses that have progressed to the chronic or 'recurrent' category and have developed a marked periosteal reaction along with chronic inflammation and associated soft tissue swelling. Less commonly, a more focal area of swelling may be present at some point along the dorsal diaphysis,[1]

which must be differentiated from a true stress fracture (see section below).

Lameness examination

Horses with acute 'bucked shins' typically exhibit a bilateral stiff or choppy forelimb gait at a trot (sometimes mimicking a foot or carpal lameness), but in those in which one metacarpus is more severely affected than the other, a distinct head nod may be evident. Lameness in these horses ranges from grade 1 to 3.[2] The most severely affected horses may acutely exhibit mild lameness at the walk. The severity of the lameness will vary greatly with the stage of the disease and the timing of the examination in relation to the last speed work.

Diagnostic confirmation

Diagnostic analgesia Diagnostic analgesia is generally not necessary to localize the source of pain in a horse with acute 'bucked shins'. High palmar analgesia (high palmar nerve block) with a dorsal ring block in the proximal metacarpus can be helpful in confirming the location of pain in those horses with subacute or chronic 'bucked shins'.

Nuclear scintigraphy Bone-phase (delayed-phase) nuclear scintigraphy classically reveals *diffuse* moderate-to-intense abnormal increased radiopharmaceutical uptake along the dorsal diaphyses of the affected MC-III[3] (Fig. 17.1).

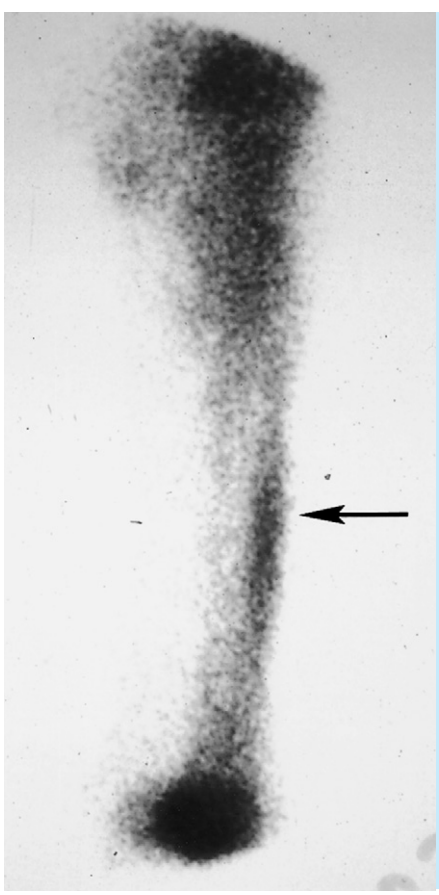


Fig. 17.1 Lateral bone-phase scintigraphic image of the right metacarpus of a 2-year-old Thoroughbred race horse with clinical 'bucked shins'. Notice the diffuse moderate-to-intense abnormal increased radiopharmaceutical uptake along the dorsal diaphysis of MC-III (arrow).

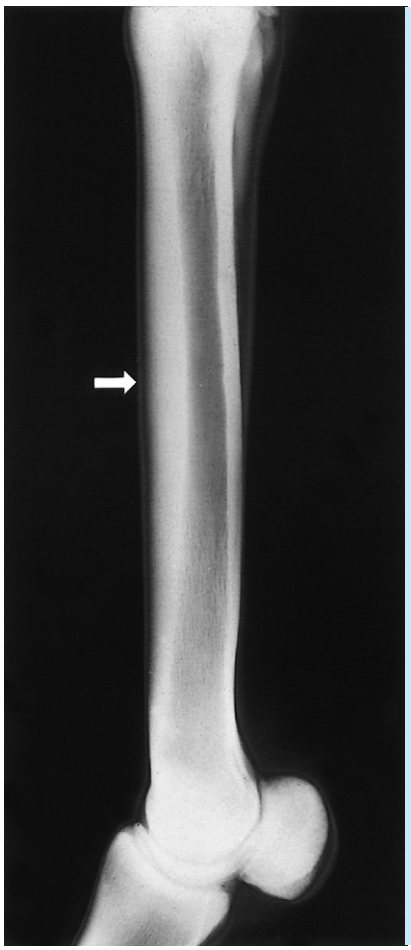


Fig. 17.2 Lateral radiograph of the left metacarpus of a 2-year-old Thoroughbred race horse with clinical 'bucked shins'. Notice the diffuse low-density periosteal proliferative reaction and subperiosteal osteolysis along the dorsal diaphysis of MC-III (arrow).

Radiography Radiographic findings vary with each case and the stage of disease. Radiographs in mildly affected horses or in the very early stages of the disease (subclinical) are often negative or equivocal for osseous abnormalities. In more severely affected horses diffuse subperiosteal osteolytic change in combination with smooth, low-density periosteal proliferative reaction is typically seen along the dorsal and dorsomedial diaphysis of MC-III (Fig. 17.2). High-detail radiographic or xeroradiographic films are superior for detecting the subtle abnormalities. Soft tissue swelling, when present, will also be evident radiographically in this location.

Thermography Thermography has recently been shown to be a valuable diagnostic aid for the detection of abnormalities in the metacarpi of racing Thoroughbreds, with up to 60% of 2 year olds in training exhibiting abnormal findings.[4]

Treatment and prognosis

Therapeutic aims

The goals of treatment for acute 'bucked shins' are two-fold: decrease or eliminate further excessive cyclic strains on MC-III and shift the balance from net bone resorption to net bone apposition, and reduce acute inflammation.

Therapy

Exercise restriction The degree of exercise restriction depends on several factors, of which the severity of clinical signs, in conjunction with radiographic and/or scintigraphic findings, is the most important.

Initially, all horses diagnosed with acute 'bucked shins' should be confined to a stall until soft tissue swelling and pain on palpation of the dorsum of MC-III have subsided. A program of controlled exercise can begin. In horses without extensive periosteal new bone formation or other severe radiographic changes, 2 weeks of stall rest with daily hand-walking (10–15 minutes once or twice a day) are initially recommended. Once horses are sound at a trot in-hand then formal training can commence, ideally employing a modified exercise protocol (see below).

Horses with moderate-to-marked periosteal reaction and/or subperiosteal osteolytic change, along with moderate-to-intense abnormal increased radiopharmaceutical uptake scintigraphically, require a more extended period of rest and controlled exercise. Generally, this encompasses 4 weeks of hand-walking, followed by 4–8 weeks of turnout exercise in a small paddock or 'shed row' exercise daily. The duration and extent of exercise restriction is modified based on the specifics of each case. Horses with chronic or recurrent 'bucked shins' (i.e. those that have had several acute episodes with or without an appropriate period of convalescence) should be allowed a total of 90–120 days' rest and in many instances they are simply turned out for the remainder of the season and training is resumed the following year.

Follow-up radiographic and scintigraphic examinations can help guide the recommendations for resumption of training in those cases where this is economically feasible.

Anti-inflammatory therapy Anti-inflammatory therapy should be initiated immediately in cases of acute 'bucked shins' and continue until signs of swelling and 'shin sensitivity' (pain) subside. Up to 30 minutes of cold hosing or icing, several times a day, along with bandaging, are generally effective. Anecdotally, application of a poultice or antiphlogistic dressing (e.g. Gel-o-cast®) for several days may also help decrease swelling.

The use of NSAIDs for their anti-inflammatory and analgesic effects in patients with inflammatory bone disorders is becoming increasingly controversial in light of the gathering body of evidence that these drugs, when used chronically at high doses, may impair bone healing in horses.[5] However, it is this author's opinion that a brief period (i.e. a few days) of NSAID treatment during the acute stage of 'bucked shins' is warranted in horses with moderate-to-severe signs. Phenylbutazone or flunixin meglumine at standard doses is generally effective. Long-term NSAID treatment is contraindicated, in this author's opinion, for the reasons noted above.

Modified training protocol The key to preventing 'bucked shins' is to stress the dorsal cortices of the developing metacarpi in such a way as to stimulate adaptation to the cyclic compressive loads under conditions that are similar to those experienced during a race, i.e. to train at racing speeds.[6] Traditional training strategies for flat-racing Thoroughbreds have employed a basic scheme of daily galloping exercise for extended distances (e.g. 1–2 miles) with speed work or 'breezes' at shorter distances (e.g. 2–6 furlongs) weekly to every third week. In immature (untrained) horses the timing (too infrequent) and distance (too long) of the high-speed work sets up a state of maladaptive remodeling in which bone resorption outpaces apposition and fibrous periosteal new bone predominates.[6] Eventually, this inferior bone develops microfractures and resulting inflammation, which manifests clinically as periostitis or 'bucked shins'.

To prevent or mitigate the potential for this vicious cycle, horses should be trained in such a way as to increase the frequency of high-strain cyclic compressive loading (high-speed exercise or 'breezes') and decrease the total distance at which they are galloped.[6] It is recommended that horses be worked at or near racing speed at least twice a week, initially at very short distances, for example 1 furlong. The distance of the speed work is increased gradually (e.g. adding 1 furlong every 1–2 weeks) and then as the horse is asked to go faster, the distance is reduced and the process repeated until the horse is conditioned to race. Throughout this process, daily galloping is limited,[6] for example to no more than 1 mile/day. Upon resumption of training, horses are continually monitored for signs of 'shin soreness', lameness or dorsal metacarpal swelling and exercise intensity should be modified accordingly.

Traditional or alternative therapies Over the course of time, seemingly endless 'traditional' therapies or essentially 'home remedies' have been promoted for treating 'bucked shins', as well as the many other inflammatory lesions and injuries of race horses. Many have gone by the wayside but a handful have persisted and remain in use today (see Table 17.1) and other 'alternative' therapies continue to arise on almost a daily basis. Unfortunately, many of these modalities have not undergone the necessary scientific scrutiny to enable rational conclusions regarding their efficacy. It is beyond the scope of this chapter to cover this subject in great detail but some of these therapies are summarized in Table 17.1.

Prognosis

The prognosis for the vast majority of horses with 'bucked shins' is generally very good if appropriate intervention is undertaken and adhered to. Recurrence is rare; however, a variable proportion of horses will experience repeated episodes or 'chronic' DMD. Horses not given adequate convalescence and those that have not had their training protocol modified (see above) are at high risk for recurrence. 'Bucked shins' is quite rare in older horses (> 4 years of age)[7] once the immature bone has remodeled and changed its inertial properties in response to the demands of high-speed exercise. However, horses that have experienced clinical 'bucked shins' as 2 or 3 year olds are in the high-risk group for dorsal cortical stress fractures (see section below).[8]

Table 17.1 Traditional and alternative therapies for metacarpal injuries

Modality	Technique	Rationale	Scientific support?	Comments
'Paints'	Topical application of a rubefacient liquid. (Numerous products and mixtures exist.)	Topical counterirritation to create hyperemia, which facilitates healing.	None for treating periostitis.	A reduction in soft tissue swelling is primarily attributable to the associated massage and bandaging.
'Blisters'	Topical application of a vesicant (agent causing cutaneous vesicles). As with 'paints', numerous products exist.	Potent counterirritation, creating deep hyperemia. Creates acute inflammation within chronically inflamed tissues to accelerate healing.	None for treating periostitis.	Any actual benefit is derived from the extended period of enforced rest, which traditionally accompanies 'blistering'.
'Pin firing'	Thermocautery: cutaneous application of a hot metallic rod or probe in multiple sites creating focal burns of varying depth.	A severe form of counterirritation.	None for treating periostitis.	As with 'blisters', the enforced rest is the primary benefit of 'pin firing'.
'Freeze firing'	Cryotherapy: cutaneous application of a liquid nitrogen-cooled metallic probe in multiple sites (similar to hot iron firing).	Method to create long-lasting local analgesia. Many practitioners consider this to be another method of creating counterirritation as well.	Scientific data support cryotherapy as having analgesic effects under certain circumstances. As with the above modalities, there is no evidence that counterirritation (if created) facilitates healing of periostitis.	Analgesia to the degree needed to mitigate that associated with 'bucked shins' is easily achieved using ice, cold water and NSAIDs. Analgesia to enable continued training is of questionable merit as the premature resumption of exercise is contraindicated.
Periosteal 'picking'	Percutaneous irritation of the periosteum in multiple sites using a hypodermic needle. (The periosteum is picked or scratched with the needle tip.)	A form of counterirritation involving direct periosteal trauma purported to accelerate healing of periosteal microfractures.	No specific studies on healing of metacarpal periostitis. In general, induced periosteal trauma does stimulate a proliferative response.	All reports on the efficacy of this treatment remain anecdotal. Further periosteal trauma is unnecessary in acute cases of 'bucked shins'.
Blood injection	Injection of an autogenous blood sample subcutaneously/ supraperiosteally in the dorsal metacarpus.	Another variation on counterirritation. Purported to accelerate healing.	None for treating periostitis.	All reports on the efficacy of this treatment remain anecdotal.
Extracorporeal shockwave therapy	Application of high-frequency shockwave energy along the dorsal metacarpus using a customized handpiece or probe.	A form of deep counterirritation purported to accelerate bone healing.	No *controlled* studies for treatment of periostitis in horses. Increasing anecdotal evidence suggests this modality *may* have a positive effect on bone healing.	Further 'stimulation' is unnecessary for the healing of acute periostitis. This modality may have merit for treating chronic DMD/stress fractures, but further investigation is needed.

Etiology and pathophysiology

The reader is referred to the chapter on stress-induced bone disease and maladaptive remodeling syndromes (Chapter 7) for a detailed discussion of this topic.

Epidemiology

Historically, DMD and, more specifically, 'bucked shins' have been and continue to be an extremely common problem in young flat-racing horses in early training. In the US, a prevalence of 65–70% in Thoroughbreds has been reported[12,13] and in Australia the prevalence has been estimated at 42–80%.[14–16] Similarly, estimates of 5–50% have been given for the prevalence in racing Quarter horses in the US.[17] DMD also affects racing Arabians. In contrast, the incidence of DMD is comparatively low in the UK, with an estimate of 17% in young Thoroughbreds in one large study.[10] This difference could be attributed to a number of variables, but differences in training surface (predominantly grass in the UK and predominantly dirt in the US) are regarded by many to be a primary factor.[9]

In stark contrast is the very low incidence of DMD in Standardbred race horses.[12] This has been attributed to differences in speed and gait between Standardbreds and Thoroughbreds, which result in different strains imposed on MC-III, and not to an inherent difference in bone material properties between the breeds.[18]

Prevention

The most effective way to prevent or decrease the incidence of 'bucked shins' is to modify the training scheme as outlined previously (see under Therapy). Essentially, this involves decreasing the daily distance worked at a gallop and increasing the frequency of short intervals of high-speed work or 'breezes'. The distance of the speed work is initially very short and is increased gradually.

Different training surfaces may also affect the incidence of 'bucked shins'. Training on wood chip-based surfaces or grass appears to be superior to the traditional dirt of most tracks in the US.[9,10] For example, in one 2-year study of Thoroughbred race horses, 55.8% of those trained on dirt experienced 'bucked shins' compared to only 26.1% of those trained on a wood chip-based surface.[9] This study did not rigidly control for differences in training methods, however.

Prevention also involves close monitoring of the horse for signs of impending shin problems. Along with physical examination for shin soreness, thermography and scintigraphy are useful imaging modalities for screening high-risk horses. In one study, pre-race detection using physical examination to screen horses for signs of DMD resulted in reduction in post-race diagnoses of lameness attributable to DMD, and more predictable race results, on Thoroughbred tracks in Australia.[11]

Dorsal cortical stress fractures of MC-III ('saucer fractures', metacarpal fatigue fractures)

- Fatigue fractures seen in racing Thoroughbreds, Quarter Horses and Arabians.
- Horses experiencing previous 'bucked shins' are at high risk.
- Short, oblique, intracortical fracture seen most commonly in the mid-diaphysis of the left MC-III (in Thoroughbreds in the US).
- Acute onset of moderate-to-severe lameness following high-speed work ('breeze') or a race.
- Fractures are often slow to heal and chronic or recurrent fractures are common if initially undiagnosed or mismanaged.
- Surgical treatment is preferred for the majority of fractures and involves osteostixis, screw fixation or a combination of the two.
- Prognosis is generally very good for return to racing.
- New or recurrent fractures develop on occasion.

Recognition

History and presenting complaint

Horses with an acute dorsal cortical stress fracture of MC-III typically exhibit a moderate-to-severe lameness immediately following high-speed work ('breeze') or a race. Less commonly, the lameness will not be evident until several hours after the horse has 'cooled out'. Acutely, these horses are too lame to continue training. There is almost invariably a focal area of soft tissue swelling, focal periosteal irregularity and sensitivity at the fracture site along the dorsal aspect of MC-III.

Some horses have a history of low-grade, chronic or intermittent lameness on the affected limb for several weeks prior to the acute onset of a more severe lameness once overt fracture has occurred. Another subset develops signs of acute fracture upon resumption of training after a brief period of lay-up (a few to several weeks) for an unrelated illness or injury.

Some horses may become sound enough to train or even race after extended rest, but continue to be plagued by recurrent lameness and poor performance. This is a common scenario for those with chronic stress fractures that have gone undiagnosed. Almost all horses with dorsal cortical stress fractures of MC-III will have a history of clinical 'bucked shins' in the 6–12 months preceding the fracture.[19]

Physical examination

For horses with acute fracture, physical examination will classically reveal a focal area of soft tissue swelling along the dorsum of the metacarpus at the site of the fracture, with a corresponding bony 'knot' or periosteal irregularity (hard swelling or exostosis) along the dorsal or dorsolateral diaphysis of MC-III. Firm digital pressure at the fracture site will consistently elicit a painful response. These signs are less dramatic in horses with chronic or subacute fractures. Horses with multiple fractures may have signs more suggestive of 'bucked shins' (i.e. diffuse pain and swelling along the diaphysis). Fractures are almost always unilateral in Thoroughbreds (in contrast to 'bucked shins') and involve predominantly the left forelimb in the US.[20–23] Bilateral fractures occur, but are rare.

Lameness examination Acutely, horses exhibit a moderate-to-severe lameness on the affected limb, which is typically grade 3–4.[2] Many are lame at a walk and all are profoundly lame at a trot. With a brief period of rest (a few days to a few weeks), horses generally walk comfortably but exhibit a mild-to-moderate lameness at a trot in-hand (grade 2–3). Horses with chronic fractures may exhibit only mild lameness at a trot in-hand. Firm pressure applied over the fracture site will exacerbate the lameness in most acute and subacute cases.

Diagnostic confirmation

Diagnostic analgesia Diagnostic analgesia is rarely necessary to localize the source of lameness in horses with acute and subacute dorsal cortical stress fracture of MC-III (owing to the specificity of clinical signs) and in fact, it is arguably contraindicated in these horses. Diagnostic analgesia *can* be useful for this purpose in horses with chronic fractures when clinical signs are less specific. High palmar analgesia (a 'high palmar block') will be positive.

Scintigraphy Bone-phase (delayed-phase) nuclear scintigraphy will reveal a *focal* (or multifocal in horses with multiple fractures) area of moderate-to-intense abnormal increased radiopharmaceutical uptake in the dorsal diaphysis of the affected MC-III in acute and subacute cases (Fig. 17.3). The intensity of radiopharmaceutical uptake will be less intense in chronic cases and will vary with the time course of the injury.[3]

Radiography The classic radiographic abnormality is a short, oblique intracortical (unicortical) fracture line in the dorsal or dorsolateral cortex of MC-III (Fig. 17.4). Most commonly the fractures are diaphyseal and are oriented dorsodistal to palmaroproximal at a 30–45° angle with the dorsal cortex. Most extend to the junction of the middle and palmar third of the dorsal cortical width and do not enter the medullary cavity. Occasionally, a complete fracture will extend proximodorsally out through the dorsal cortex (a true 'saucer fracture'). Metaphyseal fractures, those that begin and propagate in a dorsoproximal-to-palmarodistal direction, and those that enter the medullary cavity are less common.

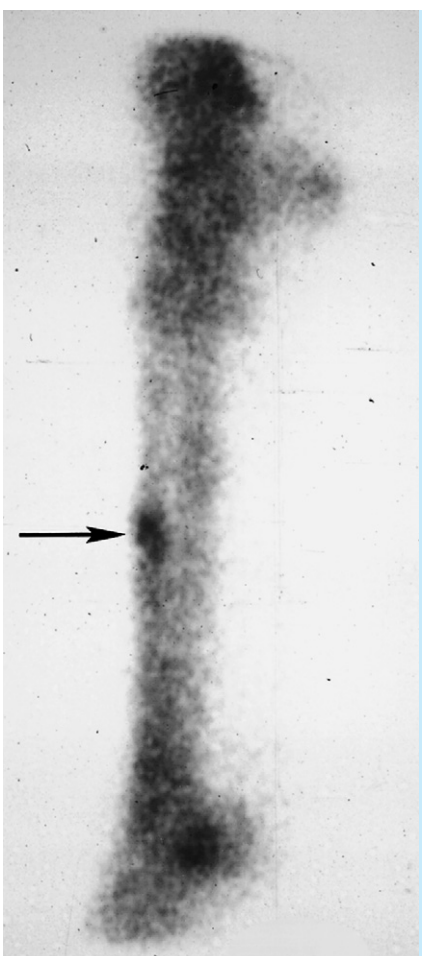


Fig. 17.3 Lateral bone-phase scintigraphic image of the left metacarpus of a 3-year-old Thoroughbred race horse with a dorsal cortical stress fracture of MC-III. Notice the focal area of moderately intense abnormal increased radiopharmaceutical uptake in the dorsal cortex (arrow).

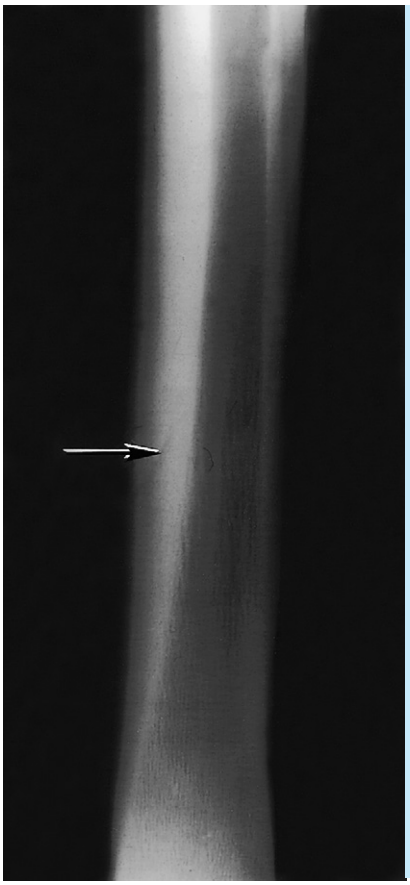


Fig. 17.4 Lateral radiograph of the left metacarpus of a 3-year-old Thoroughbred with a typical dorsal cortical stress fracture (arrow).

A full series of radiographs (four views: lateral, dorsopalmar, DMPLO and DLPMO) of the entire MC-III should be taken. Multiple fractures are sometimes present. In rare cases fracture lines may propagate or radiate away from the primary fracture site.[24] The majority of fractures are oriented in a frontal or near-frontal plane, but occasionally sagittally oriented fractures are seen.[25] Variable degrees of periosteal and endosteal callus may be present, as will soft tissue swelling and more diffuse osteolytic and proliferative periosteal reaction associated with previous 'bucked shins' in many horses.

Radiographs may be negative in acute cases. As with other stress fractures, high-detail radiographic films or xeroradiographs are advantageous for detecting subtle cortical abnormalities. When initial radiographs are negative or have equivocal findings, and clinical signs and/or scintigraphic findings are highly suggestive of stress fracture, follow-up radiographs should be taken in 7–10 days.

Treatment and prognosis

Therapeutic aims

The primary goal of treatment for dorsal cortical stress fractures of MC-III is to promote fracture healing and, although uncommon, minimize the potential for catastrophic fracture.

Therapy

Complete cessation of exercise (stall confinement) and anti-inflammatory treatment are the initial steps in the immediate postfracture period. A light padded bandage and local cold therapy (hosing/icing as previously described), along with NSAID treatment for a few days, are helpful to reduce soft tissue swelling and improve comfort in the acute phase.

Non-surgical management There is debate among clinicians regarding the merits of surgical and non-surgical management of dorsal cortical stress fractures of MC-III. These fractures are notorious for being slow to heal or for following an unpredictable course between horses.[12,19] Fractures in younger horses (2 and 3 year olds), those that enter the medullary cavity or that involve the metaphyseal regions are the most likely to heal expediently without surgical intervention. In general, this involves a period of 3–4 months of controlled exercise; however, it is not unusual for some fractures to require 4–6 months or longer for satisfactory healing.[26]

When non-surgical management is chosen, 4–6 weeks of stall confinement with daily hand-walking is recommended. This is followed by 6–8 weeks of controlled exercise in the form of small paddock turnout or very light jogging. Some form of controlled exercise is important to stimulate remodeling and fracture healing.[20,21] Complete cessation of exercise for a prolonged period (e.g. long-term stall confinement) favors the development of a chronic fracture (i.e. a delayed or non-union).

Follow-up radiographs should be taken every 4–6 weeks to assess healing before increasing the intensity of exercise or for determining whether surgical intervention is warranted (to overcome delayed healing). Follow-up scintigraphic scans can also help in making these decisions.[3] A radiographically visible fracture exhibiting low or diminishing scintigraphic activity would warrant strong consideration as a candidate for surgery.

Surgical management With the above exceptions, the majority of horses with acute dorsal cortical stress fractures of MC-III, and *all* horses with chronic fractures, are candidates for surgical intervention. Surgical treatment stimulates healing, thereby assuring a more rapid and predictable convalescence, and in the hands of an experienced surgeon carries a low rate of complications.

Surgery involves either osteostixis (fenestration), screw fixation (either positional or compression) or a combination of the two. One clear disadvantage of screw fixation over osteostixis alone is the need for a second surgical procedure to remove the screw. For any technique, the procedure can be performed with the horse under general anesthesia or standing under sedation and using local anesthesia (high palmar analgesia with a dorsal ring block). This author prefers sedation and local anesthesia unless the temperament of the horse is exceptionally fractious. There is a slight increase in risk for non-catastrophic complications (e.g. contamination/infection or drill bit or tap breakage if the horse moves unpredictably), but the risk of catastrophic fracture during recovery, although rare, and other potential anesthetic-related problems is eliminated and the overall length of the procedure is minimized.

The surgical approach is similar with any method, although if just a single screw is being placed some surgeons elect to perform this through a small stab incision. After routine aseptic preparation and draping, the fracture should be localized using radiopaque markers. (In many cases it is not possible to accurately identify the fracture simply through surgical exposure and periosteal elevation.) A row of stainless steel skin staples or hypodermic needles inserted perpendicular to the skin is placed along the dorsal metacarpus in the region of the fracture and a lateral (or slightly oblique if appropriate) radiograph is taken.

Osteostixis A 4–6 cm longitudinal incision is created between the digital extensor tendons, centered over the fracture, and extended through all tissues, including the periosteum, in a single cut. Self-retaining retractors (Gelpi, sharp Weitlaner) are used to maintain exposure and the periosteum is elevated. Four to six holes in a diamond pattern are then drilled across the fracture line perpendicular to the long axis of MC-III and entering the medullary cavity, using the preplaced markers as a guide. It is appropriate to monitor hole placement radiographically and therefore a radiograph should be taken after the first hole is drilled to ensure proper location. Successive holes are then drilled using the first hole as a reference point.

Drill bit preference varies with surgeon but 2.5–3.5 mm diameter bits are appropriate. Smaller bits (e.g. 2.0 mm) are more easily broken in the standing patient and larger holes may unnecessarily weaken the bone, as does an excessive number of holes.[27] Distance between holes should be kept at approximately 1.0 cm. A large number of holes placed close together can result in sequestrum formation or resorption of a core of bone or significantly weaken MC-III. Copious lavage during drilling, and frequent cleaning of the bit, are important to minimize the potential for the bit to break. After final radiographic confirmation of adequate hole placement the extensor tendons, subcutaneous fascia and skin are closed routinely in separate layers and a padded bandage is applied.

Horses are confined to a box stall for a total of 4–6 weeks following surgery. Skin sutures are removed 12–14 days postoperatively, at which time daily hand-walking exercise should commence. A bandage is maintained for 2–3 weeks after surgery. After this period of stall confinement and hand-walking, horses are allowed daily turnout exercise in a small paddock for 4 weeks. If at that point follow-up radiographs reveal good progression of healing, daily light jogging exercise can begin. Harder training should not commence until fractures have sufficiently healed radiographically. Drill holes may persist radiographically for many months (beyond the point of fracture healing), even while horses are training at speed. Based on studies in other species[28] and on clinical observation in horses,[21] it is assumed that these holes should no longer act as stress risers by that stage.

Osteostixis is believed to accelerate or promote healing by facilitating access of mesenchymal cells and other osteogenic medullary elements to the fracture line.[7,29] The 'cores' of new bone that form across the fracture line may act to stabilize the fracture and further promote healing.[30] Osteostixis may also

stimulate fracture healing through activation of the 'regional acceleratory phenomenon'.[31]

Screw fixation If osteostixis is to be employed along with screw placement, the surgical approach is identical to that described above. If a single screw is being used without osteostixis a smaller (~1.0 cm) 'stab' incision can be used. A 3.5 or 4.5 mm ASIF cortical screw is appropriate. Regardless of the technique, either compression ('lag screw') or positional ('neutral'), screws are placed in a unicortical manner. Transcortical screws that engage the palmar cortex are contraindicated and no longer recommended, as they are associated with a higher incidence of osteolysis around the implant and implant-associated pain,[12] as well as fracture and the risk of suspensory ligament damage during placement.[32]

Unicortical screws placed in lag fashion to create compression provide the greatest degree of stability, but the technique is challenging given the width of the fragment/cortex. Standard ASIF techniques are employed and great care is required to ensure adequate position and depth of the glide hole. Once the glide hole is created the pilot hole is drilled and tapped, the hole is countersunk and a screw of appropriate length is inserted. Screws should be placed as close to perpendicular to the fracture line as possible. For positional screw placement the technique is similar but a glide hole is not created. Osteostixis, if employed, is then performed as previously described and the incision is closed routinely (skin sutures may only be necessary for smaller stab incisions).

Bandaging and initial aftercare are similar to that described for osteostixis. Screw removal is usually performed between 2 and 3 months after surgery. Proponents of the combination of a positional screw and osteostixis feel that 2 months is generally adequate.[20] The decision for screw removal is based on adequate progression of healing on follow-up radiographs. Screws are removed with the horse standing and using sedation and local anesthesia. An additional period of controlled exercise is recommended before resuming training following screw removal. This period varies from 2 to 8 weeks.[20,33] Unicortical screws in the dorsal cortex of MC-III do not cause pain in all horses upon resumption of training and return to racing.[32] However, screw removal in the early postoperative phase (i.e. at the 2–3 month point) obviates the need to take the horse out of training if pain develops and it eliminates the screw being implicated as the cause for any number of unrelated problems in the future.

The benefits of interfragmentary screw compression ('lag screw' technique) in fracture healing are quite clear and well understood. The mechanisms by which a neutral or positional screw acts specifically to promote or accelerate healing of stress fractures of the dorsal cortex of MC-III remain incompletely understood. In a recent uncontrolled study,[20] dorsal cortical stress fractures of MC-III treated surgically by a combination of screw fixation using a positional (non-compression) screw and osteostixis were reported to heal faster (95% of fractures healed in 2 months) than fractures treated with osteostixis alone (3–4 months for radiographic healing).[21,23] Differences in postoperative exercise regimens between studies may have influenced the results, but interfragmentary stabilization and the 'regional acceleratory phenomenon' have been proposed as mechanisms by which screws facilitate fracture healing over osteostixis alone.[20]

Prognosis

The prognosis for horses to return to racing following healing of dorsal cortical stress fractures of MC-III is generally very good. Eighty-two to 89% of Thoroughbreds in the US returned to race at least once following osteostixis.[21–23] One report on the outcome following screw fixation and osteostixis in Thoroughbreds indicated that 94% raced at least once postoperatively.[20] The majority of horses in all studies returned to compete at their prefracture levels.

A small percentage of horses experience repeat fracture or new fractures upon resumption of training and racing, regardless of treatment modality.[20,21] Recurrent fractures presumably result from inadequate healing (i.e. delayed union) and this may occur up to a year or more following treatment and return to training. New fractures developing at the site of an osteostixis hole have been reported.[21] Development of new fractures may also be related to training methodology in these horses (see below). Catastrophic fracture upon resumption of training and racing, although uncommon, has also been reported in Thoroughbreds.[22]

Etiology and pathophysiology

Dorsal cortical stress fractures of MC-III are a classic example of fatigue fractures that result from failure of bone to adapt to accumulated high-strain cyclic loading.[34,35] The reader is referred to the chapter on stress-induced bone disease and maladaptive remodeling syndromes (Chapter 7) for a detailed discussion of this topic.

Epidemiology

See the previous section on 'bucked shins' for additional details of the epidemiology of DMD.

Almost all Thoroughbreds with dorsal cortical stress fractures of MC-III experience a previous episode of clinical 'bucked shins'[19] and the same observation has been made in Quarter horses.[1] It has been estimated from older studies that 10–15% of Thoroughbreds which develop 'bucked shins' will go on to experience a true stress fracture in 6–12 months.[12,19] Therefore, this subgroup of DMD cases in Thoroughbreds is slightly older than the 'bucked shins' group, typically 3–5 years of age, but even horses older than 5 occasionally present with this injury. In contrast, dorsal metacarpal stress fractures in Quarter horses are seen predominantly in 2 year olds.[1]

In Thoroughbreds, these fractures appear to be more common in males than females,[20–23] but whether this simply reflects a referral bias or a true physiologic difference between males and females remains incompletely understood.[21,36,37]

Fractures most commonly involve the left forelimb in Thoroughbreds in the US (72–91%).[20–22] This has been

attributed to increased strains on this limb as a result of the counterclockwise direction of racing in this country.

Prevention

The reader is referred to the discussion of DMD prevention under 'bucked shins' (previous section) for details on the role of training modification and altering training surfaces.

Prevention of stress fractures in horses with DMD also involves early detection of bone disease or the 'prefracture state'. In addition to a high index of suspicion that should be maintained for horses that have experienced an earlier episode of 'bucked shins', careful physical examination and the use of diagnostic imaging modalities such as nuclear scintigraphy and thermography to detect prefracture pathology should enable identification of horses at risk of impending fracture.

Condylar fractures (parasagittal or longitudinal fractures of the distal third metacarpus and metatarsus)

- Condylar fractures are high-speed injuries affecting race horses of all breeds.
- The lateral condyles in the forelimbs of young Thoroughbreds are most commonly affected.
- Condylar fractures are presented as an acute injury during or shortly after a race or workout.
- Horses are markedly lame and clinical signs are highly consistent with a fetlock injury.
- Surgical treatment involves interfragmentary screw compression.
- Some non-displaced fractures can be managed non-surgically with a favorable outcome.
- The prognosis for return to racing for most horses with non-displaced lateral condylar fractures is favorable.
- The prognosis for most horses with displaced lateral condylar fractures is guarded.
- Medial condylar fractures are associated with a significant risk for catastrophic fracture of the affected bone.
- Treatment of medial condylar fractures may necessitate supplemental internal fixation to mitigate catastrophic failure.
- The prognosis for future athletic soundness for most horses with medial condylar fractures is favorable if catastrophic fracture is avoided.

Condylar fractures are common high-speed injuries in race horses of all breeds.[38–43] However, they most commonly affect the lateral condyle of MC-III in Thoroughbreds[39,42,43] and are only rarely seen in non-race horses.

Fractures can involve the medial or lateral condyles. Lateral fractures are categorized as incomplete, complete/non-displaced or complete/displaced. Medial condylar fractures fall into three categories: 'short' (simple, sagittally oriented fractures involving only the distal metaphysis/diaphysis); 'spiral' (fractures that propagate proximally in a spiral configuration and remain a simple fracture); and 'Y fractures' (long sagittal fractures that abruptly change configuration or direction in the mid-diaphysis) (Fig. 17.5).

Recognition

History and presenting complaint

The classic presentation of a horse with a condylar fracture is an acute onset of moderate-to-severe lameness during or immediately after a race or high-speed work. In most cases the rider or driver is immediately aware that the horse has sustained an injury. In others, the horse successfully finishes the race or workout with lameness immediately obvious after pulling up (slowing down). Less commonly, the injury will not become apparent until several hours after the horse has 'cooled out' or even until the following day. Acutely, most horses exhibit lameness of varying degrees at a walk. Joint effusion and periarticular soft tissue swelling may also be noted.

The vast majority of horses are not able to continue training. On rare occasions a horse with a chronic fracture (generally short and incomplete) will be presented with a history of recurrent lameness and/or poor performance that is exacerbated with exercise. Some horses have a history of seemingly minor or low-grade 'soreness' on the affected limb or other concerns of an 'ankle problem', for several days or weeks prior to overt acute fracture (see discussion of pathophysiology below).

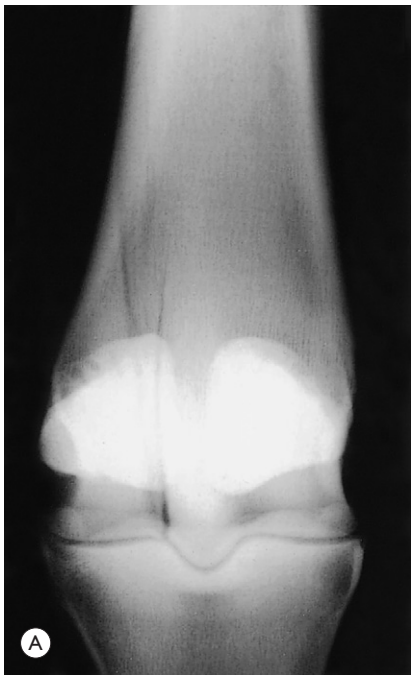
Physical examination

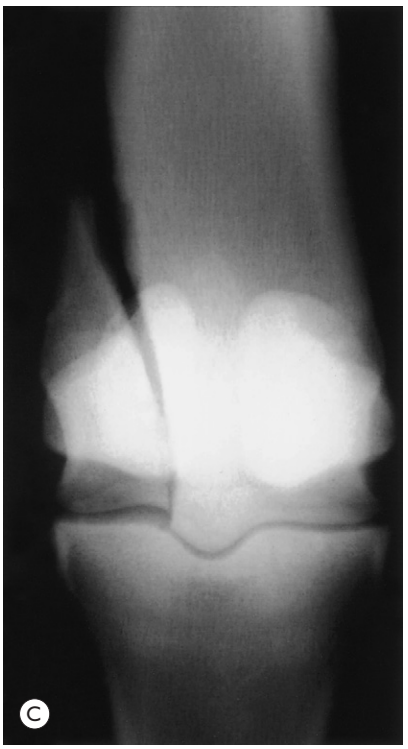
In the majority of horses with acute condylar fractures there is little difficulty identifying the location of the injury. Most horses have obvious heat and effusion of the involved fetlock joint and flexion will elicit a marked painful response. In horses with displaced lateral condylar fractures there is typically soft tissue swelling over the affected condyle and a noticeable deviation in the contour of the metaphysis. The same is true for horses with medial condylar fractures that have become displaced or have failed catastrophically in the diaphysis. (Open and/or unstable fractures in this category are common and are not a diagnostic challenge.)

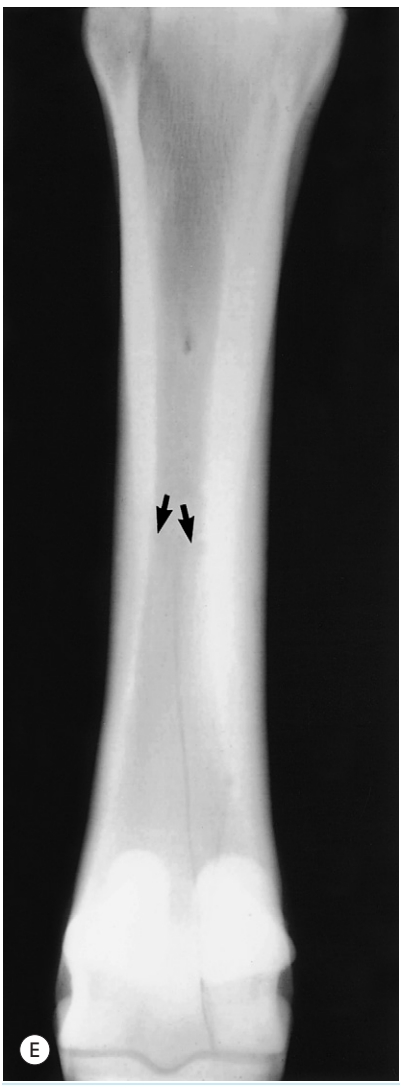
Horses with chronic fractures (typically a non-displaced, short, lateral condylar fracture) tend to have less soft tissue swelling, but joint effusion and pain on lower limb ('fetlock') flexion persist, although the degree will vary from horse to horse.

Lameness examination

Radiographs should be taken *first* in all cases of suspected condylar fracture before proceeding with a formal lameness examination. Owing to the severity and relative specificity of the clinical signs, a full diagnostic lameness evaluation is generally unnecessary in these horses.







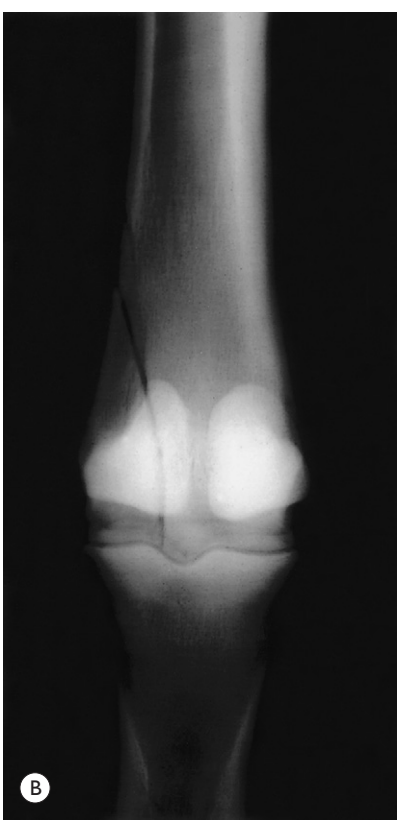


Fig. 17.5
Dorsal-palmar/plantar radiographs of the metacarpo/metatarsophalangeal joints and distal MC-III/MT-III of various horses depicting different configurations of condylar fracture. (A) Incomplete lateral condylar fracture. (B) Complete, non-displaced lateral condylar fracture. (C) Complete, displaced lateral condylar fracture. (D) Medial condylar fracture with spiral configuration. (E) Medial condylar fracture with mid-diaphyseal 'Y' configuration (arrow).

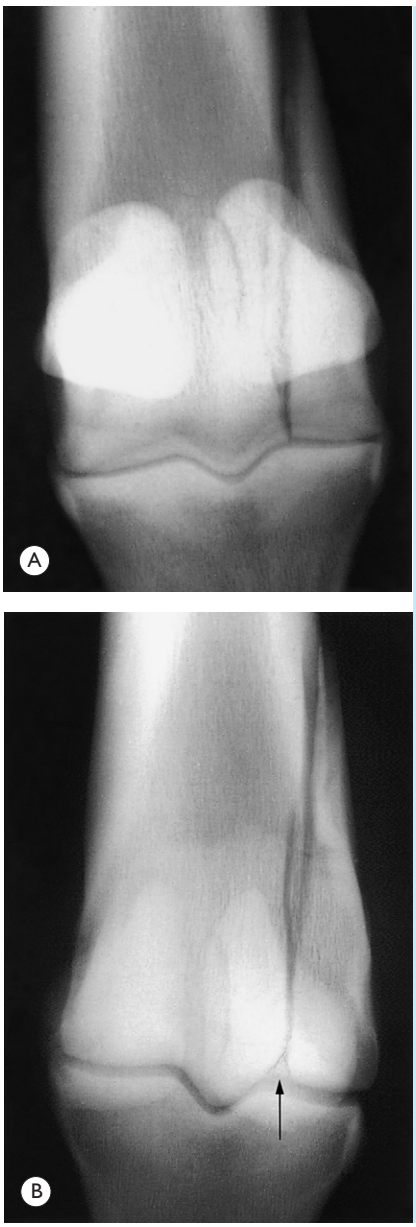


Fig. 17.6 (A) Routine dorsopalmar radiograph of the metacarpophalangeal joint of a horse with a complete, displaced condylar fracture of MC-III. (B) Flexed 125° dorsopalmar projection of the same joint revealing a comminuted fragment at the palmar aspect of the metacarpal condyle (arrow).

Acutely, the majority of horses with a condylar fracture exhibit mild-to-moderate lameness at a walk. Some exhibit limited weight bearing but generally after a few days of rest, bandaging and anti-inflammatory treatment, most will bear full weight and walk readily. In the early postfracture period these horses generally remain moderately to severely lame at a trot in-hand (grade 2–4 of 5). Horses with chronic, incomplete fractures typically exhibit mild-to-moderate lameness at a trot (grade 1–3 of 5). Lameness in horses with chronic displaced fractures is often quite severe as degenerative joint disease progresses.

Diagnostic confirmation

Diagnostic analgesia Diagnostic analgesia is rarely needed to localize the site of pain in horses with condylar fractures and is contraindicated in *all* horses with clinical signs typical of acute fracture given the risks for exacerbation of the injury (i.e. development of a complete or even catastrophic fracture). In the exceptional case of a horse with a chronic, incomplete or unicortical lateral condylar fracture[44] (a horse that has been able to continue some level of exercise or does not have a history of acute onset of marked lameness and joint effusion), a full lameness examination with diagnostic analgesia would be acceptable. In these horses a low palmar/plantar nerve block or intra-articular local anesthetic block of the fetlock joint will result in improvement of the lameness.

Scintigraphy Nuclear scintigraphy is rarely needed to assist in the diagnosis of condylar fracture. Nonetheless, condylar fractures are readily detected scintigraphically and occasionally are identified on scans of horses with acute lameness for which specific clinical signs are lacking or equivocal.

Scintigraphy is of greatest value in identifying chronic condylar fractures. Depending on the stage of disease (chronicity), these appear as focal areas of mild-to-intense abnormal increased radiopharmaceutical uptake in the distal metacarpus/metatarsus. Scintigraphic activity is often most intense in the palmar/plantar aspect of the condyle.

Radiography Four standard radiographic projections (lateral, dorsopalmar/plantar, DLPMO, DMPLO) of the involved fetlock are indicated for all cases of lateral condylar fracture. Ideally, these should include the full length of the metacarpus/metatarsus because on rare occasions fracture lines will extend proximally into the diaphysis. Radiographs of the full metacarpus/metatarsus are *mandatory* for all cases of medial condylar fracture given the propensity for these fractures to extend into the proximal diaphysis, and the concerns of mid-diaphyseal comminution and the associated potential for catastrophic fracture.[45]

A flexed dorsopalmar/plantar projection[46,47] is also recommended to evaluate the palmar/plantar aspect of the condyles for the presence of a comminuted fragment at the articular surface (Fig. 17.6). Similarly, the proximal sesamoid bones should be scrutinized for the presence of any associated fractures – in particular, axial fractures of the lateral proximal sesamoid, which are most commonly associated with displaced lateral condylar fractures[42,48] (Fig. 17.7). It is important to note the presence of any additional pathology such as dorsal P1 chip fractures (flexed lateral radiographs are beneficial here), so that these can be addressed at the time of surgery, or signs of degenerative joint disease so that their potential impact on the horse's prognosis can be appropriately considered.

Treatment and prognosis

Therapeutic aims

The goals in treating condylar fractures are to reduce healing time and minimize the potential for further degenerative changes in the affected joint. Optimal anatomic reconstruction of the articular surface and stabilization of the fracture

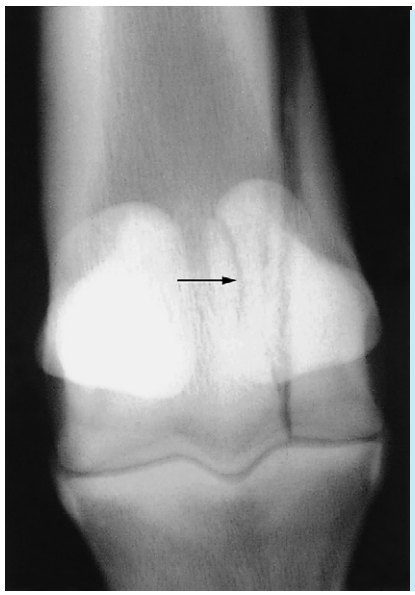


Fig. 17.7 Dorsopalmar radiograph of the metacarpophalangeal joint of a horse with a lateral condylar fracture and associated axial fracture of the lateral proximal sesamoid bone (arrow) (same case as in Fig. 17.6).

are the keys. When dealing with medial condylar fractures (and the rare lateral fracture that extends into the mid-diaphysis), prevention of a catastrophic fracture is also paramount.

Therapy

Emergency treatment Horses with acute condylar fractures should be confined strictly to a stall. The majority of non-displaced or incomplete lateral condylar fractures can be managed by coaptation with a firm, padded bandage pending definitive treatment (see below). Horses with displaced lateral condylar fractures are initially best managed by more rigid coaptation with the distal limb in a neutral or 'equinus' position (oriented such that the metacarpus/metatarsus and digit are in line). This can be accomplished with a dorsally applied splint and bandage that extends from the toe to just distal to the carpus or tarsus (such as a Kimzey splint®). This type of coaptation is important until the full extent of the injury can be assessed to rule out concurrent suspensory apparatus pathology and to prevent further fracture displacement and damage to the fetlock joint.

Horses with short medial condylar fractures should at least be managed with a rigid heavily padded bandage (such as a Robert-Jones bandage), with the addition of splints a prudent option. In horses with radiographically identifiable fracture lines in the mid-diaphysis, dorsally and laterally applied splints in the forelimb (extending to the elbow) or plantar and lateral splints in the hindlimb extending to the point of the hock are recommended. Rigid coaptation with a bandage and splints or application of a well-constructed full-limb cast should also be considered prior to transportation given the propensity for catastrophic failure.[42,45]

NSAIDs are administered as needed for analgesia.

Non-surgical management In certain cases of short, incomplete condylar fractures, particularly those in which economic considerations preclude surgery, non-surgical treatment can result in a good outcome.[39,42,49] The distal limb is kept in a bandage for 2–3 weeks to help minimize any soft tissue swelling and to provide some support. NSAIDs are administered only as needed to provide analgesia. Generally, the majority of horses in this category are quite comfortable within a few days to a week or so following the injury. Horses initially should have 1–2 months of strict stall rest, followed by another 1–2 months of stall confinement with daily hand-walking exercise. Follow-up radiographs are repeated 3 months from the time of fracture and if healing is progressing well, exercise in the form of small paddock turnout can begin. Under ideal circumstances, fractures heal in approximately 4 months.

The major disadvantage of non-surgical treatment is the tendency for fractures to exhibit delayed healing at the articular surface.[39,49,50] Resumption of training should not commence until fractures have completely healed and this may take up to 6 months or longer in some horses treated non-surgically. However, in a small percentage of horses a gap or defect in the subchondral bone may persist indefinitely well beyond the point at which the fracture has healed, which can complicate the decision on when to resume training.

Surgical treatment of lateral condylar fractures With the exceptions noted above, interfragmentary screw compression[33,51] is the treatment of choice for the majority of horses with lateral condylar fractures. Surgical treatment is imperative for all horses with displaced fractures, regardless of their intended future use. The severity of the degenerative joint disease that develops in horses with untreated displaced fractures, even within a few months, is crippling and horses that are not surgical candidates should be euthanized.

Surgery is performed with the horse in lateral recumbency under general anesthesia with the affected limb up. The limb is clipped and aseptically prepared from the foot to the carpus or tarsus and draped to allow access to the fetlock and distal metacarpus/metatarsus.

Non-displaced fractures are compressed and stabilized using 4.5 mm or 5.5 mm cortical screws placed in lag fashion through stab incisions. The most distal screw is inserted first and should be centered in the epicondylar fossa. Screw position should be monitored radiographically or fluoroscopically throughout the procedure. Countersinking is not necessary for this screw since the contour of the bone at this level accepts the head of the screw. Given the density of the trabecular bone in this location, it is not necessary for this screw to engage or exit the trans (medial) cortex to achieve adequate holding power and compression. This avoids having the tip of the screw impinging on or irritating the medial collateral ligament.

Subsequent screws are placed proximally at 1.5–2.0 cm intervals and in contrast to the most distal screw, these holes must be countersunk (Fig. 17.8). Care should be taken not to place a screw too close to the apex (proximal extent) of complete fractures since this may cause fragmentation when the screw is tightened. Arthroscopic exploration of the joint is optional (unless chip fractures or other lesions are present), but this does allow thorough evaluation, which may identify radiographically occult pathology.

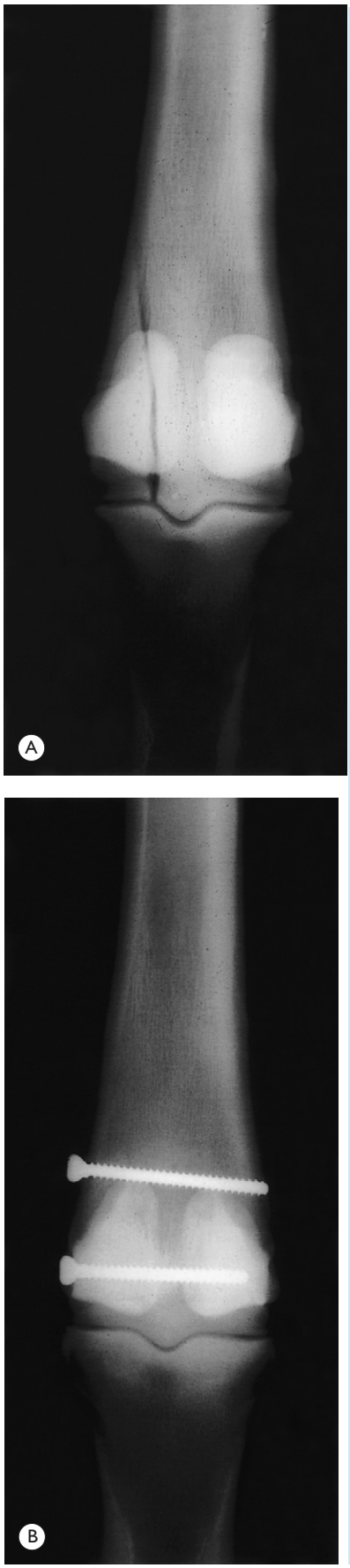


Fig. 17.8
(A) Preoperative dorsopalmar radiograph of the metacarpophalangeal joint of a horse with an incomplete lateral condylar fracture. (B) Postoperative radiograph following interfragmentary screw compression using 4.5 mm cortical screws in lag fashion.

Displaced lateral condylar fractures must be reduced prior to screw compression. Different techniques can be employed depending on individual preferences and the degree of displacement. If the fracture is not more than a few days old reduction can often be achieved under arthroscopic visualization while manipulating the limb and fragment. Alternatively, reduction can be monitored through a small incision near the apex of the fracture or through a small arthrotomy. Arthroscopy has the advantage of allowing thorough evaluation of the joint and some debridement of the fracture gap to facilitate reduction.

Fractures that are more chronic or any that require extensive debridement that cannot be accomplished arthroscopically must be reduced through a large dorsal arthrotomy. This incision is located over the fracture line and extends from the apex of the fracture to the distal insertion of the fetlock joint capsule on P1. Any blood clots, fibrin and bone fragments are cleaned from the fracture line and the fracture is then reduced.

Reduction is maintained with self-retaining bone reduction forceps. Alternatively, a 2 mm drill bit can be inserted through the fragment and into the parent bone to maintain reduction. Screws are inserted in a manner similar to that described for non-displaced fractures. Screw position and articular alignment are checked radiographically or fluoroscopically prior to closure and recovery from anesthesia. Failure to anatomically reconstruct the articular surface is an inexcusable technical error.

Stab incisions are closed with simple interrupted skin sutures using a 2-0 monofilament. Arthrotomies are closed in multiple layers, consisting of joint capsule/deep fascia, subcutaneous fascia and skin. A sterile dressing is applied to cover all incisions. Horses should be recovered from anesthesia in a half-limb fiberglass cast, although some surgeons do not customarily apply casts for horses with incomplete fractures. A customized compression boot (e.g. Farley boot®) is an alternative. Assistance during recovery in the form of head and tail ropes should be provided where feasible.

Casts or splints are removed within 24 hours of recovery and a firm, padded bandage is maintained for 2–3 weeks following surgery. NSAIDs are administered for a few days to provide analgesia and help decrease the inflammatory response in the joint. For the majority of horses antibiotics are limited to a single preoperative dose of an intravenous broad-spectrum antimicrobial or combination of antimicrobials. For horses undergoing an arthrotomy, antibiotic treatment is continued for 24–48 hours. Skin sutures are removed 10–14 days after surgery. Horses receive strict stall confinement for 1 month, followed by 1–2 months of stall rest with increasing daily hand-walking exercise. Follow-up radiographs are taken 2–3 months postoperatively and if healing is progressing satisfactorily, horses are allowed a minimum of 1–2 months of small paddock turnout before gradually resuming training.

Screw removal is not customarily recommended following repair of lateral condylar fractures. However, screw-associated pain in some horses upon resumption of high-speed exercise has historically been a concern. Subchondral

bone reaction ('subchondral stiffening') or collateral ligament irritation, associated with the most distal screw, have been proposed as possible causes.[52,53] Another possible explanation is simply pain and lameness associated with degenerative joint disease or from an unrelated injury, with the screw being implicated as the cause. In the author's experience, screw-associated pain is very rare. Surgeons that advocate screw removal generally do so between 3 and 4 months following surgery. Others remove screws only when there is strong reason to suspect them to be causing problems. In any situation, this can usually be accomplished with the horse standing under sedation and using local anesthesia. Screws are identified (using radiographs if necessary) and removed through stab incisions. An additional 2 months of rest and controlled exercise are recommended before resuming hard training.

Surgical treatment: medial condylar fractures 'Short' medial condylar fractures (sagittally oriented fractures that do not extend proximal to the distal diaphysis) are repaired in a manner similar to that described for non-displaced lateral condylar fractures.

Medial condylar fractures that extend proximally in a spiral configuration are approached through a long dorsal incision that splits the digital extensor tendons. The periosteum is elevated and the fracture line inspected for any signs of radiographically inapparent comminution or mid-diaphyseal divergence of fracture lines. The most distal screws are inserted through separate stab incisions (as above) and subsequent screws are inserted perpendicular to the fracture plane at 2.0–2.5 cm intervals through the long dorsal incision. Application of a dorsal or dorsolaterally positioned dynamic compression plate (DCP) is an alternative to help minimize the potential for catastrophic failure (see below).[54]

Care should be taken not to unnecessarily traumatize the splint bones, suspensory ligament or other soft tissues during drilling and tapping. Screw length and position should be monitored radiographically or fluoroscopically to ensure that they do not engage soft tissues or the splint bones. Similarly, screws that are placed through a fracture line can significantly weaken the bone and increase the risk for catastrophic fracture[51] and this should be avoided.

Long sagittally oriented fractures that exhibit mid-diaphyseal comminution or the so-called 'Y' configuration are at high risk for catastrophic failure, either preoperatively or in the early postoperative period. Fractures of this nature are almost exclusively seen in MT-III.[42,45] However, because of the potential adverse consequences, all medial condylar fractures should be regarded as having the possibility of catastrophic failure. These fractures should be treated with a combination of interfragmentary screw compression followed by application of a broad DCP that spans the length of MT-III.

Screws that compress the sagittal (distal) component are inserted through a combination of stab incisions (for the condylar screws) and through the long dorsal incision as previously described. Alternatively, plate screws inserted in lag fashion can be used to compress the fracture, although they will not be absolutely perpendicular to the fracture plane. A 4.5 mm, broad DCP of appropriate length is then applied along the dorsal or dorsolateral aspect of the bone, using 4.5 mm or 5.5 mm cortical screws and routine ASIF techniques. Again, care should be taken not to place a screw through a fracture line.

The dorsal incision is closed routinely in multiple layers and stab incisions are closed with skin sutures. Unless a pool recovery system is available, horses with medial condylar fractures that have not been plated should be recovered from anesthesia in a full-limb cast and recovery should be assisted. A cast is also prudent for cases in which plates have been applied but the risks of a full-limb cast, particularly in the hindlimbs, should be taken into consideration.

Postoperative care and exercise restriction are similar to that for lateral condylar fractures with a few exceptions. Hand-walking exercise does not begin until 2 months postoperatively in cases of spiral or long sagittal fracture. Antimicrobial treatment may be extended for an additional 24–48 hours in cases of plate application.

Horses that are intended to resume athletic careers must have plates and any independent screws placed in a dorsal-palmar/plantar direction removed prior to resumption of training. This is generally performed 3–4 months postoperatively under local anesthesia and is followed by an additional 2 months of convalescence.

Prognosis

The prognosis for horses with non-displaced lateral condylar fractures is generally very good. Results of retrospective studies indicate that 61–86% of Thoroughbreds with non-displaced fractures will race successfully following surgical treatment.[39,42,49,53,54] The prognosis for horses with displaced fractures is less favorable, with a reported range of 18–48% successfully returning to racing following surgical repair.[39,42,49,53,54] Fractures in the hindlimbs carry a more favorable prognosis, with 34% versus 76% of horses with complete fractures, and 79% versus 93% of horses with incomplete fractures of the front and hindlimbs, respectively, returning to racing in one study.[42]

Differences in prognosis between displaced and non-displaced fractures can be attributed to several factors, including a greater degree of articular and periarticular trauma associated with the original injury or with an open surgical approach, or technical errors during surgery for displaced fractures resulting in poor reduction and realignment of the articular surface.

The presence of a concurrent axial fracture of the proximal sesamoid (typically the lateral sesamoid) has also been shown to impart a poor prognosis for racing in Thoroughbreds with condylar fractures.[42]

Convalescent time (time from injury to first postoperative start) for horses with lateral condylar fractures generally ranges from 6 to 12 months, with an average of 8–9 months. This time is generally slightly shorter for non-displaced fractures and longer for horses with displaced fractures, but will vary considerably depending on the specifics of each case.

The propensity for catastrophic fractures to occur in horses with medial condylar fractures is now well recognized. The prevalence of this complication has been reported at 25–40% and can occur even up to several weeks following surgery if supplemental plate application is not utilized.[39,42,45] However, if catastrophic failure is not encountered, the prognosis for these horses to return to racing soundness is generally quite good following implant removal.[42,45,54] It should be noted that convalescent time for horses with medial condylar fractures tends to be longer than for those with fractures of the lateral condyles and has been attributed to a prolonged period of controlled exercise associated with implant removal.[42,54]

Etiology and pathophysiology

Etiology

There is increasing evidence to suggest that condylar fractures are another form of fatigue fracture in horses associated with repetitive trauma, or cyclic strain, incurred during high-speed exercise (see Pathophysiology below).

Pathophysiology

It is recognized that condylar fractures originate in the palmar/plantar articular surface of the condyles of distal MC-III/MT-III.[39,44,49,55] In race horses, the subchondral bone in the region of the condyles undergoes intense adaptive and maladaptive remodeling in response to the strains of high-speed exercise.[55–57] There is ample evidence, both grossly and histologically, of degenerative changes in the subchondral bone associated with lateral condylar fractures[58] (Fig. 17.9). These findings suggest that condylar fractures are another manifestation of a cyclic fatigue injury, rather than an acute fracture in otherwise normal bone.

A recent series of morphologic studies in Thoroughbred race horses has added further support to this theory. Riggs et al (1999)[59] demonstrated that as training progresses, high-speed strains stimulate subchondral sclerosis in the palmar/plantar aspect of the condyles of MC-III/MT-III. This results in the development of a steep density gradient between the subchondral bone of the condyles and the adjacent sagittal ridge. The investigators proposed that this density gradient results in stress concentration in this region of MC-III/MT-III (the 'condylar groove'), which is the location of the majority of condylar fractures. A related post-mortem study demonstrated that small fissures develop first in the zone of calcified cartilage in this area.[60] When sufficient pathologic forces are generated on the condyle, overt fracture may then occur. Because the trabecular bone in the distal metaphyses is organized into sagittally oriented plates[61] – an adaptation to resist the strong bending loads applied in the dorsal-palmar/plantar direction – these fractures propagate in a characteristic sagittal configuration and course axially or abaxially depending on the location of the fracture (i.e. medial or lateral condyle).[60]

It is reasonable to conclude that cyclic fatigue initiates the pathologic changes that predispose the bone to fracture. However, from a purely biomechanical standpoint, it has been proposed that overt fracture occurs in association with excessive dorsiflexion (hyperextension) of the fetlock joint and disruption of the normal synchronous rotation of P1 on MC-III/MT-III at the end of the weight-bearing phase of the stride.[62–66] Several recent post-mortem epidemiologic studies on racing Thoroughbreds in the US have implicated shoes with toe grabs and poor dorsopalmar hoof balance (specifically long toe/low heel or 'under-run' heel conformation) as *potential* risk factors.[67,68] Presumably, these shoe and hoof characteristics may biomechanically contribute to, or exacerbate, the abnormal forces that predispose to condylar fracture.

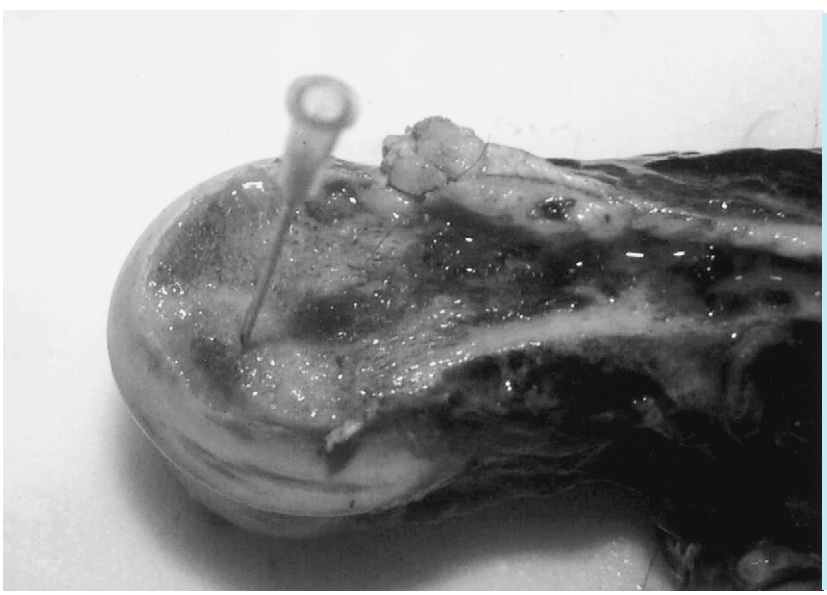


Fig. 17.9
Post-mortem photograph of the lateral condyle of MC-III from a horse with a complete, displaced lateral condylar fracture. Notice the well-demarcated degenerative lesion in the subchondral bone in the palmar aspect of the condyle (needle).

Epidemiology

Condylar fractures most commonly occur in young Thoroughbred race horses but they also occur in Standardbred, Quarter Horse and Arabian race horses.[39,42,43,49] In one study in racing Thoroughbreds in Britain, condylar fractures and sagittal fractures of the first phalanx were the two most common fractures occurring during racing or race training, each accounting for approximately 15% of all fractures.[41] In another study in the US, approximately 20% of Thoroughbreds euthanized for musculoskeletal injury on California racetracks had lateral condylar fractures of MC-III.[40]

In Thoroughbreds, condylar fractures occur more frequently in the forelimbs, and lateral fractures are much more common than medial.[39,42,43,49] However, in Standardbreds there is a more even distribution between fore and hindlimbs and there may be a more equal distribution between lateral and medial fractures.[42] This difference in fracture distribution between the two breeds can presumably be attributed to biomechanical differences between the gallop or pace/trot. Among Standardbreds, pacers may be more commonly affected than trotters.[42]

Prevention

While the vast majority of condylar fractures present as an acute injury there is increasing evidence that condylar fractures are fatigue fractures (see Etiology and pathophysiology above). In theory, early detection of pathologic changes in the subchondral bone of the distal metacarpus or metatarsus should enable intervention prior to fracture. At present, bone-phase nuclear scintigraphy offers the most sensitive means for detecting maladaptive remodeling processes in the clinical setting.[55–57] Horses with abnormal increased radiopharmaceutical uptake in the distal palmar or plantar subchondral bone of MC-III/MT-III should be regarded as being at increased risk for condylar fracture, and modifications in training intensity would be warranted. Common sense would also dictate that horses with clinical signs of a problem in the fetlock joint be thoroughly evaluated.

Proliferative periostitis of the small metacarpal/metatarsal bones/interosseous desmitis ('splints')

- Inflammatory lesions affecting primarily young athletic horses of all breeds and uses.
- Recognized as a focal area of firm, painful swelling along the shaft of the affected splint bone.
- Lesions on MC-II are most common, but all splint bones can be affected.
- Lameness is generally mild to moderate, with acute or insidious onset.
- Caused by exercise-associated strain and tearing of the interosseous ligament with associated periostitis.
- Others caused by external trauma and resulting primary periostitis.
- Majority respond to exercise restriction and anti-inflammatory therapy.
- Surgery reserved for chronic or recalcitrant cases.
- Prognosis is generally favorable.

'Splints' are inflammatory lesions resulting from repetitive strain during exercise, or from external trauma, that affect the small metacarpal/metatarsal bones or splint bones (MC-II/IV, MT-II/IV), and are seen in all varieties of athletic horses.

Recognition

History and presenting complaint

Horses with 'splints' typically are presented with a mild-to-moderate lameness having either an acute or insidious onset. Many horses can continue training, albeit with impaired performance, while others must be taken out of work. Lameness may also be intermittent and quickly improve with rest, but recurs upon resumption of exercise if the lesion has not been allowed adequate time to heal. Whether or not lameness improves, worsens or remains static *during* exercise is also highly variable, but in most horses lameness worsens as exercise progresses.

In addition to lameness, the other chief complaint or clinical sign is a variable degree of focal swelling at the site of the lesion. Astute trainers or owners may also recognize the lesion to be painful on palpation. There is a subset of young horses that develop 'splints' without overt lameness and in these cases the cosmetic blemish is the primary concern.

Physical examination

A 'splint' is recognized as a focal swelling along the shaft of the affected bone that is smooth and firm to hard on palpation. In some cases the swelling is located axially and the lesion can only be detected by palpation. Axially located 'splints' are most easily palpated with the limb held in flexion while running the fingers along the shaft of the splint.

There may be a single lesion or multiple lesions affecting the same bone but, overall, a single lesion is most common. Multiple lesions are most common on MC-II in young horses associated with early training. In this group, 'splints' are also commonly bilateral.

Horses exhibit variable degrees of pain on palpation of the 'splint'. Pain is most severe in the acute stages and does not always correlate well with the degree of swelling/exostosis. Chronic 'splints' or those that have healed clinically are not sensitive to palpation, but some horses react to firm skin pressure and this can give a false-positive response.

Open wounds or abrasions may be present over the lesion when the cause is external trauma.

Lameness examination

Lameness, when present, typically is mild to moderate (grade 1–3 of 5).[2] The majority of horses walk comfortably and only exhibit lameness during exercise. Acutely, most horses will exhibit lameness at a trot in-hand and the lameness tends to be exacerbated with the affected bone on the inside of a circle when working on a lunge line. Horses that are affected bilaterally may exhibit a 'choppy' or 'stiff' gait bilaterally and not a distinct 'head nod' or 'hip hike' per se. Firm digital pressure on the splint will often exacerbate the lameness.

Other horses are only affected when working at speed. Classic examples are the Standardbred race horse that is bearing in or out, or is 'on a line' or 'getting over on a shaft', or the performance horse that will not take or maintain the appropriate lead.

Diagnostic confirmation

Diagnostic analgesia High palmar/plantar analgesia (a 'high palmar/plantar block') will reduce lameness in horses with 'splints'. Selectively blocking just the medial or lateral nerves provides greater specificity. Local infiltration of anesthetic directly over the lesion is also an alternative method for localizing the site of pain. Local infiltration may be less effective if a substantial component of the pain is related to inflammation of the interosseous ligament and the anesthetic is deposited superficially (abaxially). The same is true if there is suspensory ligament impingement as a component of the lameness. In these horses a combination of successive blocks may be necessary to pinpoint the problem.

Scintigraphy As with other inflammatory bone disorders, nuclear scintigraphy is a very sensitive method for detecting increased bone remodeling at the site of a 'splint'. It should be noted that the majority of acute 'splints' can be diagnosed on physical examination. Nuclear scintigraphy, like diagnostic analgesia, has its strongest application in ruling in or out other potential causes for lameness, as well as monitoring healing in exceptional cases.

Focal abnormal increased radiopharmaceutical uptake will vary from mild to intense, depending on the stage of disease (Fig. 17.10). As with many other conditions, scintigraphy will often be positive when radiographs are negative or equivocal in the acute stages. Scintigraphic activity also tends to persist after the lesions have healed clinically and therefore, results of physical/lameness examination, diagnostic analgesia, radiographs and clinical experience are necessary to formulate a therapeutic plan.

Radiographs Radiographic abnormalities may not be evident with many acute 'splints', even in cases where considerable external swelling is present (see Pathophysiology below). For that reason, and because treatment for young horses in early athletic training is not necessarily modified based on radiographic findings, many clinicians do not recommend an initial set of radiographs in every case. However, radiographs are essential to rule out a fracture and to assess the nature and extent of any periosteal reaction – which is particularly important in horses with chronic or recalcitrant

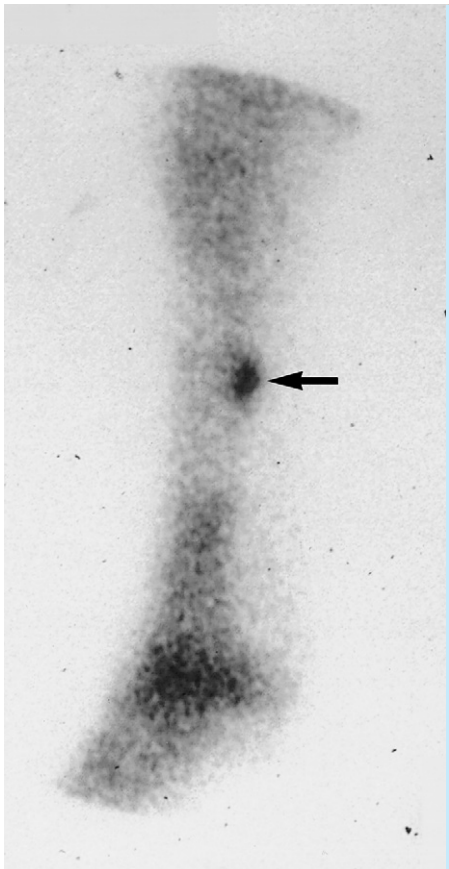


Fig. 17.10 Lateral bone-phase scintigraphic image of the left metacarpus of a horse with an active proliferative periostitis lesion ('splint'). Notice the focal area of moderately intense abnormal increased radiopharmaceutical uptake affecting MC-IV (arrow).

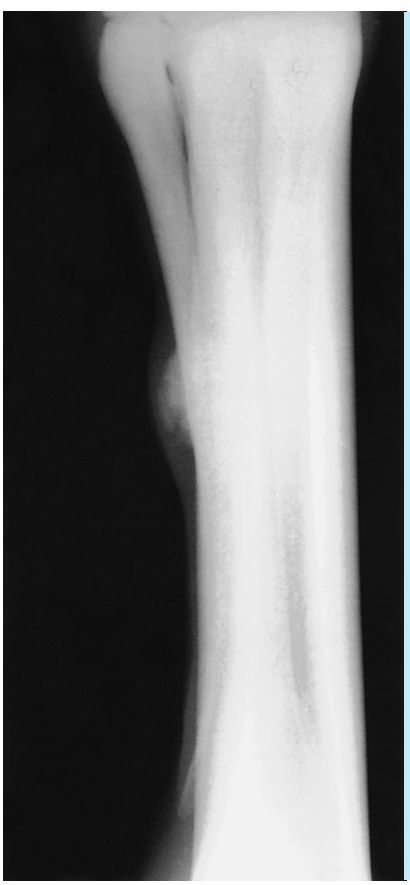


Fig. 17.11 Dorsomedial-to-palmarolateral oblique radiograph of the left metacarpus of a horse with a proliferative periostitis lesion ('splint') affecting MC-II. Notice the exuberant irregular periosteal reaction, which is typical of lesions resulting from external trauma.

'splints', cases where lameness is profound, those with a large swelling/exostosis and certainly any with a draining wound.

Four views (lateral, dorsopalmar/plantar, DMPLO, DLPMO) of the affected metacarpus/metatarsus are recommended, although most information is obtained on the appropriate oblique view that isolates the affected bone(s). Lesions that are the result of internal trauma (exercise-associated cyclic strain) most commonly have a variable degree of focal, smooth periosteal reaction along the shaft of the affected splint bone. In addition, there may be evidence of subtle osteolytic change along the axial aspect of the bone (the region of the interosseous ligament) as well as subtle or mild proliferative and lytic changes in the underlying cannon bone. Lesions resulting from external trauma are more likely to have an irregular and exuberant periosteal reaction (Fig. 17.11). It is important to note that superimposition of normal and periosteal new bone can result in misdiagnosis of a fracture in some cases if radiographs are not interpreted carefully.

Ultrasound A sonogram is important for evaluation of concurrent suspensory ligament pathology in cases with potential impingement on this structure by a large exostosis.

Thermography In the hands of an experienced operator, thermography can be useful in identifying active lesions.

Treatment and prognosis

Therapeutic aims

The goals of therapy for 'splints' are to reduce or eliminate the inciting cause, reduce inflammation, minimize the size of the exostosis and allow the lesion to become quiescent or 'set up' (see Pathophysiology below).

Therapy

Exercise restriction The extent of exercise restriction varies with each case and depends on the duration and severity of clinical signs and, to some extent, the use of the horse and stage of training.

Most horses should be confined to a stall with exercise limited to daily hand-walking until lameness and the majority of the focal pain have subsided. In most cases this will be a period of 2–6 weeks. However, this will also vary depending on response to treatment. Exercise intensity is increased gradually and, as above, the specific protocol will vary with each case.

Anti-inflammatory treatment As with exercise restriction the extent of anti-inflammatory treatment for 'splints' will vary with each case. The NSAIDs phenylbutazone or flunixin meglumine are administered systemically at standard doses for several days in most cases, or up to a few weeks in exceptional cases. As in other inflammatory disorders, long-term NSAID treatment is becoming more controversial due to its potentially negative impact on bone healing. Promoting metacarpal/metatarsal fusion (see Pathophysiology) is desirable but how NSAIDs affect this process is unclear. NSAIDs, along with corticosteroids (see below), may be of greatest importance in minimizing the development of an exuberant exostosis.

Local cold therapy, in the form of cold hosing or icing (bucket or ice boot) administered for 20–30 minutes several times daily for several days in the acute stages, is also beneficial to reduce soft tissue swelling and inflammation in the affected tissues.

Local injection of corticosteroids can also be highly beneficial, particularly with respect to decreasing the fibrous and osseous proliferative response. Local injection of corticosteroids is particularly efficacious for managing lameness associated with 'splints' in horses whose competition schedules will not allow an extended period of lay-up.

Corrective shoeing Corrective trimming and shoeing plays an important role in reducing or eliminating the tendency for interference when this form of external trauma is the cause of a 'splint'.

Boots and protective bandages In cases in which interference is the primary cause, 'shin boots' or other protective wraps or bandages are helpful to prevent further trauma.

Surgery The vast majority of 'splints' respond well to non-surgical management.[32,69] Refractory cases associated with chronic or recurrent lameness, cases with exuberant exostoses and suspected suspensory ligament impingement and those with osteitis associated with an open wound are appropriate candidates for surgery. Surgery is also occasionally undertaken to improve the cosmetic appearance of show horses.

Surgery involves either a partial ostectomy (osteotomy just proximal to the lesion with excision of the distal aspect of the splint bone) or surgical debridement of the exostosis with preservation of the bone. The option chosen depends on the nature and location of the lesion, the bone involved and in some cases the surgeon's preference. With the exception of MT-IV,[70] excision of more than the distal two-thirds to three-quarters of a splint bone will result in instability of the remaining proximal portion, which can lead to chronic lameness of various origins.[71] This is particularly true when dealing with MC-II. Therefore, when considering surgery for a large impinging exostosis affecting the proximal portion of a splint bone, debridement of the exostosis and preservation of the bone are appropriate.

Fortunately, 'splints' resulting from cyclic internal trauma (exercise-associated repetitive strain) that affect the proximal aspect of the bone rarely become chronic problems once allowed to 'set up' (formation of a stabilizing synostosis or fusion – see Pathophysiology), and surgical intervention is therefore not a consideration. 'Splints' of this nature that are most likely to result in chronic lameness generally affect the midshaft of the splint bone and in the author's opinion they are candidates for partial ostectomy.

Surgery is performed with the horse in lateral recumbency under general anesthesia. A tourniquet is helpful but not essential. The limb is clipped and aseptically prepared from midpastern to carpus/tarsus and draped to allow access to the full metacarpus/metatarsus. An incision is made directly over the splint bone and extends from a few centimeters proximal to the lesion to just distal to the distal aspect or 'button'. Sharp and blunt dissection is used to expose the portion of the bone to be excised. Care is taken to avoid trauma to the suspensory ligament and neurovascular structures in the

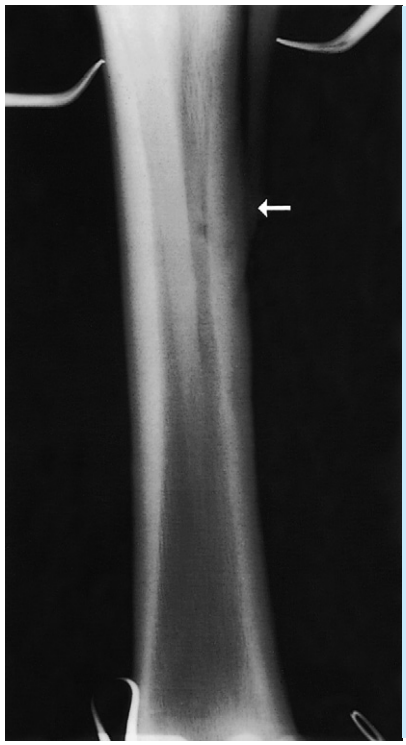


Fig. 17.12 Intraoperative DMPLO radiograph of the right metacarpus following ostectomy of the distal portion of MC-II (arrow) in a horse with a chronic proliferative periostitis lesion ('splint').

area (particularly when dealing with MT-IV). A 6–12 mm osteotome and mallet are used to transect the splint bone just proximal to the lesion, at a 30–45° angle with the long axis of the bone (Fig. 17.12). The distal portion is then excised, beginning distally and working proximally. Mayo scissors can be used to cut the heavy fibrous tissue attached to the most distal aspect and then an osteotome or chisel and mallet are used to undermine and separate the more proximal portion from the cannon bone. The periosteum is removed with the bone. Remaining bone fragments and fibrous tissue are carefully debrided and a bone rasp is used to smooth the remaining proximal stump and cannon bone where needed. Excessive rasping or other trauma to the cannon bone should be avoided. The surgical field is lavaged copiously to remove small bone fragments. Intraoperative radiographs are helpful to identify small fragments that may not be readily seen. A Penrose drain is not essential, but does help prevent seroma formation in some cases. The wound is closed routinely in multiple layers and a dressing containing rolled or folded sterile gauze pads is applied over the incision to provide increased direct pressure and help minimize swelling and seroma formation prior to application of a padded bandage.

The surgical approach for debridement of a large exostosis is similar, but with a shorter incision centered over the lesion. After reflecting the soft tissues an osteotome (or chisel) and mallet are used to carefully separate the proliferative periosteal bone from the surfaces of the underlying splint and cannon bones. The periosteal bone is usually softer and more irregular than the normal cortical bone and in most cases is easily identified. All overlying periosteum is removed with the exostosis, taking care not to unnecessarily traumatize bone that is left behind. Intraoperative radiographs may help identify foci of remaining periosteal new bone. Lavage, closure and bandaging are similar to that for ostectomy.

Postoperatively, horses are treated with an NSAID for 3–7 days. Broad-spectrum antibiotics are initiated preoperatively and continued for 24–48 hours postoperatively. If excessive soft tissue swelling or a seroma develops, antibiotic treatment is continued at the discretion of the surgeon. Sutures are removed in 12–14 days and a bandage is maintained on the limb for 3–4 weeks to help minimize swelling. Horses are confined to a stall for 6–8 weeks, with light hand-walking exercise beginning after suture removal. Exercise intensity gradually increases over the ensuing 6–8 weeks. Early resumption of harder exercise predisposes horses to inflammation at the site of the ostectomy and sets up the possibility of chronic problems postoperatively.

Traditional and alternative therapies Many of the numerous traditional therapeutic modalities mentioned in the section on 'bucked shins' continue to be used by some lay persons and veterinarians for treating 'splints'. As with 'bucked shins', the efficacy of these techniques for treating 'splints' has not been substantiated scientifically, but many clinicians remain strong advocates based on anecdotal evidence and personal experience. A detailed discussion of this topic is beyond the scope of this chapter. In addition to those modalities listed in Table 17.1, soft lasers, therapeutic ultrasound and magnet boots have been employed in the treatment of 'splints'.[69] The efficacy and scientific rationale of these treatments also remain controversial.

Prognosis

The prognosis for most horses with 'splints' is generally very good if appropriate intervention is undertaken and adhered to. This is particularly true for 'splints' that develop in young horses in early training. The majority of horses will recover and their athletic potential will not be impaired. Most chronic or recurrent problems develop in situations where the lesion initially goes undiagnosed or horses are not allowed an adequate time to heal and undergo fusion or synostosis (see Pathophysiology below).

'Splints' that develop in older horses, either from internal or external trauma, tend to take longer to heal and are more likely to fall into the chronic or recurrent category. Other exceptions are cases of chronic interference where repeated external trauma cannot be corrected or rare proliferative lesions that affect the very proximal aspect of the bone and contribute to problems with the carpometacarpal/tarsometatarsal joints.

The prognosis for athletic soundness following partial ostectomy is also generally fair to good if appropriate case selection, surgical technique and aftercare are adhered to.[72] Prognosis is guarded for horses undergoing proximal ostectomy, with or without supplemental stabilization of the remaining portion.[73] Recurrence of the exostosis following surgical debridement has been a recognized problem[69] and owners should be cautioned accordingly. Careful removal of the associated periosteum appears to minimize this complication.[74]

Etiology and pathophysiology

Etiology

'Splints' can be caused by internal or external trauma. Internal trauma is in the form of repetitive or cyclic strains incurred during exercise. External trauma is essentially blunt force or concussive trauma, resulting either from a kick or interference.

Pathophysiology

'Splints' caused by cyclic strains during exercise (internal trauma) are initiated by tearing and inflammation of the interosseous ligament and underlying periosteum of the cannon and splint bones. In immature horses the splint bones are mobile relative to the adjacent cannon bone. As such, during exercise, axial forces applied to the proximal aspect of the splint bones by the overlying carpal or tarsal bones result in strain and shearing of the interosseous ligament and periosteum. As exercise continues a focal desmitis and periostitis develop, which in turn results in the clinical signs of focal swelling and lameness. The swelling is initially a combination of soft tissue edema and fibrosis, and progresses to periosteal new bone or exostosis.

This type of 'splint' is most common in younger horses in early training and the small metacarpals, and in particular MC-II, are most frequently affected. The small metacarpal bones have larger articulations with the overlying carpal bones, and more extensive soft tissue attachments, than do the small metatarsal bones. Functionally, it is assumed that the small metacarpal bones play a more important role in stabilizing the carpus and experience greater stresses during exercise than the small metatarsals.

Eventually, a synostosis between the splint and cannon bones develops at the site of a 'splint' – termed 'metacarpal fusion'[75] – and it is hypothesized that this results in stabilization and resistance to further strain and shear.[75] 'Splints' at this stage are said to have 'set up' and no longer appear to cause clinical problems. Given that metacarpal fusion has an estimated prevalence of over 95%, with 78% of horses over 2 years old having two or more sites of fusion,[75] it is reasonable to assume that the process is not always associated with an inflammatory reaction severe enough to produce clinical signs of 'splints' and, in fact, may be a normal adaptive process as the skeleton matures.

Poor conformation is also implicated as a risk factor for the development of 'splints',[50] presumably by exacerbating the shearing forces applied on the splint bones and interosseous ligament. Specifically offset or 'bench knees' appear to favor development of splints of MC-II.[50,75] Carpal or tarsal valgus or varus deformities may also potentiate the development of 'splints'.

In contrast to the above, 'splints' caused by external trauma begin as a primary focal periostitis/osteitis of the affected splint bone, although a primary interosseous desmitis may also be initiated by the event.[50] Exercise can aggravate and perpetuate this inflammatory process and presumably a secondary interosseous desmitis and periostitis of the cannon bone may result. Base narrow, toe-out conformation, which may exacerbate the tendency for interference – specifically trauma to the contralateral MC-II – has been suggested as one risk factor.[69]

Regardless of the underlying cause, if the exostosis becomes exuberant and projects axially a secondary, focal suspensory desmitis may develop in some cases. However, in the author's experience, this condition is uncommon but is more likely with the marked exostosis that tends to develop following external trauma.

Epidemiology

'Splints' resulting from cyclic strains associated with exercise are common in young performance horses of many breeds and uses. As previously mentioned, MC-II is the bone most commonly affected in this group, followed by MT-II, but the lateral splint bones (MC-IV, MT-IV) can certainly also be affected. Lesions are very commonly bilateral and multiple 'splints' affecting a single bone are not unusual, particularly on MC-II.

'Splints' are very common problems in race horses of all breeds aged 2–4 years and, as with 'bucked shins', many trainers still consider them to be almost a 'rite of passage'. In performance horses other than race horses, 'splints' can develop at any age but are common in those aged 3–10 years (young adults). 'Splints' also develop in weanling and yearling horses that are not in formal training and in the author's experience, these are frequently fast-growing or overconditioned animals. Overnutrition has been cited as an associated risk factor by others.[69]

'Splints' resulting from external trauma can affect horses of any age and involve any of the splint bones. Obviously, those resulting from interference are most likely to occur during performance and affect MC-II. However, this type of splint is also frequently seen on MT-IV resulting from a kick or contact with natural or manmade objects.

Prevention

In theory, with training modifications it should be possible to prevent or minimize the incidence of 'splints' that develop in young horses in early training as a result of cyclic trauma that exceeds the physiologic limits of the tissues and their capacity to adapt to the imposed stresses. In reality, it is impossible at this stage to outline a specific training regimen that would be appropriate for each breed and use of athletic horse. Early detection using physical examination and diagnostic imaging techniques such as thermography and scintigraphy, to then enable timely intervention, is a more realistic goal. Correction of gait abnormalities that predispose to interference should minimize the incidence of traumatic 'splints' in the individual horse. In horses with a tendency for interference, long-term use of shin boots or other protective wraps is also an option.

Fractures of the small metacarpal/metatarsal bones (splint bone fractures)

- Splint bone fractures occur in all types of performance horses.
- Fractures of the distal third are the most common type.
- Fractures of the middle and proximal aspect result from trauma associated with interference.
- Fractures of the head may be caused by torsional forces or be avulsions.
- Distal fractures are treated by surgical excision.
- Middle and proximal fractures are treated by excision or internal fixation.
- The prognosis is generally favorable for all fracture types.
- Concurrent suspensory desmitis is the limiting factor with distal fractures.

Splint bone fractures can occur during exercise or randomly as a result of some form of external trauma. The following will deal exclusively with fractures that occur in athletic horses during performance. The most common in this category are fractures of the distal third. Others include fractures of the midshaft or proximal portion (head) resulting from interference, and oblique fractures of the head that may result from torsional forces or be avulsions associated with the extensive soft tissue attachments.

Recognition

History and presenting complaint

Acute lameness and swelling are the primary clinical signs of splint bone fractures.

Degree of lameness in horses with fractures of the distal portion is highly variable and may have an acute or more insidious onset. Most horses develop an acute lameness during or immediately after exercise. Lameness is generally mild to moderate. Many horses are able to resume exercise after a period of rest, but have lingering problems with low-grade lameness. Acutely, mild soft tissue swelling and sensitivity are usually present near the fracture site. Horses may have a history or clinical signs of suspensory desmitis. Some chronic distal fractures are incidental findings.

Lameness with fractures of the proximal portions of the splint bones is generally acute in onset, ranges from moderate to severe and generally persists despite rest. The majority of these horses are too lame to continue exercise. Soft tissue swelling ranges from mild to marked and abrasions or wounds may be present.

Physical examination

Horses with distal splint bone fractures generally have very mild to moderate local soft tissue inflammation. The degree varies with the chronicity of the injury. Fractures that are more than a week or two old may have minimal residual associated swelling. Distal splint fractures have a high incidence of associated suspensory desmitis and therefore suspensory enlargement, most commonly of the associated branch, may also be present. Focal pain is common on firm palpation of the fracture site. If the fracture is chronic, a callus can often be palpated, along with instability if the distal tip or 'button' is pressed axially.

Variable degrees of soft tissue swelling and pain on palpation of the fracture site are the hallmarks of fractures of the more proximal portions of the splint bones. Open wounds or abrasions may be present if the fracture is the result of interference.

Lameness examination

Lameness in horses with splint bone fractures ranges from very mild to relatively severe and depends in great part on the type of fracture and the chronicity.

Horses with acute fractures of the distal aspect generally exhibit mild-to-moderate lameness at a trot and in some cases exhibit mild lameness at a walk (grade 1–4). Horses with chronic distal fractures generally exhibit only mild lameness at a trot, but performance is impaired at high speeds. Lameness may be exacerbated on a circle. Lower limb ('fetlock') flexion may exacerbate the lameness, particularly if concurrent suspensory desmitis is present.

Horses with acute fractures of the middle and proximal portions of the splint bones generally exhibit severe lameness at a trot and many are markedly lame at a walk (grade 2–4 of 5). Lameness in chronic cases is highly variable. Lameness is exacerbated with the fractured bone on the inside of a circle in many horses. Carpal or tarsal flexion may be positive in horses with fractures affecting the head of the splint.

Diagnostic confirmation

Diagnostic analgesia Diagnostic analgesia is rarely needed to definitively localize the source of pain in horses with most acute splint fractures. Diagnostic analgesia becomes important in the work-up of horses with chronic fractures involving either the distal aspect or the head of the splint, in which soft tissue swelling and lameness have improved considerably. In horses with distal splint fractures, response to low palmar/plantar analgesia is variable. High palmar/plantar analgesia will consistently be positive in all cases of splint bone fracture, with the exception of those involving the articular aspect, in which the response is variable. In these cases, intra-articular analgesia of the carpometacarpal (via the middle carpal joint) or tarsometatarsal joint will be positive or result in substantial improvement.

Scintigraphy Nuclear scintigraphy is unnecessary for diagnosis of acute splint bone fractures. This modality is beneficial in the work-up of horses with chronic fractures when attempting to rule in or out other potential causes of lameness.

Radiography Radiographs are necessary to confirm the diagnosis. Four views (lateral, dorsopalmar/plantar, DMPLO and DLPMO) of the full metacarpus/metatarsus are required. In

cases of fractures involving the head of the bone (articular fractures) a full series of the associated carpus/tarsus is also warranted.

Ultrasonography A sonogram should be performed to evaluate the suspensory ligament in cases where concurrent desmitis is suspected.

Treatment and prognosis

Therapeutic aims

Therapy for distal fractures is directed at eliminating a source of chronic irritation/inflammation. Goals of therapy for fractures involving the midshaft include minimizing the convalescent time and mitigating the tendency for development of delayed or non-union and formation of exuberant callus/exostosis. Goals in treating proximal fractures include promoting primary bone healing, preservation of the stability of the proximal portion and minimizing the potential for degenerative joint disease.

Therapy

First aid Initial treatment for all splint bone fractures includes bandaging and anti-inflammatory therapy, as previously discussed for other metacarpal/metatarsal injuries. Horses should be confined to a stall pending decisions on definitive treatment. Wound care and antibiotics are administered as needed.

Treatment of distal fractures There is no strong consensus on the most appropriate way to manage distal splint fractures. Many will heal or become quiescent as non-unions and no longer appear to cause problems.[77,78] Residual lameness/poor performance is generally attributed to chronic suspensory desmitis. However, because the distal portion of the splint bone is highly mobile, healing is often slow and associated with considerable callus (Fig. 17.13). The fragment and associated inflammation appear to cause chronic irritation in some horses. Surgical excision of the fragment reduces the convalescent period and eliminates the fracture as a continued cause for concern. Therefore, it is this author's opinion that *acute* or *clinically active* distal splint fractures are best treated by surgical excision.

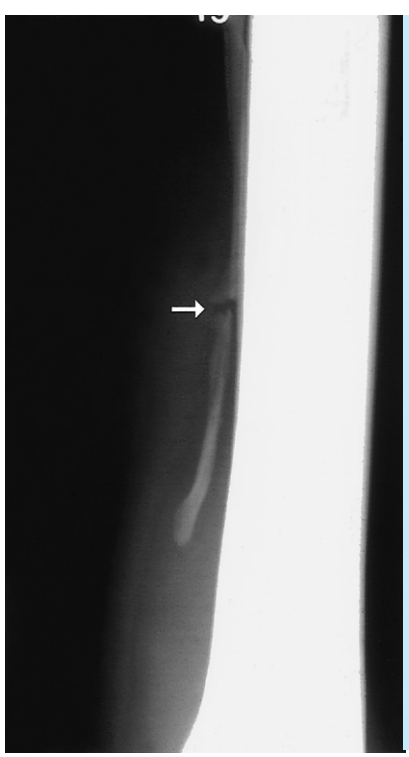


Fig. 17.13 Dorsolateral-to-plantaromedial radiograph of the right metatarsus of a horse with a chronic fracture of the distal aspect of MT-IV. Notice the callus and evidence of non-union (arrow).

Surgery is generally best performed under general anesthesia, but excision under local anesthesia is a viable alternative in some cases. The preparation and approach are similar to that described for splint ostectomy in the previous section, but the incision is considerably shorter. Fractures of the distal third involve the portion of the splint bone not attached to the interosseous ligament. Therefore, excision is relatively easy and can be performed with heavy scissors, again working from distal to proximal while grasping the 'button' to elevate it. The distal fragment, callus and a small segment of the proximal fragment (that involved with the callus), along with associated periosteum, are excised. A small osteotome or bone rongeur can be used for transecting the proximal fragment. Closure and bandaging are carried out in a routine manner.

Aftercare involves 2–4 weeks of stall confinement with increasing daily hand-walking exercise, followed by 2–4 weeks of small paddock turnout or other form of light exercise. Exceptions are horses with concurrent suspensory desmitis, in which case rest and controlled exercise, and other adjunct therapy, are dictated by the extent of the ligamentous injury (the reader is referred to the chapter on tendon and ligament injuries (Chapter 20)). A bandage is maintained for 2–3 weeks and sutures are removed 10–14 days postoperatively. NSAID and antibiotic treatment are at the discretion of the surgeon, but neither is required for an extended period.

Treatment of midbody fractures Treatment for fractures of the midportion of the splint bones involves partial ostectomy, and the technique and aftercare are similar to that described for managing chronic 'splints' in the previous section. Because of motion at the fracture site, healing is often delayed and frequently results in exuberant callus or exostosis, along with chronic pain/lameness, which may be considered as another manifestation of proliferative periostitis/interosseous desmitis or 'splints' (Fig. 17.14).

Treatment for proximal fractures The consequences of partial ostectomy alone for treating fractures of the proximal third of a splint bone are well recognized.[71] These fractures must be managed by either ostectomy with supplemental internal fixation to stabilize the remaining proximal portion or by primary repair using internal fixation. Failure to do so leads to loss of stability of the proximal portion and chronic lameness will result. The exception is MT-IV, in which the entire bone can be excised with a good outcome in many cases.[70]

With respect to fractures that occur during performance, the most common proximal splint fracture is an oblique fracture involving the head, most commonly MC-II

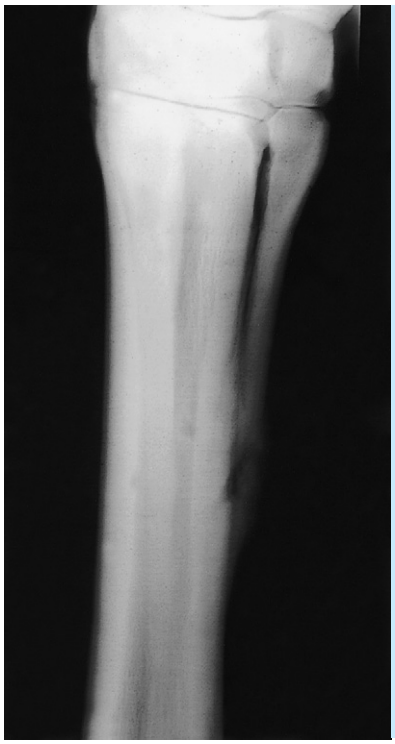
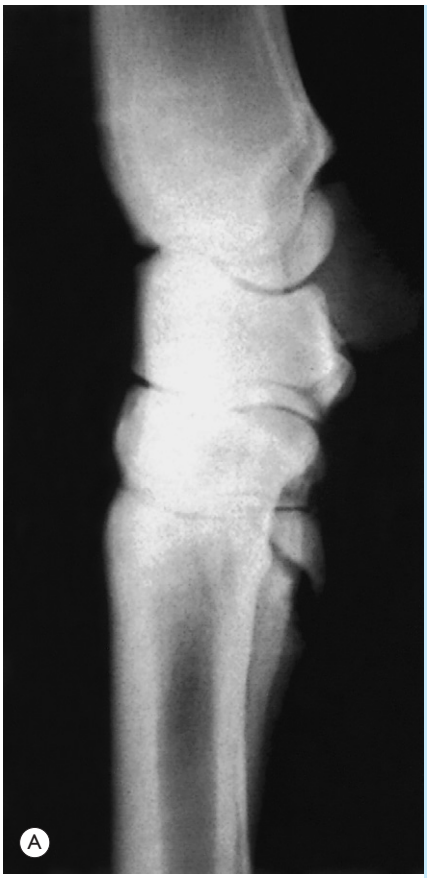


Fig. 17.14 Dorsomedial-to-palmarolateral oblique radiograph of the right metacarpus of a horse with a chronic fracture of the midbody of MC-II.



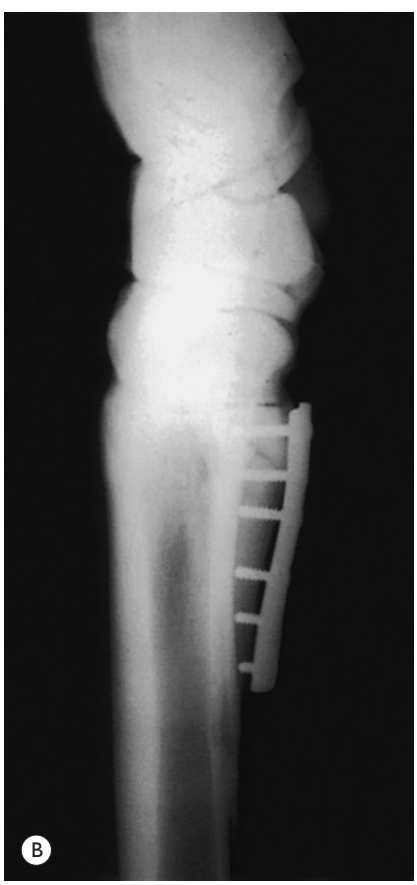


Fig. 17.15 (A) Lateral radiograph of the proximal left metacarpus and carpus of a Thoroughbred race horse that sustained an oblique fracture of the proximal portion of MC-II during a race. (B) Postoperative radiograph following open reduction and internal fixation using a 3.5 mm narrow dynamic compression plate. Note that screws do not engage MC-III.

(Fig. 17.15A). The fractures involve the articular aspect and are almost always displaced. Surgical repair involves open reduction and internal fixation using a small bone plate. An incision of appropriate length is centered over the proximal aspect of the bone along the palmaromedial or palmarolateral aspect of the limb. Sharp dissection is carefully carried out using a sharp elevator or scalpel to sever the heavy ligamentous attachments and expose the bone. The fracture line is debrided as needed to allow reduction. A 4–6 hole, narrow, 3.5 mm DCP is appropriately contoured and applied using 3.5 mm cortical screws. Screws should not engage the MC-III (Fig. 17.15B). Screws crossing the fracture line can be inserted in lag fashion but this may be difficult, depending on fragment width and fracture configuration, and is not essential if the fracture is well reduced. The incision is closed in multiple layers and a tight, padded bandage is securely applied.

Broad-spectrum antibiotics are administered for 24–48 hours and NSAIDs are administered for 3–5 days postoperatively. A bandage is maintained for 2–3 weeks and skin sutures are removed 12–14 days postoperatively. Horses are confined to a stall for 2 months. Daily hand-walking begins after suture removal. Exercise in a small paddock can begin at the 2-month point. Implants are removed 3 months postoperatively. This can be performed under local or general anesthesia but because of the heavy soft tissue covering is easier under general anesthesia, particularly for implants in MC-II. Screws are removed through stab incisions and the plate is elevated and removed through a small incision over the distal end. An additional 4–6 weeks of limited exercise are allowed before resumption of training once fractures have healed radiographically.

Prognosis

The prognosis for fractures involving the distal aspect of the splint bones is generally very good if there is no concurrent suspensory desmitis.[78,79] The prognosis for horses with suspensory ligament injury is directly related to the severity of the desmitis.

The prognosis following partial ostectomy for management of fractures of the midportion of the splint bones is fair to good and is similar to ostectomy for treatment of recalcitrant 'splints'.[80] In this author's experience, problems tend to arise if horses are not allowed an appropriate period of convalescence and training is resumed too quickly.

The prognosis for the oblique fractures involving the heads of the splint bones treated with internal fixation, in the author's experience, appears to be good but reports involving large numbers of this specific fracture type are lacking.

Etiology and pathophysiology

Etiology

Many distal splint fractures are associated with either axial compressive forces exerted through the proximal aspect of the bone or tension imparted by the attachments to the suspensory ligament. Most fractures of the middle and proximal portions of the splint bones are the result of blunt external trauma. Some oblique fractures of the head of the splint bone, specifically MC-II, may be avulsion fractures or the result of internal torsional forces.

Pathophysiology

Unlike the middle and proximal portions of the splint bones, the distal portion is not tightly adhered to the cannon bone through the interosseous ligament. It is therefore relatively mobile and has fascial attachments to the adjacent branch of the suspensory ligament. During exercise, compressive axial forces on the bone in some cases, or in others flexion and extension of the fetlock joint with the associated elongation and retraction of the suspensory ligament, create cyclic strain on the distal splint bone. If this proceeds at a rate that exceeds the bone's ability to adapt, it weakens and eventually fracture occurs. However, fractures appear clinically as an acute injury. The inherent motion at this location commonly leads to delayed or non-union or healing with a considerable callus.

Enlargement of the suspensory branch, as occurs with desmitis, displaces the distal splint bone abaxially, which may exacerbate the strain on the bone. Local inflammation associated with the desmitis may also lead to osteitis and a predisposition to fracture. However, the temporal relationship between desmitis and fracture is not completely understood and fracture may precede desmitis in some cases.

Blunt trauma from interference in the mid-to-proximal portion of the splint generally results in a short oblique or transverse fracture, but comminuted fractures or fracture of a crescent-shaped fragment are also seen. On rare occasions these fractures are open. (Conversely, open fractures are very common in non-exercise related cases.) Strains exerted on the proximal aspect of the bone (see previous section on 'splints') invariably result in motion and healing with a large callus or exostosis.

Fractures of the head of the splint bone can result from blunt external trauma, but they are also suspected to result from torsional stresses during exercise[69] and in some cases maybe avulsions. In this author's opinion, the oblique fractures of the head of MC-II appear in many cases to be avulsion fractures that presumably occur during hyperextension of the carpus. In addition to the medial collateral ligament of the carpus, the flexor carpi radialis and extensor carpi obliquus muscles insert on the proximal aspect of MC-II.

Epidemiology

Distal splint fractures affect performance horses of all breeds and uses, but are particularly common in race horses. Overall, distal splint fractures more commonly involve the forelimbs, with the exception of Standardbred race horses. For comparison, in Thoroughbreds left MC-IV and right MC-II are the most commonly affected and in Standardbreds fractures of the left MT-II and right MT-IV are most common.[52,78,79] Distal splint fractures are unusual in immature horses (< 2 years of age) and this is thought to be due to a decrease in pliability of the suspensory ligament and an increase in brittleness of the bone as horses age.[71,79] Younger horses are also not in formal athletic training.

Fractures of the middle and proximal portions resulting from interference are seen in all performance horses. Oblique fractures of the head caused by torsional strains during performance are most common in race horses and jumpers.[69]

Prevention

The use of shin boots, and corrective trimming and shoeing to correct gait abnormalities, can minimize the incidence of splint fractures resulting from interference.

Many distal splint fractures are fatigue fractures and concurrent or pre-existing suspensory desmitis may contribute to the development of this injury. Early detection of pre-fracture pathology, using such modalities as thermography and nuclear scintigraphy, along with careful physical examination and recognition of subtle signs of soreness or lameness, should enable early intervention/prevention in some horses.

Stress remodeling ('stress reaction') and stress fracture (avulsion fracture) at the suspensory origin

- Stress reaction and stress fractures at the suspensory origin are two of the three components of the 'high suspensory syndrome'.

- Either disorder may exist as a primary, distinct entity or be associated with desmitis at the suspensory origin.
- Stress reaction affects all types of performance horses.
- Stress fractures are seen most commonly in race horses.
- Pain on palpation of the suspensory origin, but few other overt clinical signs.
- Lameness may have gradual or sudden onset with stress reaction.
- Lameness typically has an acute onset with stress fracture.
- Scintigraphy plays an important role in the diagnosis.
- Treatment involves rest and controlled exercise for 2–6 months.
- Prognosis is generally favorable for either condition.

Stress remodeling or stress reaction, which can be thought of as an enthesitis, and stress or avulsion fractures at the origin of the suspensory ligament, along with desmitis of the suspensory origin, are the three components of the 'high suspensory syndrome'. This section will focus specifically on the primary osseous disorders and the reader is referred to Chapter 20 on suspensory desmitis for details on the primary ligamentous disorder. It is important to remember that although each condition can occur as a distinct injury, an element of both osseous and ligamentous pathology may exist in many cases.

Recognition

History and presenting complaint

Horses with stress reaction typically have a progressive lameness of insidious onset, but cases with apparent acute onset are also seen. Initially, lameness may be intermittent and improve or resolve with short-term rest. Eventually, lameness becomes persistent and worsens as exercise continues, rather than being a lameness that the horse 'warms out of'. In a subset of horses the condition only causes poor performance at peak exertion. An example would be Standardbred race horses that 'bear in or out' (drift into the rail or away from the rail) or frequently break stride during a race.

Lameness in horses with stress fracture is typically acute in onset and is first evident during or shortly after high-speed or hard exercise. Most horses are too lame to continue training. Some horses have a history of low-grade or intermittent lameness (as above) prior to acute fracture.

Physical examination

There are very few overt physical abnormalities in horses with primary osseous disease at the suspensory origin. Soft tissue swelling is minimal or absent (unless concurrent suspensory desmitis is present). Some horses stand 'over' at the knee (slight carpal flexion at rest). Focal pain in the region of the suspensory origin is the primary sign. This is most easily assessed with the limb in flexion and with firm pressure applied by the thumb along the proximal palmar aspect of the metacarpus (or with fingers along the plantar metatarsus), while displacing the flexor tendons medially or laterally.

Lameness examination

Lameness in horses with stress reaction ranges from subtle to moderate – grades < 1–3 of 5. The condition may be present bilaterally, in which case an overt lameness may not be apparent and horses have a change in gait mechanics or loss of action. Lameness in horses with acute stress fracture is typically grade 2–4 of 5. Bilateral fractures are rare. Lameness with either condition may be exacerbated with firm pressure over the suspensory origin and often is more pronounced with the affected limb on the outside of a circle. Lameness may also be exacerbated on soft footing, but this is more consistent with cases of desmitis at the suspensory origin. Lameness with stress fracture may be exacerbated with carpal or tarsal flexion, but this is not consistent.

Diagnostic confirmation

Diagnostic analgesia High palmar or high plantar analgesia will be positive in horses with pain at the suspensory origin. The proximal palmar metacarpus and plantar metatarsus are regions notorious for anatomic nuances that may contribute to misinterpretation of the response to local anesthetic injections.[81] Of chief concern are the distal palmar/plantar outpouchings of the carpometacarpal (CMC)/tarsometatarsal (TMT) joints and their close relationship with the suspensory origin.[82,83]

In the forelimb, a high lateral palmar nerve block[84] is the most specific perineural block for the suspensory origin and is therefore preferred to the traditional high palmar block (high 'four-point' block) or local infiltration of the suspensory origin (see Chapter 14).[85] A comparable technique does not exist for the hindlimb but because the distal plantar outpouchings of the TMT joint are less extensive than the CMC outpouchings, inadvertent intra-articular (IA) injection is less likely in the hindlimb, but this possibility, along with deposition of anesthetic in the tarsal sheath, must be recognized.[83,85]

Similarly, intra-articular injection of anesthetic in the middle carpal (and thus, CMC) or TMT joint can result in a false-positive diagnosis of articular pathology with bony disease at the suspensory origin.

Scintigraphy Nuclear scintigraphy is invaluable in the diagnostic work-up of horses with suspected stress reaction or stress fracture at the suspensory origin.[86,87] The minimal overt clinical signs and potential for misinterpretation of diagnostic analgesia, along with the fact that radiographs are often negative or equivocal in the early stages of stress reaction, make this imaging modality particularly beneficial.

Bone-phase images will reveal focal, mild to intense, abnormal increased radiopharmaceutical uptake in the proximal palmar metacarpus/plantar metatarsus in horses with stress reaction. Uptake is typically moderate to intense in horses with acute stress fracture (Fig. 17.16).

Radiography A full radiographic study of the proximal metacarpus/metatarsus should be obtained in all cases, but the most important views in horses with stress reaction or stress fracture are the dorsopalmar/plantar (DP) and lateral

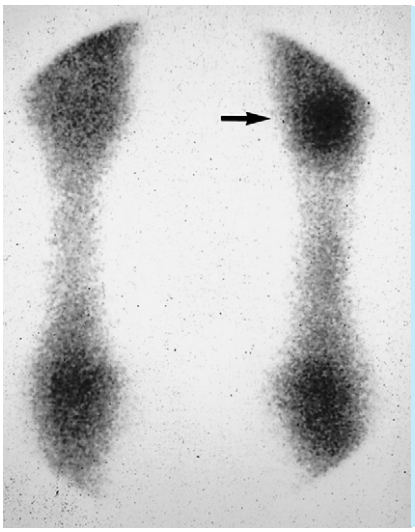


Fig. 17.16 Dorsopalmar bone-phase scintigraphic image of the metacarpal and carpal regions of a horse. Notice the focal area of intense abnormal increased radiopharmaceutical uptake in the proximal left metacarpus associated with an avulsion fracture at the origin of the suspensory ligament (arrow).

or flexed lateral. In the early or acute stages radiographs are often equivocal or may be negative, and correlation of lameness examination and scintigraphic findings is important.

Horses with stress reaction will exhibit varying degrees of trabecular bone sclerosis in the proximal palmar/plantar aspect of MC-III/MT-III at the suspensory origin. Careful evaluation may also reveal osteolytic change in the early stages in some cases. In the forelimbs this is most commonly medially and in the hindlimbs the changes are most commonly laterally (associated with the respective heads of the bipartite suspensory origin). Endosteal proliferative reaction and/or enthesiophyte formation along the palmar/plantar cortex may also be present.

Stress fractures in this location typically appear as an inverted V- or U-shaped radiolucency on the DP view and are often seen as a small crescent-shaped fragment on the lateral or flexed lateral view. Endosteal callus may be identifiable on the lateral view.

Ultrasonography A sonogram should be performed to assess the state of the suspensory ligament although, as previously mentioned, distinct changes indicative of active desmitis are inconsistent and frequently absent. Osseous abnormalities, including irregularity of the cortex or a separate avulsion fragment, may be identifiable.

Thermography In the hands of an experienced operator thermography may be useful for identifying inflammation at the suspensory origin.

Treatment and prognosis

Therapeutic aims

The goal of treatment is to reduce or eliminate strains on the affected area(s) and promote bone healing.

Therapy

Treatment for stress reaction at the suspensory origin involves anti-inflammatory therapy along with rest and controlled exercise, the specifics of which depend a great deal on the severity of the condition and the use and performance demands (i.e. competition schedule) of the horse.

In general, horses should have stall confinement with daily hand-walking exercise until lameness at a trot in-hand has resolved. Exercise is then gradually increased. Time for recovery is highly variable, but a range of 2–6 months is typical. Follow-up scintigraphic examination can be used to monitor healing and enable a more informed recommendation on increases in exercise intensity. Sclerosis will persist after scintigraphic activity has resolved, and therefore radiographs are less helpful in monitoring healing.

Local corticosteroid injection is often effective in alleviating lameness associated with stress reaction in horses whose competition schedules will not allow an extended period of rest. In addition, internal blisters (local infiltration of a counterirritant, typically an iodine-based product) are described anecdotally by many practitioners to be helpful for this condition, particularly when chronic and associated with suspensory desmitis; however, controlled studies are lacking. More recently, application of radial shock wave therapy is gaining popularity for treating this condition but, as with internal blisters, controlled studies at this stage are lacking.

Long toe/low heel conformation is often associated with this condition and may contribute to strain at the suspensory origin. Therefore, corrective trimming to shorten the toes to facilitate breakover may be helpful in these cases. Heel wedges (to elevate the heels) are contraindicated as they will actually increase suspensory ligament strain.[88]

Stress fractures usually heal readily in 3–4 months. Recommendations include 1 month of strict stall rest, followed by 1–2 months of stall confinement with daily hand-walking exercise and then 1–2 months of limited turnout in a small paddock. Follow-up radiographs (± scintigraphy) are taken at approximately 3–4 months to assess healing.

Prognosis

The prognosis for most horses with primary stress reaction or stress fracture at the suspensory origin is good if the condition has been allowed sufficient time to heal. The prognosis with concurrent desmitis at the suspensory origin is much more guarded, particularly in the hindlimbs, and therefore it is important to assess the suspensory ligament in these cases. (The reader is referred to Chapter 20 on suspensory desmitis for details.)

Etiology and pathophysiology

Etiology

Stress reaction and stress fractures at the suspensory origin are cyclic fatigue injuries associated with repetitive strain.

Pathophysiology

Repeated hyperextension of the fetlock joint during exercise with associated cyclic strain on the suspensory ligament is believed to be the primary cause of these conditions. In the

forelimbs, carpal hyperextension is also believed to be a contributing factor. As previously noted, long toe/low heel conformation may exacerbate the strain on the suspensory ligament. Stress reaction at the suspensory origin can be classified as an enthesitis resulting from tearing of Sharpey's fibers and associated inflammation of the underlying bone. Maladaptive remodeling and the onset of a stress fracture follow a pathogenesis similar to that of others and the reader is referred elsewhere for a detailed discussion. Stress fractures are most common in race horses and it is presumably the high-speed cyclic strain that promotes the development of fracture in these cases. Stress fractures can be classified as a form of avulsion fracture.

Epidemiology

Stress reaction at the suspensory origin is seen in all types of performance horses. It appears to be most common in race horses, eventers and show hunters or show jumpers.[86,87] Stress fractures at the suspensory origin are most commonly seen in race horses.[86–89] While the 'high suspensory syndrome', and in particular proximal suspensory desmitis, affects both front and hindlimbs, in the author's experience the primary osseous disorders (stress reaction and stress fracture) are seen more commonly in the forelimbs.

Prevention

Like other bone disorders associated with high-strain cyclic fatigue and/or maladaptive remodeling ('stress-induced bone disease'), prevention of stress reaction and stress fracture at the origin of the suspensory ligament, in theory, should involve both modification of the training regimen and early detection of the subclinical pathologic changes. In actuality, it is impossible to make a blanket recommendation on appropriate training schemes for all ages and uses of athletic horses. Detection of early pathologic changes using advanced diagnostic imaging modalities such as scintigraphy and thermography during the evaluation of horses at high risk for these conditions, or those exhibiting early clinical signs typical of pain at the suspensory origin, with subsequent modification in training intensity is a more realistic approach.

Long toe/low heel conformation exacerbates strain on the suspensory ligament. Therefore, corrective trimming and shoeing to improve hoof balance and shape is also important. However, elevating the heels with wedges and the use of egg bar shoes actually increases strain on the suspensory ligament[88] and their application in these horses should be avoided.

Other proximal metacarpal/metatarsal fractures in performance horses

This group consists of incomplete longitudinal fractures of the proximal palmar cortex of MC-III, dorsomedial articular fractures of proximal MC-III and dorsolateral articular fractures of proximal MT-III. All of these fractures are relatively uncommon compared to other metacarpal/metatarsal injuries and are seen almost exclusively in race horses. Recommended treatment for all is extended rest (3–6 months). The prognosis for the two metacarpal fracture types is generally good.[90–92] The prognosis for the dorsolateral articular fractures of proximal MT-III is more guarded.[93,94] This may be related to the association with osteoarthritis of the TMT joint.

References

1. Goodman NL, Baker BK. Lameness diagnosis and treatment in the Quarter Horse racehorse. Vet Clin North Am Equine Pract 1990; 6(1):85–108.
2. Swanson TD. Lameness grading system. In: Guide for veterinary service and judging of equestrian events, 3rd edn. Golden, CO: American Association of Equine Practitioners; 1984.
3. Koblik PD, Hornof WJ, Seeherman HJ. Scintigraphic appearance of stress-induced trauma of the dorsal cortex of the third metacarpal bone in racing Thoroughbred horses: 121 cases (1978–1986). J Am Vet Med Assoc 1988; 192(3):390–395.
4. Turner TA, Pansch J, Wilson JH. Thermographic assessment of racing Thoroughbreds. Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners; 2001; 344–346.
5. Rohde C, Anderson DE, Bertone AL, et al. Effects of phenylbutazone on bone activity and formation in horses. Am J Vet Res 2000; 61(5):537–543.
6. Nunamaker DM, Provost MT. The bucked shin complex revisited. Proceedings of the 37th Annual Convention of the American Association of Equine Practitioners; 1992; 757–762.
7. Copelan RW. Incidence, location, and principles of treatment of stress fractures of the third metacarpal bone. Proceedings of the 25th Annual Convention of the American Association of Equine Practitioners; 1979; 159–162.
8. Nunamaker DM. The bucked shins complex. Proceedings of the 32nd Annual Convention of the American Association of Equine Practitioners; 1986; 457–460.
9. Moyer W, Spencer PA, Kallish M. Relative incidence of dorsal metacarpal disease in young Thoroughbred racehorses training on two different surfaces. Equine Vet J 1991; 23(3):166–168.
10. Jeffcott LB, Rossdale PD, Freestone J, et al. An assessment of wastage in Thoroughbred racing from conception to four years of age. Equine Vet J 1982; 14:185–198.
11. Griffiths JB, Steel CM, Symons PJ, et al. Improving the predictability of performance by prerace detection of dorsal metacarpal disease in Thoroughbred racehorses. Aust Vet J 2000; 78(7):466–467.
12. Norwood GL. The bucked shins complex in Thoroughbreds. Proceedings of the 24th Annual Convention of the American Association of Equine Practitioners; 1978; 319–336.
13. Stover SM, Pool RR, Morgan JP, et al. A review of bucked shins and metacarpal stress fractures in Thoroughbred racehorses. Proceedings of the 34th Annual Convention of the American Association of Equine Practitioners 1988; 129–134.

14. Buckingham SHW, Jeffcott LB. Shin soreness: a survey of Thoroughbred trainers and racetrack veterinarians. Aust Equine Vet 1990; 8:148–152.
15. Bailey CJ. Wastage in the racing industry – approaches to study. Proceedings of the Rural Industries Research and Development Corporation Epidemiology Workshop for Equine Research Workers; 1998; 43–52.
16. Jeffcott LB, McCarthy RN, Buckingham SHW, et al. Shin soreness in racehorses. University of Melbourne, Melbourne: Equine Clinical Research Unit, Department of Veterinary Science; 1991; 5–23.
17. Goodman NL. Quarter Horse racetrack practice. Proceedings of the 33rd Annual Convention of the American Association of Equine Practitioners; 1987; 835–841.
18. Nunamaker DM, Butterweck DM, Black J. In vitro comparison of Thoroughbred and Standardbred racehorses with regard to local fatigue failure of the third metacarpal bone. Am J Vet Res 1991; 52(1):97–100.
19. Nunamaker DM. Metacarpal stress fractures. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 195–199.
20. Dallap BL, Bramlage LR, Embertson RM. Results of screw fixation combined with cortical drilling for treatment of dorsal cortical stress fractures of the third metacarpal bone in 56 Thoroughbred racehorses. Equine Vet J 1999; 31(3):252–257.
21. Hanie EA, Sullins KE, White NA. Follow-up of 28 horses with third metacarpal unicortical stress fractures following treatment with osteostixis. Equine Vet J 1992; 24(suppl 11): 4–9.
22. Cervantes C, Madison JB, Ackerman N, et al. Surgical treatment of dorsal cortical fractures of the third metacarpal bone in Thoroughbred racehorses: 53 cases (1985–1989). J Am Vet Med Assoc 1992; 200(12): 1997–2000.
23. Specht TE, Colahan PT. Osteostixis for incomplete cortical fracture of the third metacarpal bone – results in 11 horses. Vet Surg 1990; 19(1):34–40.
24. Spurlock GH. Propagation of a dorsal cortical stress fracture of the third metacarpal bone in two horses. J Am Vet Med Assoc 1988; 192(11):1587–1589.
25. Watt BC, Foerner JJ, Haines GR. Incomplete oblique sagittal fractures of the dorsal cortex of the third metacarpal bone in six horses. Vet Surg 1998; 27:337–341.
26. Norwood GL, Haynes PF. Dorsal metacarpal disease. In: Mansmann RA, McAllister ES, eds. Equine medicine and surgery, 3rd edn. Santa Barbara, CA: American Veterinary Publications; 1982; 1110–1114.
27. Specht TE, Miller GJ, Colahan PT. Effects of clustered drill holes on the breaking strength of the equine third metacarpal bone. Am J Vet Res 1990; 51(8):1242–1246.
28. Burstein AH, Currey J, Frankel VH, et al. Bone strength. The effect of screw holes. J Bone Joint Surg 1972; 54-A:1143–1156.
29. Williams JGP. Recalcitrant stress fracture: a case managed by drilling. Br J Sports Med 1979; 13:84–85.
30. Richardson DW. Dorsal cortical fractures of the equine metacarpus. Comp Cont Educ Pract Vet 1984; 6:248–255.
31. Frost HM. The regional acceleratory phenomenon: a review. Henry Ford Hosp Med J 1983; 31:3–9.
32. Bertone AL. The metacarpus and metatarsus. In: Stashak TS, ed. Adam's lameness in horses, 5th edn. Philadelphia, PA: Lippincott Williams and Wilkins; 2002; 800–830.
33. Richardson DW. The metacarpal and metatarsal bones. In: Auer JA, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia, PA: Saunders; 1999; 810–821.
34. Carter DR, Hayes WC. Compact bone fatigue damage: a microscopic examination. Clin Orthop 1977; 127: 265–274.
35. Nunamaker DM, Butterweck DM, Provost MT. Fatigue fractures in Thoroughbred racehorses: relationships with age, peak bone strain, and training. J Orthop Res 1990; 8:604–611.
36. Nunamaker DM, Butterweck DM, Provost MT. Some geometric properties of the third metacarpal bone: a comparison between the Thoroughbred and Standardbred racehorse. J Biomech 1989; 22:129–134.
37. Stover SM, Sprayberry K, Pool RR, et al. Incomplete cortical fractures of the Thoroughbred third metacarpal bones. Trans Ann Vet Orth Soc Mtg 1988; 15:19.
38. Ferraro GL. Lameness diagnosis and treatment in the Thoroughbred racehorse. Vet Clin North Am Equine Pract 1990; 6(1):147–178.
39. Ellis DR. Some observations on condylar fractures of the third metacarpus and third metatarsus in young Thoroughbreds. Equine Vet J 1994; 26(3):178–183.
40. Johnson BJ, Stover SM, Daft BM, et al. Causes of death in racehorses over a 2-year period. Equine Vet J 1994; 26(4): 327–330.
41. Bathe AP. 245 fractures in Thoroughbred racehorses: results of a 2-year prospective study in Newmarket. Proceedings of the 40th Annual Convention of the American Association of Equine Practitioners; 1994; 175–176.
42. Bassage LH, Richardson DW. Longitudinal fractures of the condyles of the third metacarpal and metatarsal bones in racehorses: 224 cases (1986–1995). J Am Vet Med Assoc 1998; 212(11):1757–1764.
43. Zekas LJ, Bramlage RM, Embertson RM, et al. Characterization of the type and location of fractures of the third metacarpal/metatarsal condyles in 135 horses in central Kentucky (1986–1994). Equine Vet J 1999; 31(4): 304–308.
44. Kawcak CE, Bramlage LR, Embertson RM. Diagnosis and management of incomplete fractures of the distal palmar aspect of the third metacarpal bone in five horses. J Am Vet Med Assoc 1995; 206(3):335–337.
45. Richardson DW. Medial condylar fractures of the third metatarsal bone in horses. J Am Vet Med Assoc 1984; 185(7):761–765.
46. Hornof WJ, O'Brien TR. Radiographic evaluation of the palmar aspect of the equine metacarpal condyles: a new projection. Vet Radiol 1980; 21(4):161–167.
47. Pilsworth RC, Hopes R, Greet TRC. A flexed dorso-palmar projection of the equine fetlock in demonstrating lesions of the distal third metacarpus. Vet Rec 1988; 122: 332–333.
48. Barclay WP, Foerner JJ, Phillips TN. Axial sesamoid injuries associated with lateral condylar fractures in horses. J Am Vet Med Assoc 1985; 186(3):278–279.
49. Rick MC, O'Brien TR, Pool RR, et al. Condylar fractures of the third metacarpal bone and third metatarsal bone in 75 horses: radiographic features, treatments, and outcome. J Am Vet Med Assoc 1983; 183(3):287–296.
50. Stashak TS. The metacarpus and metatarsus. In: Stashak TS, ed. Adam's lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1987; 596–624.
51. Schneider RK, Jackman BR. Fractures of the third metacarpus and metatarsus. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 179–194.
52. Richardson DW. Third metacarpal/metatarsal condylar fractures. In: White NA, Moore JN, eds. Current practice of equine surgery. Philadelphia, PA: JB Lippincott; 1990; 617–622.

53. Martin GS. Factors associated with racing performance of Thoroughbreds undergoing lag screw repair of condylar fractures of the third metacarpal or metatarsal bone. J Am Vet Med Assoc 2000; 217(12):1870–1877.
54. Zekas LJ, Bramlage LR, Embertson RM, et al. Results of treatment of 145 fractures of the third metacarpal/metatarsal condyles in 135 horses (1986–1994). Equine Vet J 1999; 31(4):309–313.
55. Ross MW. Scintigraphic and clinical findings in the standardbred metatarsophalangeal joint: 114 cases (1993–1995). Equine Vet J 1998; 30(2):131–138.
56. Martinelli MJ, Chambers MD, Baker GJ, et al. A retrospective study of increased bone scintigraphic uptake in the palmar-plantar fetlock and its relationship to performance: 50 horses (1989–1993). Proceedings of the 40th Annual Convention of the American Association of Equine Practitioners; 1994; 53–54.
57. Arthur RM, Constantinide D. Results of 428 nuclear scintigraphic examinations of the musculoskeletal system at a Thoroughbred racetrack. Proceedings of the 41st Annual Convention of the American Association of Equine Practitioners; 1995; 84–87.
58. Stover SM, Read DH, Johnson BJ, et al. Lateral condylar fracture histomorphology in racehorses. Proceedings of the 40th Annual Convention of the American Association of Equine Practitioners; 1994; 173.
59. Riggs CM, Whitehouse GH, Boyde A. Structural variation of the distal condyles of the third metacarpal and third metatarsal bones in the horse. Equine Vet J 1999; 31(2): 130–139.
60. Riggs CM, Whitehouse GH, Boyde A. Pathology of the distal condyles of the third metacarpal and third metatarsal bones of the horse. Equine Vet J 1999; 31(2): 140–148.
61. Boyde A, Haroon Y, Jones SJ, et al. Three dimensional structure of the distal condyles of the third metacarpal bone of the horse. Equine Vet J 1999; 331(2): 122–129.
62. Rooney JR. Distal condylar fractures of the cannon bone in the horse. Mod Vet Pract 1974; 52:113–114.
63. Meagher DM. Lateral condylar fractures of the metacarpus and metatarsus in horses. Proceedings of the 22nd Annual Convention of the American Association of Equine Practitioners; 1976; 147–154.
64. Turner AS. Surgical repair of fractures of the third metatarsal bones in a Standardbred gelding. J Am Vet Med Assoc 1977; 171(7):655–658.
65. Baker RH. Comments on the incidence and repair of cannon bone fractures extending into the fetlock joint. Proceedings of the 25th Annual Convention of the American Association of Equine Practitioners; 1979; 163–164.
66. Pool RR, Meagher DM. Pathologic findings and pathogenesis of racetrack injuries. Vet Clin North Am Equine Pract 1990; 6(1):1–29.
67. Kane AJ, Stover SM, Gardner IA, et al. Horseshoe characteristics as possible risk factors for fatal musculoskeletal injury of Thoroughbred racehorses. Am J Vet Res 1996; 57(8):1147–1151.
68. Kane AJ, Stover SM, Gardner IA, et al. Hoof size, shape, and balance as possible risk factors for catastrophic musculoskeletal injury of Thoroughbred racehorses. Am J Vet Res 1998; 59(12):1545–1552.
69. Ray C, Baxter GM. Splint bone injuries in horses. Comp Cont Edu Pract Vet 1995; 17(5):723–730.
70. Baxter GM, Doran RE, Allen D. Complete excision of a fractured fourth metatarsal bone in eight horses. Vet Surg 1992; 21(4):273–278.
71. Doran R. Fractures of the small metacarpal and metatarsal (splint) bones. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 200–207.
72. Bramlage LR, van Hoogmoed L, Embertson R, et al. Treatment of refractory exostoses of the midportion of the splint bones. Proceedings of the 43rd Annual Convention of the American Association of Equine Practitioners; 1997; 126–127.
73. Welling EK. Evaluation of the efficacy of surgical intervention on middle and proximal splint bone injuries in 95 Standardbred horses. Vet Surg 1993; 22:293.
74. Barber SM, Caron J, Pharr J. Metatarsal/metacarpal exostosis removal – a prospective study. Vet Surg 1987; 16:82.
75. Les CM, Stover SM, Willits NH. Necropsy survey of metacarpal fusion in the horse. Am J Vet Res 1995; 56(11): 1421–1432.
76. Verschooten F, Gasthuys F, de Moor A. Distal splint bone fractures in the horse: an experimental and clinical study. Equine Vet J 1984; 16(6):532–536.
77. du Preez P. Fractures of the small metacarpal and metatarsal bones (splint bones). Equine Vet Edu 1994; 6(5):279–283.
78. Jones RD, Fessler JF. Observations on small metacarpal and metatarsal fractures with or without associated suspensory desmitis in Standardbred horses. Can Vet J 1977; 18(2):29–32.
79. Bowman KF, Evans LH, Herring ME. Evaluation of surgical removal of fractured distal splint bones in the horse. Vet Surg 1982; 11:116–120.
80. Bowman KF, Fackelman GE. Surgical treatment of complicated fractures of the splint bones in horses. Vet Surg 1982; 11:121–124.
81. Dyson S. Some observations on lameness associated with pain in the proximal metacarpal region. Equine Vet J 1988; 20(suppl 6):43–52.
82. Ford TS, Ross MW, Orsini PG. Communications and boundaries of the middle carpal and carpometacarpal joints in horses. Am J Vet Res 1988; 49(12):2161–2164.
83. Dyson SJ, Romero JM. An investigation of injection techniques for local analgesia of the equine distal tarsus and proximal metatarsus. Equine Vet J 1993; 25(1):30–35.
84. Wheat JD, Jones K. Selected techniques of regional anesthesia. Vet Clin North Am Large An Pract 1981; 3:223–246.
85. Ford TS, Ross MW, Orsini PG. A comparison of methods for proximal palmar metacarpal analgesia in horses. Vet Surg 1989; 18(2):146–150.
86. Pleasant RS, Baker GJ, Muhlbauer MC, et al. Stress reactions and stress fractures of the proximal palmar aspect of the third metacarpal bone in horses: 58 cases (1980–1990). J Am Vet Med Assoc 1992; 201(12):1918–1923.
87. Edwards RB, Ducharme NG, Fubini SL, et al. Scintigraphy for diagnosis of avulsions of the origin of the suspensory ligament in horses: 51 cases (1980–1993). J Am Vet Med Assoc 1995; 207(5):608–611.
88. Riemersma DJ, van den Bogert AJ, Jansen MO, et al. Influence of shoeing on ground reaction forces and tendon strains in the forelimbs of ponies. Equine Vet J 1996; 28(2):126–132.
89. Bramlage LR, Gabel AA, Hackett RP. Avulsion fractures of the origin of the suspensory ligament in the horse. J Am Vet Med Assoc 1980; 176(10):1004–1010.
90. Ross MW, Ford TS, Orsini PG. Incomplete longitudinal fracture of the proximal palmar cortex of the third metacarpal bone in horses. Vet Surg 1988; 17(2):82–86.
91. Ross MW, Martin BB. Dorsomedial articular fracture of the proximal aspect of the third metacarpal bone in Standardbred racehorses: seven cases (1978–1990). J Am Vet Med Assoc 1992; 201(2):332–335.
92. Lloyd KCK, Koblik P, Ragle C, et al. Incomplete palmar fracture of the proximal extremity of the third metacarpal bone in

horses: 10 cases (1981–1986). J Am Vet Med Assoc 1988; 192(6):798–803.
93. Ross MW, Sponseller ML, Gill HE, et al. Articular fracture of the dorsoproximal aspect of the third metatarsal bone in five Standardbred racehorses. J Am Vet Med Assoc 1993; 203(5):698–700.
94. Pilsworth RC. Incomplete fracture of the dorsal aspect of the proximal cortex of the third metatarsal bone as a cause of hind-limb lameness in the racing Thoroughbred: a review of three cases. Equine Vet J 1992; 24(2):147–150.

CHAPTER 18

The carpus

Christopher E. Kawcak

Diseases of the carpus commonly affect race horses, in which repeated stress from training and racing can lead to degradative changes within synovium, joint capsule, articular cartilage, subchondral bone and ligaments. These chronic changes often lead to acute problems ranging from synovitis to catastrophic injuries. Identification of the chronic processes prior to the development of acute disease would be ideal and newer diagnostic methods, such as magnetic resonance imaging (MRI), computed tomography (CT) and biomarkers, may help. Most of the acute manifestations of carpal diseases lead to synovial effusion and pain on flexion and radiographic imaging and diagnostic arthroscopy are often necessary to characterize the disease process. Carpal disease in race horses is common and the lesions occur in consistent areas. This permits in-depth clinical study of carpal diseases, allowing practitioners to give an accurate prognosis for a particular injury based on these studies.

Carpal injuries can also affect any other type of equine athlete; however, these disease processes are usually manifested as acute, traumatic injuries which sometimes occur in uncommon areas of the carpus. Consequently, determining prognosis for these types of injuries is often difficult due to the unusual nature of the damage and the lack of large clinical studies.

Synovitis

- Variable lameness with synovial effusion.
- Radiographs are often unremarkable.
- Intra-articular medication is often effective for eliminating signs.
- Horses with synovitis often respond well to medical therapy.

Recognition

History and presenting complaint

Synovitis manifests itself primarily as a lameness associated with significant synovial effusion. Synovial effusion alone in young race horses that are not showing lameness or training problems is not uncommon. However, the effusion may be significant if there is a history of training-associated problems or lameness with the horse.

Physical examination

Synovial effusion in the carpal joints can occur in both the dorsal and palmar aspects. A grading scheme, developed by Ray & McIlwraith (unpublished data, 1995) can be used to grade synovial effusion from 1 to 4. Grade 1 is mild effusion palpable on the dorsal aspect of the carpal joints, while grade 4 is palpable effusion that can also be detected on the palmar aspect of the joint. It is typical to see pain with static flexion in horses with synovitis and pinpoint pain on palpation can sometimes be appreciated in those with synovitis and other injuries leading to synovitis. Heat on palpation is not uncommon in horses with synovitis; however, the presence of topical medications and recent bandaging may influence surface heat.

Most horses with synovitis will be lame at the trot and, in carpal lameness in particular, wide movement to the forelimbs is appreciable. This wide movement occurs because horses with synovitis, and the resulting pain in the carpal joints, do not want to flex their carpi. Consequently, they will

circumduct the limb, leading to a wide moving gait. Furthermore, in cases of carpal synovitis, it is quite common to see worsening of the lameness after flexion.

Special examination

Regional anesthesia of the carpus, although often unnecessary for diagnosis of synovitis, can be accomplished by performing a median and ulnar nerve block after perineural anesthesia below the carpus has been performed. Intra-articular anesthesia is usually not necessary to diagnose synovitis of the carpal joints but occasionally may be needed to confirm carpal disease and rule out other diseases in the limb. As an example, it may be prudent to block the carpal joints and eliminate the lameness there in order to document additional lameness in another area of the limb. Although carpal joint blocks have been described elsewhere, it is important to remember that the radiocarpal and intercarpal joints should be blocked separately. Because heat can be experienced in joints with synovitis, the use of thermography can help to regionalize the area of injury. Furthermore, radiographs are usually negative. However, good-quality radiographs in multiple views are necessary to rule out any small or subtle injuries. In many cases of primary synovitis, it is not uncommon to see soft tissue thickening or dorsal displacement of the fat pad on the dorsum of the carpus on the radiographs.

Advances in ultrasonographic examination of joints have given clinicians a better impression of soft tissue injuries. Because soft tissue injuries can lead to synovitis, documentation of capsular and synovial lining thickening and edema can help not only to diagnose the primary problem but also to monitor therapy over time. Ultrasound also allows the clinician to rule out extracapsular thickenings such as hygromas and synovial hernias. An in-depth review of ultrasonographic examination of joints has been documented.[1]

Synovial fluid can also be evaluated subjectively. It is not uncommon in cases of synovitis to see a watery, clear to light yellow fluid. In some cases, there is increased opacity and flocculants in the fluid. In cases such as this, laboratory examination of the synovial fluid may be necessary to rule out septic arthritis.

Laboratory examination

Synovial fluid analysis results can be variable in cases of synovitis although most white blood cell counts are less than 1000 cells/mm^3 and total protein concentrations are generally between 2.5 and 4.0 g/dL. Biomarker data often show elevated concentrations of prostaglandin E_2.[2,3]

Diagnostic confirmation

The lack of radiographic findings, which rules out osteochondral fragmentation and fracture, is often enough to lead to a diagnosis of synovitis, although a negative diagnostic arthroscopy is needed to be totally convinced that intra-articular ligament disease is not present. It is often difficult to justify diagnostic arthroscopy in cases that are most likely synovitis compared to intra-articular ligament injury; therefore most veterinarians will monitor response to medical therapy. Refractory cases are then easier to justify as needing surgery as synovitis usually responds well to intra-articular medications.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to provide timely, effective anti-inflammatory medications either systemically or locally.

Therapy

Systemic anti-inflammatory medications, such as non-steroidal anti-inflammatory medications or intravenous hyaluronic acid, are the simplest forms of therapy which are often very effective for controlling synovitis. However, intra-articular anti-inflammatory medication in the form of corticosteroids and/or hyaluronic acid may be necessary to provide effective treatment. Physical therapy methods such as ice, hydrotherapy and walking are often used in addition to medications.

Prognosis

The prognosis for synovitis is often excellent for resumption of athletic training with rapid, effective therapy barring predisposing conformational abnormalities, osteochondral disease or intra-articular ligament disease.

Etiology and pathophysiology

Acute injuries can lead to synovitis but in race horses, the chronic effects of training and racing can lead to failure of tissues to adapt properly to training. Early, chronic stress can lead to adaptive changes until a certain threshold is crossed, when degradative changes overcome adaptive changes. This can occur within any tissues. Conformational abnormalities can accelerate the degradative process due to high, focal stresses.

Epidemiology

As stated previously, young race horses typically develop some form of synovitis early in their training. However, most cases of synovitis are secondary to a primary disease entity within the joint, such as osteochondral fragmentation or fracture. Conformational abnormalities, especially offset and/or calf-kneed conformations, can increase the chances of synovitis.

Prevention

Critical evaluation of conformation is essential as gross abnormalities in conformation may cause persistent

abnormal loading and hence synovitis and ultimately osteoarthritis (OA). Careful monitoring during training is also essential as treatment and change in training early in cases of synovitis are helpful.

Capsulitis

- Capsulitis often results in joint capsule thickening.
- Restricted range of motion is common in cases of capsulitis.
- Enthesiophytes are often seen on radiographs.
- Response to treatment is often variable.

Recognition

History and presenting complaint

Capsulitis can be caused by several disease processes so the history can be quite variable. For instance, it is not uncommon to see capsulitis in horses with a history of carpal disease such as osteochondral fractures, fragmentation or ligamentous injuries. However, capsulitis can also result from non-articular diseases, such as extracapsular ligament damage or capsular injury. In some cases, capsulitis can also occur because of acute injury, which may lead to edema and possibly fibrosis of the joint capsule. In some recurrent or unresponsive idiopathic synovitis cases, capsular thickening and scarring can also result. In most of these cases in athletes, the animal will fail to train and will have chronic unresponsive joint disease.

Physical examination

Horses with capsulitis typically show soft tissue thickening over the dorsal aspect of the carpus. However, the severity of effusion can be difficult to appreciate because of this thickening. Range of motion is often restricted and maximal flexion often results in a painful response. At the jog, these horses typically move wide and are often significantly worse after carpal flexion. Occasionally, pain on palpation will be apparent on the dorsal aspect of the carpus, especially in acute cases. Although capsular swelling is difficult to appreciate on the palmar aspect of the joint, it is the author's experience that horses with palmar capsular pain are extremely sensitive to carpal flexion.

Special examination

Horses with acute capsular changes may show no radiographic changes; however, those horses with capsular tearing, especially at the insertion of the capsule into the bone, will often show enthesiophyte formation several weeks after injury (Fig. 18.1). Enthesiophytes can vary in severity and location; however, in most equine athletes, especially race horses, enthesiophyte formation on the dorsal aspect of the carpal bones is quite common. Ultrasound examination of the joint capsule in horses with acute capsulitis will often show edema formation within the capsular tissues, and thickening of those tissues. Thermography may be of some use in acute cases due to the heat and inflammation that commonly occur with capsulitis and capsular tearing. Nuclear scintigraphy may also be helpful in some cases, especially in the flow and soft tissue phases. CT examination may be of little use in these cases unless a primary osteochondral disease process is leading to the capsular change. MRI, on the other hand, would be very helpful in assessing capsular disease and in qualifying the severity of damage.

Laboratory examination

Synovial fluid analysis in horses with capsular damage is often quite variable.

Diagnostic confirmation

As mentioned previously, radiographs are usually only suggestive of capsular changes. In particular, enthesiophyte formation certainly indicates previous capsular insertional damage and periarticular lysis may indicate acute inflammation at the insertion. Even though capsular damage can occur by itself, other intra-articular diseases must be ruled out, either by the special examinations mentioned above or, as in most cases by diagnostic arthroscopy.

Finally, capsulitis is sometimes diagnosed based on response to therapy. For instance, some cases of acute capsular tearing may respond well to intra-articular anti-inflammatory medications. Unlike secondary capsulitis, which occurs in response to other osteochondral diseases, primary capsular damage will usually respond to medical therapy. However, this is dependent upon the severity of damage.

Treatment and prognosis

Therapeutic aims

The principal therapeutic aim is to remove the primary disease. In cases of secondary capsular damage, the primary objective is to remove the intra-articular damage that is leading to capsulitis. Second, inflammation must be reduced by either systemic or intra-articular methods. Finally, because capsular disease often leads to scar tissue formation, methods that help restore function and range of motion are essential to decreasing scar tissue formation. For instance, this author commonly uses passive range of motion, hypothermia, massage therapy and progressive increase in exercise in an attempt to restore proper function to the joint.

Therapy

Arthroscopic removal or fixation of the primary problem is essential to overcoming capsular damage. Systemic and intra-articular anti-inflammatory medications and physical therapy, including passive range of motion, are also essential in dealing with capsular damage. Furthermore, although unsubstantiated

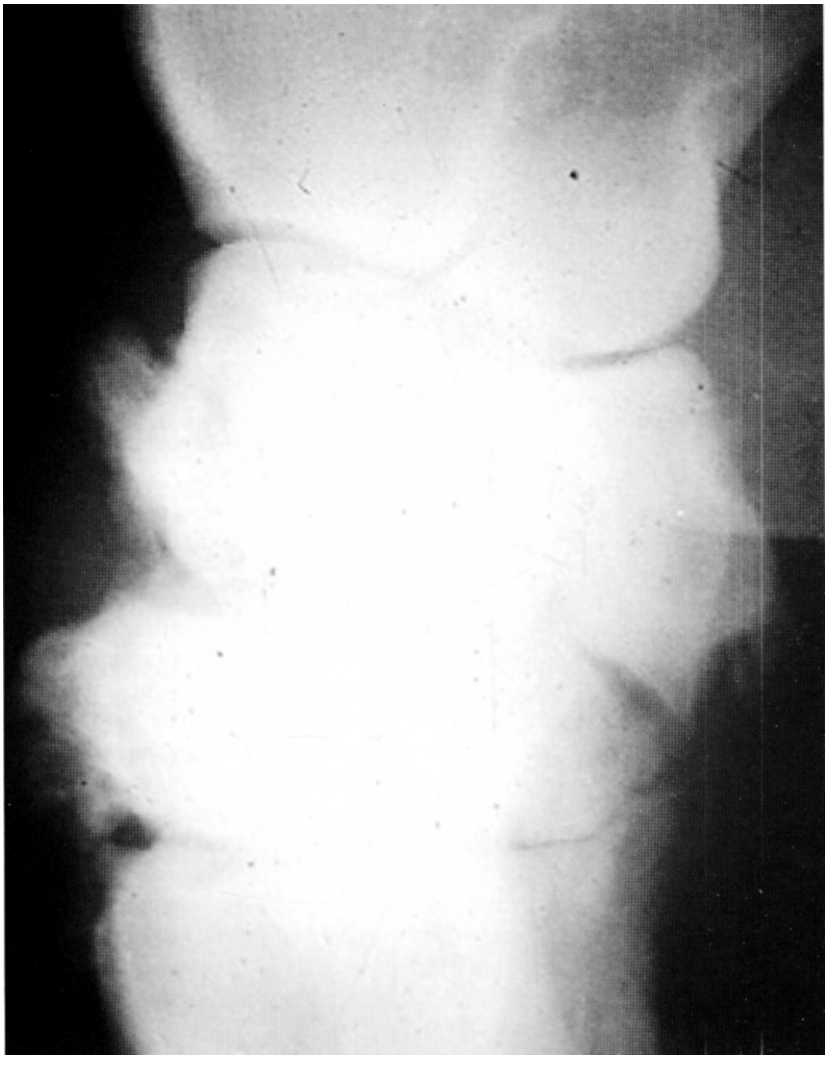


Fig. 18.1
Radiographic image of a carpus showing severe enthesiophyte formation.

experimentally, this author feels that the use of joint supplements such as chondroiton sulfates and glucosamines may be beneficial in cases in which there is capsular damage.

Prognosis

The prognosis in cases with capsular damage can be quite variable. In cases of acute, mild capsulitis or capsular damage, the prognosis is usually quite good with prompt identification of the disease process and therapy. However, severe cases of capsular damage can be quite limiting to the prognosis of an athlete and often require ongoing medical management to continue competing. Decreased range of motion and pain on flexion often hinder the horse's ability to use the limb properly. The prognosis for cases of secondary capsulitis or capsular damage is dependent on the severity and form of the primary disease process.

Etiology and pathophysiology

In most primary cases of capsular damage, an acute sprain type of injury is often the cause of the problem. However, as stated above, repetitive trauma to the joint capsule due to training and racing could lead to chronic changes in the joint capsule, and hence chronic capsulitis. Secondary forms of capsular damage often result from osteochondral damage elsewhere in the joint and failure to treat that primary disease promptly.

Epidemiology

It seems that most cases of carpal disease often result in some form of capsulitis. Only in those very acute cases of primary joint disease will capsulitis not be a factor. However, failure to treat promptly or a 'wait and see' approach to carpal disease will most likely lead to some form of capsular disease. Capsulitis is common in race horses and in retired race horses which are commonly used in other disciplines. In some of the latter cases, the primary osteochondral injury may not be treated because the horse is retired, and hence lead to capsulitis.

Prevention

Aggressive and prompt treatment of the primary cause of secondary capsulitis is essential in order to prevent capsular

damage and thickening. In some cases, failure to treat the primary problem often results in persistent capsular changes that often limit the prognosis of the animal, even though the primary disease may be mild or cured.

Desmitis (intra-articular and extra-articular ligament disease)

- Effusion often persists in the face of medical therapy.
- Radiographs are often unremarkable.
- Diagnostic arthroscopy is often required to establish a diagnosis.
- Fiber tearing is common in athletes.

Recognition

History and presenting complaint

There are no distinguishing historical characteristics for horses with desmitis of intra-articular ligaments.[4]

Physical examination

Similar to the history, it has been shown in a retrospective study that there are no distinguishing clinical characteristics for diagnosis of intra-articular ligament damage that separate it from other forms of carpal disease.[4]

Special examination

Most cases of intra-articular ligament damage present similar to cases of synovitis. In acute cases, these animals show synovial effusion and negative radiographic findings. However, in some cases of avulsion fracture, special views can identify intra-articular ligament damage and nuclear scintigraphy may show increased uptake within the intercarpal area. CT examination has revealed stress reaction in the subchondral bone adjacent to intra-articular ligament sites, which may be indicative of damage at that site.[5] In the future, MRI examination will undoubtedly show intra-articular ligament damage much as it does in humans.

Diagnostic confirmation

Although other diagnostic modalities exist, diagnostic arthroscopy is still the best method, not only to characterize the severity of damage but also to aid in debridement of the torn ligament fibers.

Treatment and prognosis

Therapeutic aims

The primary therapeutic aim is to identify the diseased tissues and debride those torn ligamentous fibers. In cases of avulsion fracture, it is best to remove the avulsed portion of bone.

Therapy

Arthroscopic debridement of tissue ends is essential for treatment of intra-articular desmitis. Furthermore, anti-inflammatory medications and joint supplements may also be beneficial, as is physical therapy.

Prognosis

The prognosis for intra-articular ligament damage is based on the severity of damage; however, in most cases the prognosis is good.

Etiology and pathophysiology

It appears that intra-articular ligament damage is quite common as most horses older than 1 year have some form of tearing.[6] It has also been shown that larger ligaments show some forms of damage at the ultrastructural level. Therefore, it appears that most of these cases are the result of chronic progressive damage, most likely due to training and racing. However, the gross changes have variable clinical effects on equine athletes.

Epidemiology

Recent reports have shown that intra-articular ligament damage is quite common and may even be incidental in most cases. This makes it difficult to determine the clinical significance of these lesions; however, seeing the damage as the only pathologic change on diagnostic arthroscopy and seeing a positive improvement with debridement leads one to believe that in some cases these are significant lesions when no other lesions are present.

Prevention

There appears to be no effective means of preventing intra-articular ligament damage other than identifying the lesions at an early stage in order to prevent secondary joint changes that could lead to OA.

Osteochondral fragmentation (chip fracture)

- Chronic disease processes often lead to osteochondral fragmentation.
- Synovitis is a common feature of osteochondral fragmentation.

- Arthroscopy is the treatment of choice.
- The prognosis is dependent on the severity of articular cartilage erosion.

Recognition

History and presenting complaint

Most horses with osteochondral fragmentation appear to have a history of acute lameness isolated to the carpal joints. However, in some cases, especially in race horses, synovial effusion or synovitis often precedes diagnosis of osteochondral fragmentation.

Physical examination

Clinical signs in horses with osteochondral fragmentation are very similar to those in horses with synovitis.

Special examination

Radiographs are often diagnostic in cases of osteochondral fragmentation; however, radiographs often underestimate the severity of damage (Fig. 18.2).[7] In some cases, the lesions have not been radiographically apparent. CT examination has proven beneficial in diagnosing unusual cases of osteochondral fragmentation, as has MRI.

Laboratory examination

Synovial fluid analysis has not been beneficial for identifying cases of osteochondral fragmentation; however, biomarker evaluation of joint disease has been beneficial in an experimental model of osteochondral fragmentation.[8] In particular, significant changes in articular cartilage matrix components and subchondral bone have been seen with osteochondral fragmentation, and monitoring these changes over time may help in identifying horses that could be prone to fragmentation.[8]

Fig. 18.2
Osteochondral fragmentation present on the distal aspect of the radiocarpal bone.

Diagnostic confirmation

Diagnostic arthroscopy is by far the best means of characterizing osteochondral fragmentation and also has the benefit of allowing for treatment of the disease. However, in most cases radiographs are appropriate for confirming the disease.

Treatment and prognosis

Therapeutic aims

Removal of the fragment is essential for restoring the joint to normal function. Accurate grading of articular cartilage lesions is also essential and, of course, much like all other cases, decreasing inflammation is also essential.

Therapy

Arthroscopic removal of the fragment and use of anti-inflammatory medications are necessary in treating these diseases. Furthermore, chondral supplementation, be it by intra-articular or systemic means, is also beneficial, especially in severe cases of osteochondral fragmentation. In particular, this author uses intra-articular polysulfated glycosaminoglycans in cases of grade 4 erosion (McIlwraith, personal communication, 1997).[10] The author also finds physical therapy to be beneficial in these cases, to limit the amount of capsulitis that can accompany osteochondral fragmentation.

Prognosis

The prognosis varies with articular cartilage erosion severity. In particular, return to racing at equal to or better than before surgery was 71.1% for grade 1 lesions, 75% for grade 2 lesions, 53.2% for grade 3 lesions and 54% for grade 4 lesions.[7]

Etiology and pathophysiology

Evaluation of post-mortem cases, especially by Poole[9] and Norrdin & Kawcak (unpublished data, 1998), has shown that most osteochondral fragments in race horses are acute manifestations of chronic disease processes. In particular, most fragments occur in areas of stress-induced subchondral bone sclerosis, in which microdamage exceeds healing and acute fragmentation results. Poole has also seen attempts at healing, as shown by the presence of granulation tissue at these sites; however, continued training had resulted in fragmentation through the granulation tissue bed.

Epidemiology

Osteochondral fragmentation of the carpus is very common in race horses, particularly in racing Quarter Horses, Thoroughbreds, and Standardbreds. However, in non-racing breeds, it is quite rare and when it does occur, it arises in unusual locations other than the dorsal aspect of the carpus.

Prevention

Again, there is no effective means of preventing osteochondral fragmentation in horses, especially in race horses. However, subtle subchondral bone lysis on radiographic examination and persistent synovial effusion may be indicative of impending osteochondral fragmentation. The genesis of biomarkers may also prove beneficial in early identification of osteochondral fragments.[8]

Osteochondral fracture (slab fracture)

- Horses with osteochondral fracture often present with significant acute lameness.
- Synovitis is a common sign of osteochondral fracture.
- Horses with osteochondral fracture are often very responsive to flexion.
- Radiographs are recommended prior to performing intra-articular anesthesia, which is often not required for diagnosis.

Recognition

History and presenting complaint

Acute, severe lameness often accompanies osteochondral fracture; however, some horses may not be lame acutely but rather may manifest severe lameness within 24 hours.

Physical examination

Horses with osteochondral fracture appear to be severely lame compared to horses with other disease processes within the carpus, and they are very responsive to carpal flexion. In some cases, the horse may actually resent even partial flexion of the carpus and the clinician must take care when performing the flexion test.

Special examination

This author does not recommend intra-articular anesthesia in cases of severe carpal lameness with severe response to flexion. Instead, a complete series of radiographs is essential, including skyline and, in some cases, special views to highlight the fractures. CT and MRI are also valuable, especially in assessing those fractures that are not absolutely clear on radiographs. However, since both modalities require general anesthesia, it is recommended that the surgeon perform these imaging studies just prior to surgery so the fracture can be repaired to prevent further comminution that may occur with recovery.

Laboratory examination

There are no synovial fluid parameters that are specific for osteochondral fracture; however, hemorrhage into the joint is not uncommon.

Diagnostic confirmation

Radiographs and diagnostic arthroscopy are helpful to confirm the diagnosis.

Treatment and prognosis

Therapeutic aims

The aim of therapy is to restore the articular surface to as normal a congruence as possible and to provide axial support to the limb.

Therapy

Internal fixation or removal of the fractured piece via arthroscopy are considered the treatments of choice. Only small fractures or fractures within the palmar aspects of the joints should be removed and usually only if they cannot hold the screw. Since there is often significant articular cartilage loss with these fractures, some form of resurfacing would enhance repair. However, those methods are still in their infancy and surgeons often look towards the use of chondroprotective agents to treat the significant cartilage loss that occurs with these diseases.

Prognosis

In general, the prognosis for successful repair of intra-articular fractures is often poor, especially in race horses; however, the prognosis for third carpal slab fractures is often dependent on the severity of articular cartilage erosion at the site.

Etiology and pathophysiology

Subchondral bone sclerosis is very common in cases of osteochondral fracture, indicating that these fractures may be the result of accumulated microdamage.[9] Furthermore, the proximal portions of these fractures often have fibrous tissue within them, indicating that a chronic pathologic condition may exist prior to acute manifestation of the fracture.

Epidemiology

Osteochondral fractures are quite common in race horses and occur most frequently within the radial fossa of the third carpal bone. Other fracture configurations can occur and fractures can occur within other bones of the carpus.

Prevention

As with the above disease entities, it is difficult to prevent osteochondral fracture. However, close monitoring of horses with persistent carpal disease is essential.

Catastrophic injury (breakdown)

- Catastrophic injury can result from chronic or acute disease processes.
- Catastrophic injuries are often life threatening.
- Aggressive first aid is often needed prior to surgical repair.
- Local and systemic stabilization of the horse is necessary.

Recognition

History and presenting complaint

Horses with catastrophic injuries of the carpus often show acute non-weight bearing lameness and axial instability at the carpal area.

Physical examination

Non-weight bearing lameness with significant instability at the carpal joint, leading to loss of axial support.

Special examination

Radiographic examination is often diagnostic in identifying multiple carpal bone fractures (Fig. 18.3).

Laboratory examination

Laboratory examination is not diagnostic, as clinical signs are absolute in localizing this problem.

Diagnostic confirmation

Diagnostic confirmation is often via radiographs.

Treatment and prognosis

Therapeutic aims

Systemic support of the animal is often essential, as most of these horses will present excited and hypotensive because of sweating. This often seems to be overlooked and acute treatment of systemic effects is critical, especially if the horse is to undergo surgical treatment. Local, effective, temporary stabilization of the carpus is also essential in promoting a good prognosis. This may also help with the horse's temperament in that localized stabilization may allow the horse some degree of weight bearing and have a calming effect. Acute stabilization entails both palmar and lateral support of the carpus via splints and bandaging as described by Bramlage.[10] Ultimate therapy or ultimate treatment for this condition will rely on surgical restoration of axial support.

Fig. 18.3
Acute, traumatic catastrophic injury of the carpus in a Warmblood after a pasture accident. The carpus was physically unstable in the lateral-to-medial direction but was axially stable, resulting in adequate stability with splint application.

Therapy

Again, aggressive first aid and sedation are essential for prompt treatment and transportation of the horse. Stabilization via splints is also essential to allow the horse some degree of comfort and to prevent further damage to the joint. Surgical reduction and internal fixation are often the definitive means of treatment for restoration of axial stability. However, the ultimate goal is pasture soundness for breeding animals. Conservative therapy has also been used in some of these cases, in which cast application, usually via a sleeve cast, has allowed for ankylosis of the joints to occur. Partial or pancarpal arthrodesis has also been used to salvage these horses for breeding.

Prognosis

The prognosis for athletic soundness in these horses is grave. However, prognosis for pasture soundness is often good with acute aggressive therapy.

Etiology and pathophysiology

Catastrophic injury of the carpus can result from either acute or chronic disease processes. As mentioned above, acute diseases can occur due to some sort of traumatic event. However, some acute injuries may be a result of pain elsewhere in the animal that causes either overloading of that limb or abnormal use of the limb. Chronic disease processes can also lead to catastrophic injury of the carpus. In particular, slab fractures that go unrecognized or are not treated, or that are compounded by an acute traumatic event, may lead not only to damage of the slab portion but also to either opposite limb injury or injury to other bones within the same joint.

Epidemiology

Catastrophic injury of the carpus is quite rare, especially in non-racing breeds.

Prevention

Again, there is no definitive means of preventing catastrophic injuries of the carpus but accurate diagnosis of early diseases may be helpful. However, especially in non-racing animals, acute injury to the carpus can occur with jumping or falling, thus limiting any means of prevention.

Stress-induced bone reaction (subchondral sclerosis)

- Failure of subchondral bone to adapt to exercise.
- Response to intra-articular anesthesia is variable.
- Nuclear scintigraphy is often diagnostic.
- Early detection and decreased training are often necessary for successful treatment.

Recognition

History and presenting complaint

Horses with subchondral sclerosis that leads to clinical disease often present with a non-specific history of lameness or, more frequently, a decrease in performance.

Physical examination

Physical examination findings typically show signs of chronic carpal joint disease consisting of joint capsule thickening and pain on flexion. However, occasionally, those signs are not present.

Special examination

Radiographic findings include sclerotic bone, usually in the third carpal bone, with lysis on the proximal joint surface. These findings are best seen on the third carpal bone skyline projection. Care must be taken not to overinterpret this finding as most athletic horses, especially race horses, have this change. The distinguishing thing in cases of clinical disease is the lysis. Nuclear scintigraphy is a good confirmatory modality as horses with stress-induced bone reaction will show intense, focal uptake in the area (Fig. 18.4). Computed tomography can also help to confirm diagnosis. Areas of intense subchondral bone thickening and lysis can be easily seen. Magnetic resonance imaging can also be used to view these changes, especially if subchondral bone edema is present.

Laboratory examination

There are no distinguishing changes in synovial fluid parameters that can lead to a diagnosis of subchondral bone stress

Fig. 18.4
Nuclear scan of a carpus showing intense, focal uptake in the intercarpal joint area.

reaction. However, early work using biochemical markers of bone turnover in synovial fluid and serum indicates that changes in osteocalcin may help to identify the change.

Diagnostic confirmation

Nuclear scintigraphy is often adequate to confirm diagnosis of subchondral stress reaction in the carpus.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to promote bone remodeling in the hope of re-establishing a more compliant subchondral bone. This can either be done through reduced training or by medication.

Therapy

Reduced training may help in re-establishing a more normal subchondral bone. The reinitiation of remodeling, including the osteoclastic function that occurs with rest, along with re-establishment of exercise may help to provide a more normal bone. However, prior to treatment, diagnostic arthroscopy may be needed if subchondral lysis has led to collapse of the overlying articular surface. In addition, some have indicated that subchondral bone forage may also help to stimulate blood flow into the area and thus reinitiate remodeling.

A few medications have also been recommended for this problem. Although not objectively established, isoxsuprine is thought to help in stimulating blood flow in bone. Bisphosphonates, which are used to control osteoporosis in humans, have recently come on the market in Europe for treating bone metabolism abnormalities in horses.

Prognosis

The prognosis for successfully treating subchondral stress reaction is dependent on the severity of the disease and the presence of articular cartilage collapse in the joint. The prognosis with articular cartilage collapse is dependent on the size of articular cartilage erosion and the depth of subchondral bone collapse.

Etiology and pathophysiology

The etiology of subchondral stress reaction has been identified as an inappropriate bone modeling response due to high loads experienced by the bone during exercise (Fig. 18.5). This high stress may be due to faulty conformation or inappropriate use of the limb. However, although not objectively identified, inherent bone metabolism could be at fault. Regardless, the subchondral bone appears to model and thicken as normal with exercise, except that it models to the point of inducing ischemia in the subchondral bone plate, leading to subchondral bone death and degeneration.[9] This degeneration then leads to loss of support and collapse of the overlying articular cartilage.

Epidemiology

Stress-induced bone response is primarily a disease of young race horses that are at the peak of bone modeling and remodeling. The radial facet of the third carpal bone is the primary area affected by the disease.

Prevention

Prevention of this disease is difficult as the onset is insidious and the disease progressive with training. Since there is no hallmark clinical sign of disease onset nuclear scintigraphy may be the only method of identifying stress-induced bone reaction in its early phases and may also be helpful in monitoring its progression. Serum and synovial fluid biomarkers could prove useful in the early detection of this disease, and hence prevention of serious damage.

Osteoarthritis (degenerative joint disease, arthritis)

- OA is usually secondary to other disease processes.
- Diagnosis is based on clinical and radiographic signs.
- Radiographic changes include joint collapse and subchondral sclerosis and lysis.
- Treatment is aimed at management.

Recognition

History and presenting complaint

Most horses with osteoarthritis (OA) have a history of previous joint injury or disease. However, in some cases, the cause is unknown and the development of the disease is insidious.

Physical examination

Most horses with OA of the carpal joints show lameness, joint capsule thickening on palpation, decreased range of motion that leads to pain in response to maximal flexion, and sometimes acquired conformational changes. These changes can include medial collapse of the carpal joints, leading to carpal varus, or persistent flexing of the carpus, leading to carpal contracture.

Special examination

Radiographic findings are often mixed but can consist of osteophyte and enthesiophyte formation, reduced joint space and a mixture of subchondral bone lysis and sclerosis. Nuclear scinti-

Fig. 18.5
A sagittal section of a carpus through the radiocarpal and third carpal articulation showing the gross evidence of subchondral and trabecular bone thickening due to exercise.

graphic findings are often mixed due to the chronic nature of the disease and the variable use of the limb. Computed tomographic findings often include variable subchondral bone sclerosis and lysis as well as the presence of osteophytes and enthesiophytes. Loss of joint space can also be seen. Magnetic resonance imaging is often the best diagnostic test to show loss of articular cartilage, which is the hallmark of OA.

Laboratory examination

Synovial fluid varies in color and viscosity, but usually is thick, orange to red and cloudy. However, in some cases synovial fluid is impossible to obtain which gives the subjective impression of a 'dry joint'. Early work using biochemical markers has shown progressive changes with OA, including reduced aggrecan and collagen content in synovial fluid and serum.

Diagnostic confirmation

Confirmation of the diagnosis is based on historical, physical examination and radiographic findings. The establishment of a chronic, progressive disease isolated to the carpus and the radiographic changes mentioned above often lead to a diagnosis.

Treatment and prognosis

Therapeutic aims

The therapeutic aims in treating OA are to realize that complete resolution of the disease is impossible and instead, management of the disease is needed. To do this, management of pain is a necessity. In some severe cases, elimination of the joint is necessary.

Therapy

The management of pain is varied based on the expected use of the horse, the severity of disease, the severity of compensatory pain and the individual horse's pain tolerance. Consequently several different management schemes must be

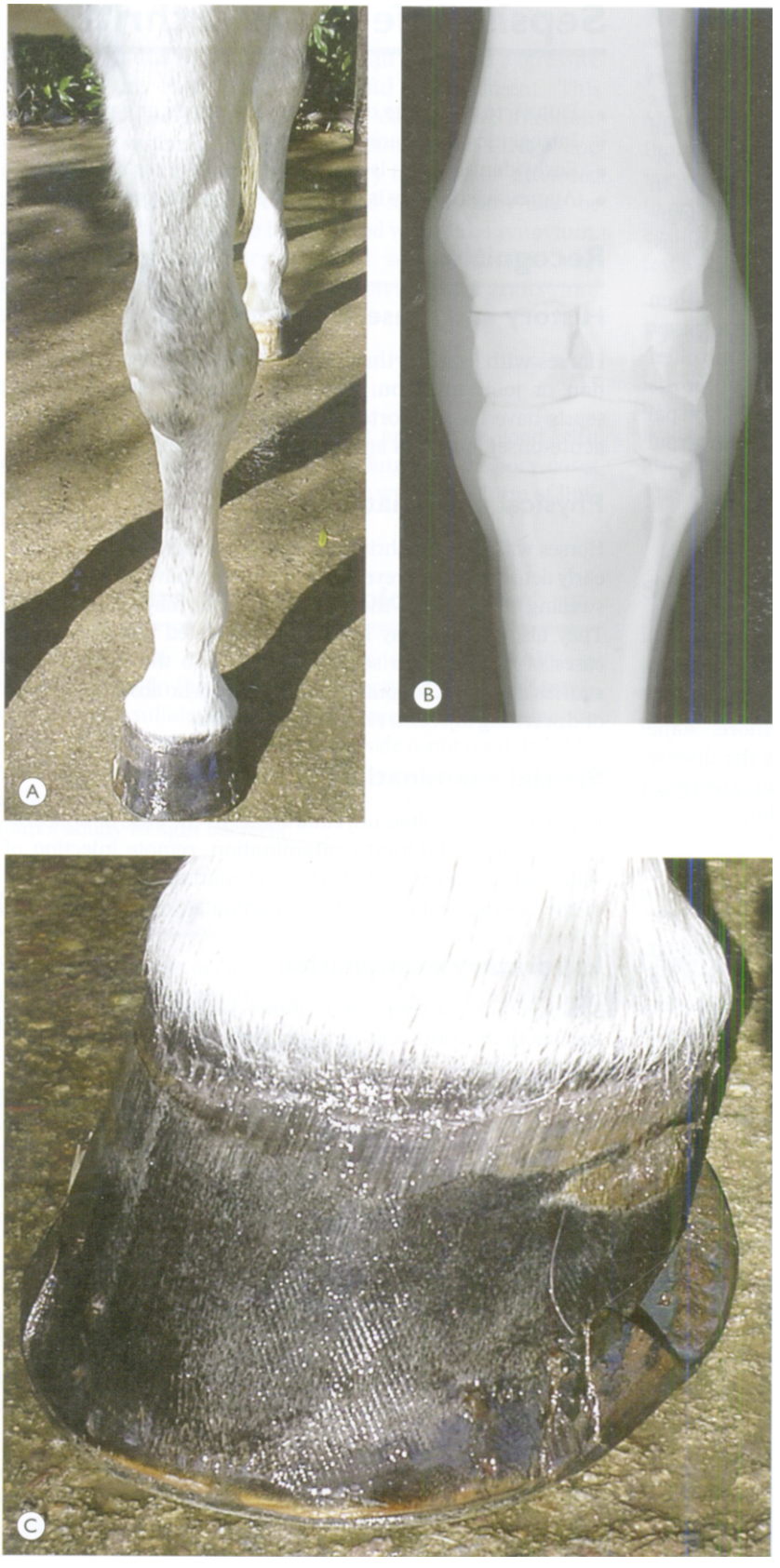


Fig. 18.6
A mare that had lifelong offset knee conformation that led to chronic pain and worsening of a carpal varus conformation. (A) Radiographs showed development of OA changes such as osteophytes and subchondral sclerosis (B), but pain and carpal varus worsening were controlled with shoeing that prevented worsening of lateral hoof breakover. (C) OA progression was prevented with shoeing in this case.

tried before one can be selected (Fig. 18.6). Pain management is often through the use of medications, supplements and/or physical therapy. Medications typically used include NSAIDs, systemic hyaluronic acid or polysulfated glycosaminoglycans and/or intra-articular administration of corticosteroids and hyaluronic acid or polysulfated glycosaminoglycans. A combination of these medications is often used (see Chapter 23). In addition, it is common to use supplements to aid in management of pain, including orally administered glucosamines, chondroitin sulfates, hyaluronic acid and various herbs.

If medical management of joint pain fails to work, then surgical fusion of the joint can be considered. In some cases, the increased likelihood of laminitis in the support limb often leads to the decision to perform surgery. Disease of either the radiocarpal or intercarpal joints justifies a partial carpal arthrodesis, or disease of both joints can lead to a pancarpal arthrodesis.

Prognosis

The prognosis for managing carpal pain due to OA is dependent on several factors, but mostly on the response to therapy. Identification of a management scheme is of the utmost importance in determining a prognosis for the owner and a trial period in which various medications are tried is needed prior to committing to a prognosis. Furthermore, some horses fail to respond to treatment over time as the disease progresses and alteration of a prognosis is needed. The prognosis for arthrodesis techniques is good for breeding animals.

Etiology and pathophysiology

The etiology of OA is varied but usually due to a primary traumatic or developmental disease. The severity of the initiating disease and the success of treatment often dictate the rate of progression of OA. Whether by progressive subchondral bone sclerosis, leading to thinning of articular cartilage, or by primary loss of articular cartilage, leading to subchondral bone sclerosis, the progressive nature of the changes in the joint at the osteochondral junction leads to pain.

Epidemiology

Osteoarthritis of the carpal joints occurs in all breeds and uses of horses, but is most common in the race horse. Many retired race horses that continue a career in another discipline run the risk of OA because of previous injury and continued athletic use. This seems to be the group of horses that require significant management for continued athletic function.

Prevention

Aggressive and prompt treatment of the primary problem and early identification of inherent problems that could lead to OA are needed in order to establish a management scheme early in the course of the disease.

Sepsis (infectious arthritis)

- Failure to recognize open joint lacerations and punctures.
- Iatrogenic causes are not uncommon.
- Early identification is critical to successful treatment.
- Aggressive therapy is critical to successful treatment.

Recognition

History and presenting complaint

Horses with septic arthritis often have a history of a laceration or joint injection, although cases of idiopathic joint sepsis have been reported. Horses with septic arthritis have acute-onset lameness and swelling of the limb.

Physical examination

Horses with septic arthritis are usually severely lame, although early detection may prevent this. They often have heat, pain and swelling in the area of the infected joint and may have cellulitis. They also may or may not have an elevated temperature. In cases of postinjection sepsis, a reaction to the injected substances must be ruled out, although there is no absolute method of discerning injection reaction from sepsis.

Special examination

Radiographs are often unremarkable. In the case of a laceration and potential joint contamination, remote injection of saline into the joint and visual confirmation of fluid flow out of the laceration documents contamination.

Laboratory examination

Synovial fluid analysis often shows white blood cell values greater than 3000 cells/mm^3 and total protein greater than 4 g/dL.

Diagnostic confirmation

Remote saline injection and visualization at the laceration is the best confirmatory method for detecting joint contamination. In the carpus, lacerations on the dorsum of the carpus are common and injection into the palmar pouches is useful to confirm the diagnosis. For established sepsis, whether by laceration or iatrogenic injection, synovial fluid analysis is often confirmatory. However, reaction to injected medication is difficult to distinguish from sepsis and it is recommended to treat cases as septic.

Treatment and prognosis

Therapeutic aims

The aims of therapy are to reduce the bacterial load and fibrin accumulation in the joint, provide appropriate antibiotic therapy and reduce inflammation and pain in the joint.

Therapy

Early recognition of septic arthritis and early and aggressive treatment are essential in successful management. This includes documenting the organism causing the infection, the use of systemic and local antibiotics and lavage and debridement of the joint. In refractory cases, open or closed suction drainage is often needed and synovectomy may be needed if infection is felt to be harbored within the synovium. Long-standing, refractory cases of septic arthritis may require arthrodesis through massive bone grafts and drains.

Prognosis

The prognosis for overcoming septic arthritis is good with early treatment. However, long-standing or refractory cases are less likely to recover or will recover with some form of limiting lameness.

Etiology and pathophysiology

Establishment of infection within a joint may be due to several factors. In the case of joint injections, the use of intra-articular polysulfated glycosaminoglycans has been shown to perpetuate infection if an aminoglycoside is not used. In addition, the basic nature of corticosteroids is to reduce inflammatory cell density in an area, hence limiting the joint's ability to fight bacteria.

Epidemiology

Septic arthritis can occur in any horse, but is more common in athletic horses which are subjected to intra-articular medications.

Prevention

Strict adherence to aseptic injection techniques and early and rapid identification of open joint lacerations are needed in order to prevent septic arthritis.

Developmental orthopedic disease

- Angular limb deformity is a common form of DOD.
- Physitis can result from conformational abnormalities and rapid growth.
- Osteochondrosis is often in the form of subchondral cystic lesions.
- Nutritional and breeding management are the only forms of intervention.

Recognition

History and presenting complaint

Most horses with developmental orthopedic disease (DOD) of the carpus are young and tend to show signs of disease at various stages of development. Angular limb deformities tend to arise early or are acquired as the horse ages. Subchondral cystic lesions can occur within the cuboidal bones and manifest as carpal lameness.

Physical examination

Horses with subchondral cystic lesions of the carpus tend to show either chronic, progressive signs or acute signs. Foals are typically born with some form of carpal valgus, but should improve over time until fully grown. The challenge lies in recognizing normal angulation for a specific age.

Special examination

Radiographs are often the only modality needed to diagnose subchondral cystic lesions within the carpus. Computed tomographic studies have been used to plan for surgical debridement of cysts and to assess follow-up.[5]

Laboratory examination

Synovial fluid analyses are often unhelpful in diagnosing DOD of the carpus; however, serum and synovial fluid biomarker analyses have shown promise in this respect.

Diagnostic confirmation

Radiographs are often all that is necessary to diagnose DOD.

Treatment and prognosis

Therapeutic aims

The primary aim is to correct the problem and then treat the resulting joint disease as described in previous sections.

Therapy

Arthroscopic examination and treatment of subchondral cystic lesions of the carpus are necessary. In addition, medical treatment of the resulting joint disease is needed.

Prognosis

Prognosis is dependent on the size of the lesion and the amount of articular cartilage erosion that is present within the joint. Fracture through a cyst or angular deviation caused by the presence of the cyst must be taken into consideration when formulating a prognosis.

Etiology and pathophysiology

The pathogenesis of DOD is complex and theoretical in some aspects. However, a few things have been proven clinically and experimentally. Trauma to the articular cartilage and subchondral bone has been shown experimentally to cause subchondral cystic lesions in the stifle.[11] The influence of body size and growth rate on the development of DOD has also been proposed, and supported in Warmbloods and Standardbreds, but again, these were shown in the tarsus and stifle.[12] Nutritional imbalances in minerals, energy and protein have also been suggested in the pathogenesis of DOD, as has heredity.[12] Because DOD manifestations other than angular limb deformity are rare in the carpus, there has been little clinical or experimental work done to gain information on the pathogenesis of disease.

Prevention

Nutrition is paramount to prevent DOD in horses. In particular, adequate energy, protein and mineral balance are critical. Furthermore, changes in feed should be gradual. It also appears that genetics may be a factor in DOD and should be considered when inquiring about a certain breeding pair. Some consider trauma to be a factor in the development of DOD and early training should be monitored closely.

Carpal canal syndrome

- Accessory carpal bone fracture commonly leads to carpal canal effusion.
- Idiopathic hemorrhage is not uncommon.
- Osteochondroma can lead to carpal canal effusion.
- Lameness severity is variable.

Recognition

History and presenting complaint

Acute or chronic carpal sheath swelling is seen with this disease with variable degrees of lameness.

Physical examination

Carpal sheath swelling with variable lameness and variable response to flexion is often seen. In chronic cases of the disease, fibrosis may be appreciated medially, but little effusion may be present.

Special examination

Radiographs often reveal an osteochondroma or a reactive area at the physis. In some cases nothing is seen and ultrasound is needed to evaluate soft tissue structures. Hemorrhage into the sheath can be appreciated with ultrasound, as can fibrin and adhesion formation.

Laboratory examination

Synovial fluid analysis is often unremarkable, although in acute hemorrhagic conditions, bright red blood may be seen.

Diagnostic confirmation

Diagnostic confirmation is dependent on the disease process that is present. For instance, osteochondroma may be confirmed radiographically, but deep digital flexor tendon tearing would be seen ultrasonographically. It is not uncommon to see deep digital flexor tendon tearing secondary to osteochondroma formation, warranting ultrasound use when osteochondroma is diagnosed.

Treatment and prognosis

Therapeutic aims

Removal of the primary disease entity and treatment with anti-inflammatory medications are needed. However, with tendon damage, prolonged rest and gradual return to exercise are essential.

Therapy

Tenoscopic exploration of the sheath is often needed, especially in the case of osteochondroma removal. Debridement of deep digital flexor tendon fibers may also be carried out during tenoscopic examination. In addition, anti-inflammatory medications are useful and viscosupplementation may be indicated to prevent adhesion formation. Without the presence of an osteochondroma, drainage and injection of corticosteroids and hyaluronic acid may provide benefit.

Prognosis

Prognosis is often good for injuries to structures within the carpal canal.

Etiology and pathophysiology

The formation of an osteochondroma is thought to be due to the presence of residual physeal tissues within the area and subsequent endochondral bone formation. Hemorrhage into the carpal canal is thought to be a result of osteochondroma fracture, generalized trauma to structures within the sheath or idiopathic.

Epidemiology

In general, carpal canal diseases are rare and can occur in any breed or use of horse.

Prevention

No good form of prevention is available for carpal canal injuries, although removal of osteochondromas is necessary to prevent chronic damage to the sheath and deep digital flexor tendon.

Periarticular disease

- Hygroma can lead to isolated dorsal swelling.
- Synovial hernia is evidenced by palpable swelling between the skin and a joint.
- Synovial fistula leads to effusion of two adjacent synovial structures.
- Synovial fistula often occurs with other lesions.

Recognition

History and presenting complaint

Horses with periarticular diseases of the carpus often present with a history of acute or chronic swelling in the carpal area. However, lameness is often absent with most of these diseases.

Physical examination

Horses with periarticular disease often show dorsal carpal swelling and in the case of synovial fistula formation, swelling may occur in two separate locations, such as two joints or a joint and an associated tendon sheath. Lameness may be absent, but in most cases of synovial fistula, other diseases such as osteochondral fragmentation or OA are present, which in themselves may cause lameness.

Special examination

Radiographs of the carpal area in horses with synovial hernia or hygroma formation are often unremarkable. In horses with synovial fistula formation, it is not uncommon to see radiographic signs of osteochondral fragmentation or OA. Intra-articular or intralesional injection of contrast agent often indicates the connection of the lesion to the joint. However, in some cases such as ganglion formation, the injection may need to be within the joint as a one-way valve may exist that would prevent passage of the contrast agent into the joint from the lesion.

Ultrasonographic examination can show the communication between a hernia and the joint, although the lack of visualization does not rule out its presence.

Laboratory examination

There are no laboratory tests that are helpful in diagnosing these lesions.

Diagnostic confirmation

Arthrographic documentation is often necessary to confirm the presence of these lesions. However, often lesions that communicate to a joint can be visualized arthroscopically.

Treatment and prognosis

Therapeutic aims

Removal of the inciting cause is often necessary.

Therapy

Anti-inflammatory medications and bandaging are often useful in resolving hygroma formation. However, persistence of the lesion occasionally results. Anecdotally, injection of contrast agents into the lesion has resulted in resolution in a few cases. However, surgical resection is sometimes needed and should be weighed against the presence of the existing lesion.

Synovial hernias are often only of cosmetic concern, but their removal is sometimes desired. Primary herniorrhaphy is needed to correct this problem, which requires the creation of an incision in the area. Again, the presence of the scar must be weighed against the cosmetic blemish of the existing hernia.

Treatment of intrasynovial fistula has been documented; however, other lesions, such as osteochondral fragmentation and fracture, should also be treated at the same time.

Prognosis

The prognosis for hygromas and hernias is good although a cosmetic blemish may persist. In the case of synovial fistula, the prognosis is dependent on the severity of the associated lesions.

Etiology and pathophysiology

Trauma is the primary etiology for these lesions.

Epidemiology

Hygroma formation is common although the others are not. Again, horses with dorsal carpal swelling should be monitored to see if they are prone to continual trauma.

Prevention

Early recognition and treatment of dorsal carpal swelling are essential to prevent persistent hygroma formation. Furthermore, careful observation of the animal may show that it persistently strikes the area during eating or play and a change in management during feeding or proximity to other animals may be needed.

Tenosynovitis of carpal extensor tendons

- Jumpers commonly exhibit this after hitting rails.
- Cross-country horses can acquire this from hitting fixed rails.
- Sepsis due to foreign bodies is not uncommon.
- Medical or surgical therapy is often needed.

Recognition

History and presenting complaint

Acute or chronic swelling of the dorsal carpal area is often reported and in some cases, the swelling may represent cellulitis and severe lameness.

Physical examination

In non-septic cases, the swelling is localized to the extensor tendons dorsal and proximal to the carpus. There may or may not be associated lameness, but in most cases there is some discomfort with carpal flexion. In septic cases, a diffuse, painful swelling is present and the horse is usually severely lame.

Special examination

In some long-standing cases, periosteal reaction may be seen on the dorsum of the radius. However, in general, radiographs are often unremarkable. Ultrasonographic examination often shows the increased fluid within the sheath and damage to the extensor tendons.

Laboratory examination

Synovial fluid analysis is essential for confirming the presence of sepsis, but non-septic conditions are often unremarkable in their presentation.

Diagnostic confirmation

Synovial fluid is confirmatory for septic cases and ultrasound is confirmatory in most other cases.

Treatment and prognosis

Therapeutic aims

Non-septic conditions require anti-inflammatory treatments and rest for management of tissue changes. Septic conditions require surgical treatment, drainage and antimicrobial therapy.

Therapy

Anti-inflammatory medications are necessary in any case of tendon sheath swelling. In septic cases, tenoscopy, foreign body removal and debridement are indicated, as is antimicrobial treatment. Persistent cases may require open drainage. Viscosupplementation is often necessary to prevent adhesion formation in any case.

Prognosis

The prognosis is good for return to athletic soundness, although a cosmetic blemish may result. Septic cases are dependent on the ability to overcome the infectious process.

Etiology and pathophysiology

Striking of the carpus on an object is often the cause of this syndrome and in septic cases, a foreign body is sometimes present.

Epidemiology

Traumatic events are usually the cause of tendon sheath swelling, so horses that are used for jumping, especially those that jump fixed structures, may be more at risk for developing the disease.

Prevention

There are no good preventive measures for this disease, except for early recognition of punctures or lacerations into the sheaths, and aggressive treatment once recognized.

References

1. Denoix J. Ultrasonographic examination in the diagnosis of joint disease. In: McIlwraith C, Trotter G, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 165–202.
2. Frisbie DD, Kawcak CE, Baxter GM, et al. Effects of 6alpha-methylprednisolone acetate on an equine osteochondral fragment exercise model. Am J Vet Res 1998; 59(12):1619–1628.
3. Frisbie DD, Kawcak CE, Trotter GW, Powers BE, Walton RM, McIlwraith CW. Effects of triamcinolone acetonide on an in vivo equine osteochondral fragment exercise model. Equine Vet J 1997; 29(5):349–359.
4. Whitton RC, Kannegieter NJ, Rose RJ. The intercarpal ligaments of the equine midcarpal joint, Part 3: Clinical observations in 32 racing horses with midcarpal joint disease. Vet Surg 1997; 26(5):374–381.
5. Kawcak C, Firth E, Herthel D, Sandler E. Clinical uses of computed tomography. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia, PA: Saunders; 2003.
6. Whitton RC, Rose RJ. Postmortem lesions in the intercarpal ligaments of the equine midcarpal joint. Aust Vet J 1997; 75(10):746–750.
7. McIlwraith CW, Yovich JV, Martin GS. Arthroscopic surgery for the treatment of osteochondral chip fractures in the equine carpus. J Am Vet Med Assoc 1987; 191(5):531–540.

8. Al-Sobayil F. Effects of exercise on synovial fluid and serum biomarkers of musculoskeletal diseases in horses with and without osteochondral fragmentation [thesis]. Fort Collins, CO: Colorado State University; 2002.
9. Poole R. Pathologic manifestations of joint disease in the athletic horse. In: McIlwraith C, Trotter G, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 87–104.
10. Bramlage L. First aid and transportation of fracture patients. In: Nixon A, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 36–42.
11. Ray C, Baxter G, McIlwraith CW, et al. Development of subchondral cystic lesions following articular cartilage and subchondral bone damage in young horses. Equine Vet J 1996; 28:225.
12. Douglas J. Pathogenesis of osteochondrosis. In: Ross M, Dyson S, eds. Lameness in the horse. Philadelphia, PA: Saunders; 2003; 534–543.

CHAPTER 19

Tarsus and stifle

Federico G. Latimer

The stifle joint is the largest and most complex in horses. It has a large range of motion and movements of the patella, distal femur and proximal tibia are highly co-ordinated and precise due to the remarkable anatomic design and function of the bony and soft tissue structures that stabilize the joint. Because of this specialized anatomic construct, injury and developmental or degenerative disease of a specific component will often cause articular instability somewhere else in the joint, making diagnosis and treatment challenging and adversely affecting prognosis for equine athletes. Stifle disease in horses can be developmental, infectious, traumatic or degenerative. Prompt recognition and localization of the disease process within the joint will maximize therapeutic options and improve the prognosis for future athletic use as most degenerative conditions in older horses are usually the result of a previous traumatic injury of a soft tissue or bony structure.

The tarsus in horses has high-motion (tarsocrural) and low-motion (proximal and distal intertarsal and tarsometatarsal) articulations. The severity, clinical presentation, joint affected and progression are variable and can be influenced by breed, conformation (skeletal or bodyweight), athletic use, age at onset and therapeutic regimens used. Many tarsal conditions can be managed medically or surgically such that a large proportion of these patients can successfully return to their previous level of athletic activity.

Stifle

Anatomy

- The equine stifle is composed of the femoropatellar and the medial and lateral femorotibial joints.
- Communication between synovial spaces is unpredictable and they should be considered separate sacs for diagnostic and therapeutic purposes.
- The trochlear groove is centered between the medial and lateral trochlear ridges of the distal femur (Fig. 19.1A).
- The medial trochlear ridge is larger than the lateral and with the patella compromises part of the stay apparatus (Fig. 19.1A).
- The medial collateral ligament and the medial meniscus are fused at the medial joint margin (Fig. 19.1A–C).
- The cranial and caudal cruciate ligaments are extrasynovial and located in the septum between the medial and lateral femorotibial joints.
- The medial and lateral collateral ligaments and three patellar ligaments (medial, middle and lateral) are all extrasynovial.
- The cupped fibrocartilaginous menisci enhance congruity of the round femoral condyles and flat tibial condyles (Fig. 19.1A, C).

Diagnosis and treatment of stifle disease in horses require an understanding of the articular anatomy and joint mechanics. It is important to obtain an adequate history to determine the age, use and duration of the lameness and whether a specific accident or injury precipitated it. Horses with stifle diseases are reluctant to flex the joint when gaiting and the cranial phase of the stride tends to be short, with the foot carried close to the ground. As a result, the gluteal rise on the involved or more severely affected side will be higher but of shorter duration. Walking on an incline or performing an upper limb or stifle flexion test will often exacerbate the lameness.

There may be visible or palpable effusion of any of the synovial sacs and atrophy of the gluteal or quadriceps muscles may accompany long-standing diseases. There may be marked periarticular or ligamentous thickening, crepitus or instability if ligamentous injuries or fractures are present. Intrasynovial anesthesia may help localize the compartment or structures involved. Due to the complexity of this joint, any improvement in the degree of lameness after intrasynovial anesthesia should warrant further investigation as involvement of multiple soft tissue or extracapsular structures may result in an incomplete response (Fig. 19.1A).

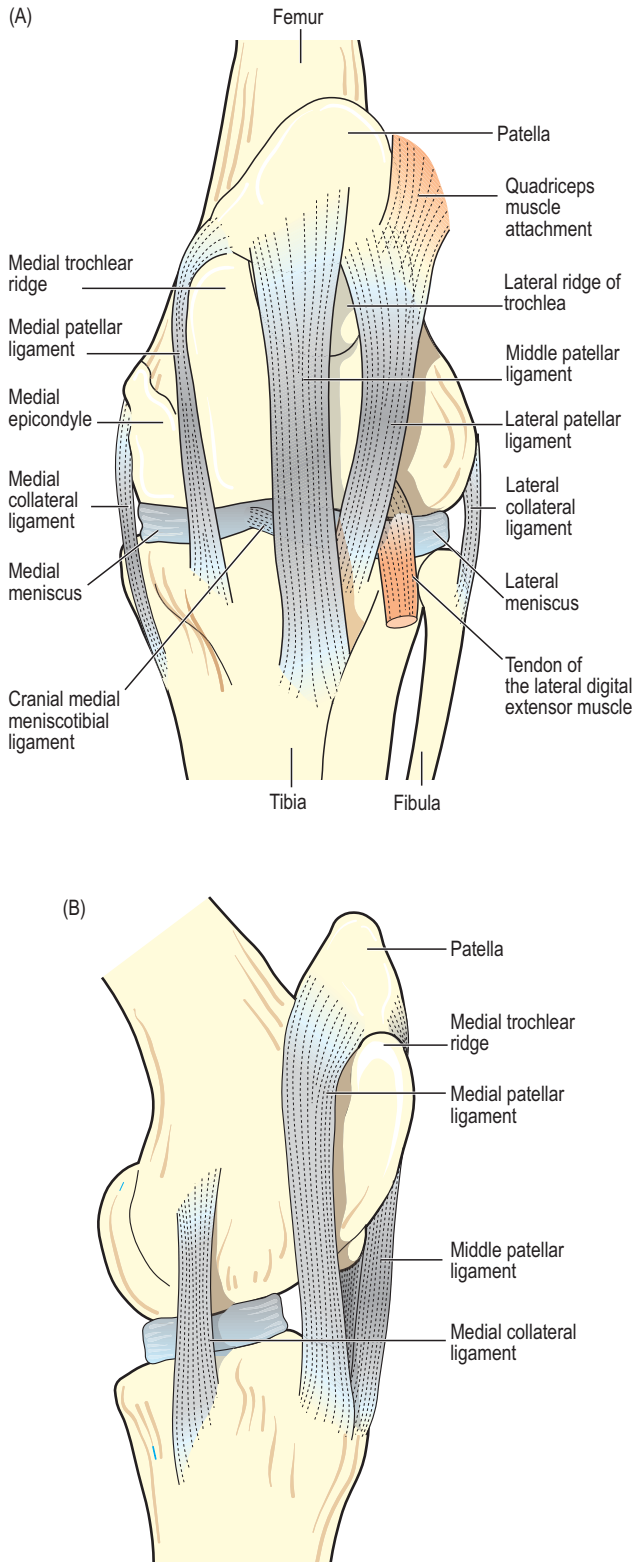


Fig. 19.1
(A) Cranial aspect of the stifle joint. (B) Medial aspect of the stifle joint.

Other diagnostic procedures that can be used for horses suspected of having stifle disease include arthrocentesis for synovial fluid analysis or cultures, radiography, ultrasonography, nuclear scintigraphy, arthroscopy and magnetic resonance imaging. Radiographic views include the lateromedial, caudocranial, 30° caudolateral-craniomedial and caudomedial-craniolateral and the cranioproximal-craniodistal oblique (skyline) of the patella. Ultrasonography can be used to evaluate the patellar, collateral and cruciate ligaments as well as the menisci and articular cartilage of the trochlear ridges (Fig. 19.1A–C). Nuclear scintigraphy will identify areas of increased skeletal or soft tissue inflammatory or metabolic activity. It is

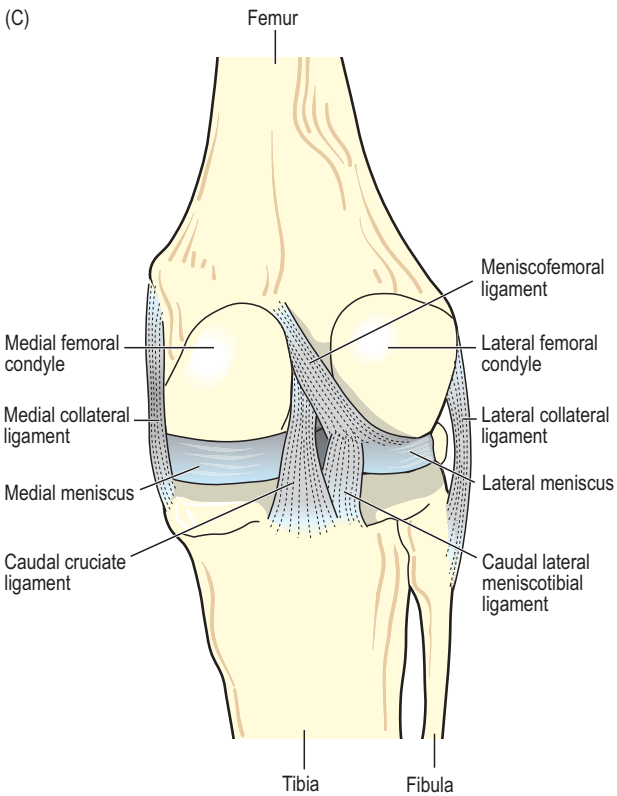


Fig. 19.1
(C) Caudal aspect of the stifle joint.

usually ineffective in identifying subchondral cysts of the medial femoral condyle in horses. Arthroscopy will permit visualization and manipulation of the intra-articular structures for therapeutic or diagnostic purposes.

Collateral ligament injuries

- The paired collateral ligaments (CoL) stabilize the stifle medially and laterally (Fig. 19.1B, C).
- The lateral CoL is reinforced by the lateral musculature of the thigh.
- The medial CoL has limited soft tissue coverage and is more frequently injured in horses.
- The medial CoL attaches to the medial meniscus (MM) at the joint space (Fig. 19.1A, B).
- Injuries to the medial CoL will often lead to significant disruptions of the MM, exacerbating stifle instability.

Horses have paired (medial and lateral) CoL that provide medial to lateral stability to the femorotibial joint.

Recognition

History and presenting complaint Horses with medial CoL injuries will usually present with an acute onset of severe lameness after a traumatic event or fall or with a less dramatic degree of rear limb lameness when the injury is milder or chronic.

Physical examination There will be a variable amount of soft tissue swelling and pain on the medial aspect of the stifle. Chronic injuries may have palpable thickening of the medial CoL, particularly when compared to the unaffected side. Horses with major disruption of the medial CoL will have obvious stifle instability and resent manipulation of the joint. Horses with more subtle injuries will have shortened anterior phase of the stride with decreased stifle flexion, toe dragging and a shorter but higher gluteal rise ('hip hike') on the affected side. Upper limb or stifle flexion and a medial CoL stress test (abduction of the limb distal to the stifle) will exacerbate the lameness.

Special examination Horses with incomplete disruptions of the medial CoL may partially improve after intra-articular analgesia of the medial femorotibial joint due to diffusion of anesthetic into the area around the ligament or because of disruption of the MM that often accompanies this injury. Caudocranial stress radiographs revealing a widened medial joint space or an avulsion fracture of the distal femur or proximal tibia are diagnostic when complete disruptions are present (Figs 19.2, 19.3).[1] Chronic injuries may demonstrate a narrowed medial femorotibial joint space and multiple osteophytes or enthesiophytes on the medial aspect on the

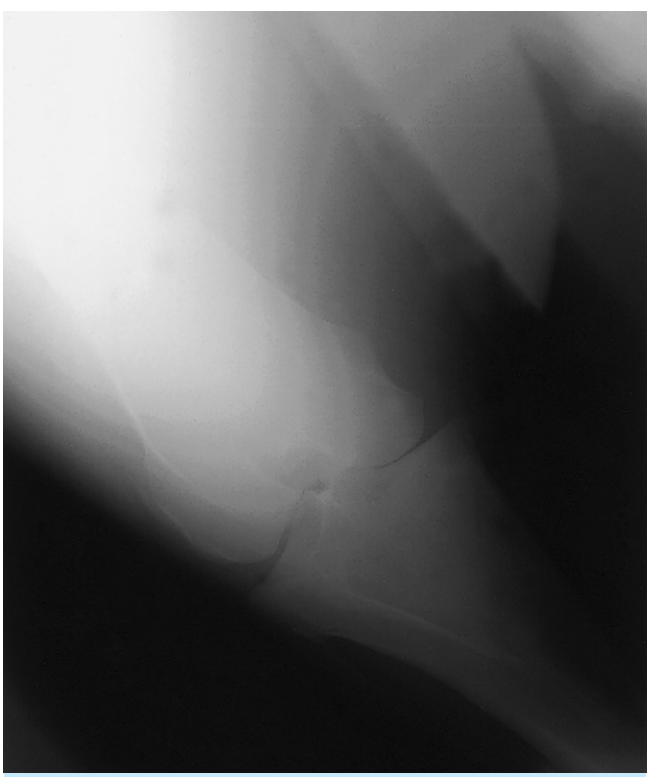


Fig. 19.2
Three-year-old Standardbred filly that presented with a grade 3 lameness of the left rear limb, medial femorotibial joint effusion and marked response to upper limb flexion. The caudocranial radiographic projection reveals narrowing of the medial joint space that was confirmed during arthroscopic surgery as a complete tear of the medial meniscus and cranial meniscotibial ligament.

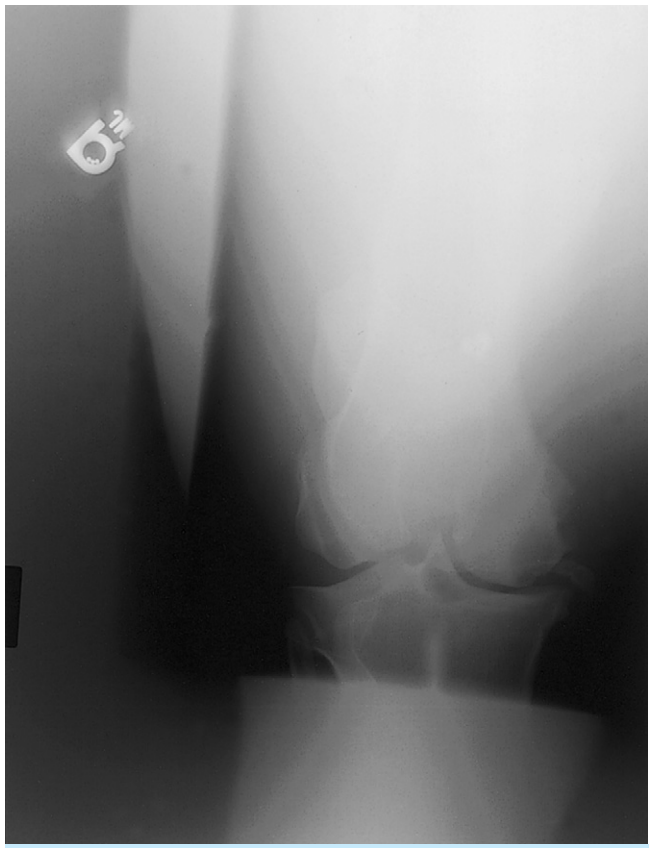


Fig. 19.3
Ten-year-old Quarter Horse mare with mineralization of the axial aspect of the meniscus, collapse of the medial joint space, periarticular osteophyte formation and the presence of a large subchondral cyst on the medial femoral condyle. Arthroscopic surgery revealed a complete tear of the medial meniscus and marked erosion of the articular cartilage of the medial femoral condyle.

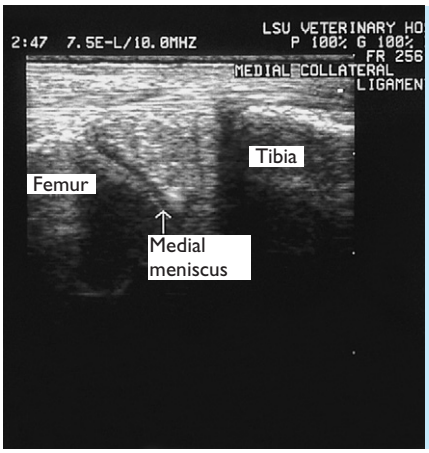


Fig. 19.4
Ultrasonographic image of a medial meniscus injury on the axial aspect of the joint space.

standard radiographic projections.[1] Ultrasonography of the medial CoL and MM can identify the extent of structural disruption and fiber discontinuity (Fig. 19.4).[2,3] The scans can be performed on the axial border of the femorotibial joint with horses standing using a 7.5–10 MHz linear probe (Fig. 19.5). The images should be obtained in a longitudinal and transverse orientation relative to the CoL.[2,3]

Necropsy examination A variable degree of disruption in the medial CoL and MM will be present. Chronic cases exhibit thickening of the medial CoL with fibrillation and erosion of the MM and articular cartilage of the medial femoral condyle along with periarticular bony proliferation.

Diagnostic confirmation Differential diagnoses include other causes of acute and severe lameness originating from the stifle such as fractures of the femur, patella or proximal tibia, cruciate or patellar ligament injuries, sepsis and traumatic patellar luxation. Chronic injuries need to be differentiated from stifle lameness caused by osteochondrosis, synovitis, meniscal injuries and degenerative joint disease secondary to instability or inflammation. The physical examination and the radiographic, ultrasonographic and arthroscopic appearance are diagnostic for medial CoL and MM injuries.

Treatment and prognosis

Therapeutic aims Prevent further damage to the structure(s) involved and reduce the inflammatory response.

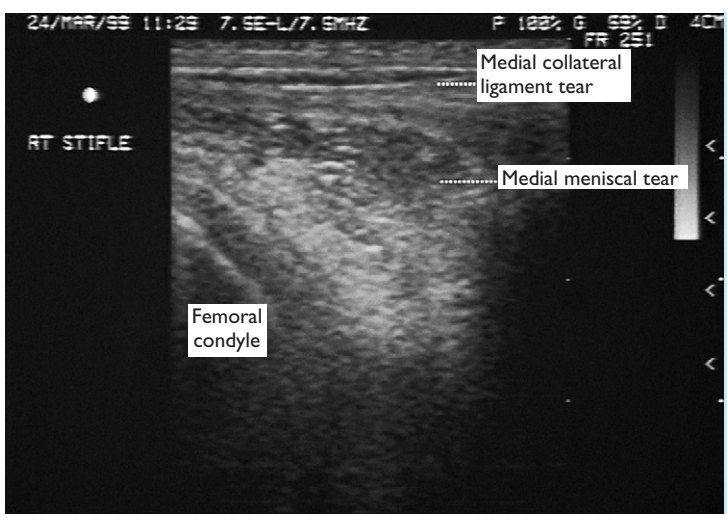


Fig. 19.5
Ultrasonographic appearance of a tear in the body of the medial meniscus in a mature sport horse.

Therapy Stall rest and systemic NSAIDs (phenylbutazone 2.2–4.4 mg/kg, p.o. per day), chondroprotective agents (polysulfated glycosaminoglycans or hyaluronic acid) and/or intra-articular anti-inflammatory therapy (hyaluronic acid and/or corticosteroids) may be beneficial in horses with acute but partial disruptions of the medial CoL. Intra-articular corticosteroids should be used judiciously to minimize inflammation, but repeated use may catabolize articular cartilage and blunt healing responses. Arthroscopic debridement of meniscal abrasions or fibrillation may reduce intra-articular inflammation, thereby preventing osteoarthritis.[4–6] Stall rest for 4–8 weeks followed by gradual increase in hand-walking for 8–12 weeks should be adequate, depending on the severity of the injury. The horse should be re-evaluated radiographically and ultrasonographically at 6–9 months for soft tissue healing and osteoarthritis before considering a return to athletic activity.

Prognosis Horses with significant disruption of the medial CoL will respond poorly to attempts at surgical repair and the ensuing stifle instability and meniscal injury make the prognosis for athletic use or pain-free life very poor.[7] The prognosis for horses with subtle injuries is guarded for athletic use and good for life, depending on the severity of the original injury, the degree of stifle instability and whether degenerative joint disease develops. Horses competing in more demanding athletic disciplines have a very guarded prognosis for full return to function.

Prevention

Proper shoeing (caulks when traction is required), avoiding strenuous activity when footing is poor or placing the horse in competitive events beyond its ability or degree of conditioning and withdrawal from competition if fatigue ensues may help prevent these injuries. Demanding disciplines in horses that are poorly conditioned, lame or schooled improperly may predispose to injuries.

Etiology and pathophysiology

Medial CoL injuries are the result of intense lateral to medial bending stresses during exercise or during a fall. Loss of footing, striking an immovable object or placement of large rotational forces on the stifle during weight bearing can result in CoL injuries in equine athletes. The paired CoL stabilize the stifle medially and laterally and disruptions of the CoL in horses will cause joint instability, impeding ambulation or pain-free exercise. Medial CoL injuries will often involve the MM, adversely affecting joint function.

Epidemiology

Collateral ligament injuries of the stifle are seen more frequently in athletes that jump (event horses, steeplechasers and hunters) or those that participate in disciplines with sudden stops or turns (barrel racing and polo).

Meniscal injuries

- Injuries of the cranial horn or ligament and body of the MM can cause lameness in equine athletes.
- Disruption of the MM can accompany CoL injuries in horses.
- Meniscal injuries can result from crushing forces when the femur rotates over the menisci with the leg in extension.
- Meniscal injuries can be a sequel to stifle instability caused by cruciate ligament disruptions.

Horses have a medial and lateral meniscus. Each cupped fibrocartilaginous meniscus functions to provide stability and congruency between the rounded femoral condyles and the flat tibial condyles at the femorotibial articulation (Fig. 19.1). Each meniscus has a cranial and caudal attachment (meniscal ligaments) to the tibia that maintains it in precise anatomic alignment during locomotion (Fig. 19.1). The medial meniscus and medial CoL are firmly attached to each other at the axial aspect of the joint space.

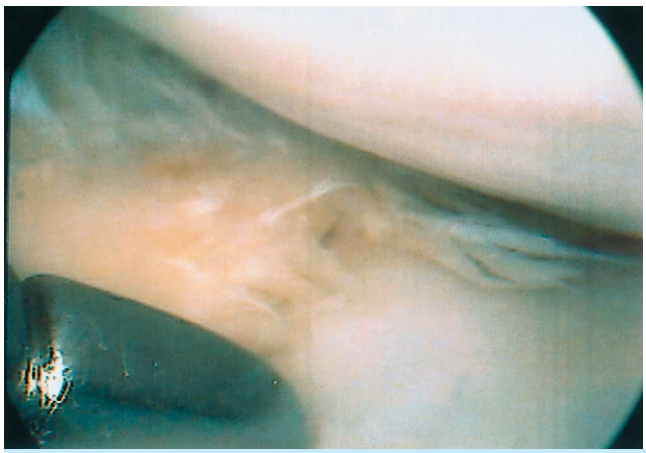
Recognition

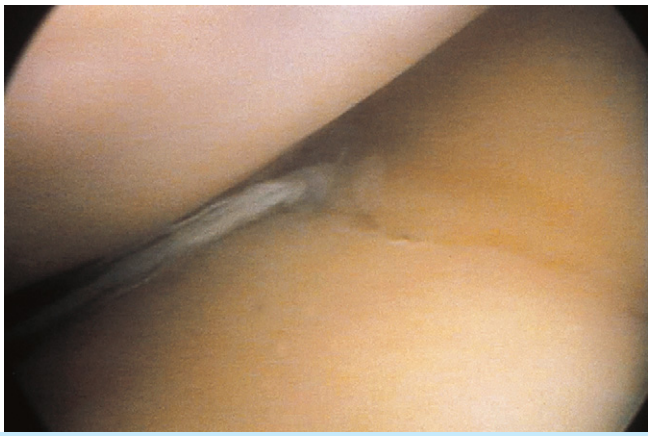
History and presenting complaint The clinical presentation is similar to horses with medial CoL injuries.

Physical examination The physical examination parameters and response to limb manipulation tests will be similar to horses with medial CoL injuries since they often occur simultaneously. The degree of lameness, periarticular thickening and effusion of the femorotibial joint will vary depending on the severity of the injury and duration. In horses with concurrent injury to the cranial cruciate ligament (CrL) the degree of stifle instability will be more pronounced.[8]

Special examination Medial femorotibial joint anesthesia will usually improve the lameness but the response is variable depending on the severity of the injury and additional extracapsular soft tissue or intra-articular cartilage structures involved. Large meniscal tears will cause collapse of the medial femorotibial joint space on the caudocranial radiographic projection (Figs 19.4, 19.5).[1] Degenerative joint disease and loss of femoral condyle cartilage will be evident in chronic cases (Fig. 19.5). Enthesiophytes or osteophytes may also be evident on the cranial aspect of the intercondylar eminence of the tibia or the edges of the femorotibial joint.[1] Ultrasonography or arthroscopy can be used to assess the integrity of the cranial and axial aspects of the MM (Figs 19.6, 19.7). Ultrasonography of the MM can be performed with a 7.5 MHz linear probe along the cranial and axial aspect of the femorotibial joint.[2,3] Defects or injuries of the MM may be imaged as hypoechoic areas in the horn or ligament at the axial or cranial portion of the structure (Fig. 19.5). Concurrent medial CoL injuries will be imaged axially at the attachment to the MM.[2,3]

Necropsy examination Findings are similar to CoL injuries with the severity of the changes dependent on the degree of MM damage and loss of congruity between the femoral and tibial condyles.





Figs 19.6, 19.7
Arthroscopic view of a tear in the medial meniscus.

Diagnostic confirmation Differential diagnoses include other causes of acute lameness originating from the stifle such as fractures, cruciate or patellar ligament injuries, sepsis and patellar luxation. Chronic injuries need to be differentiated from stifle lameness caused by osteochondrosis, synovitis and degenerative joint disease secondary to instability or inflammation. The physical examination and the radiographic, ultrasonographic and arthroscopic appearances are diagnostic for MM injuries.

Treatment and prognosis

Therapeutic aims Prevent further damage to the MM rest and surgical debridement of loose meniscal tissue that may exacerbate synovitis and accelerate the development of osteoarthritis.[8]

Therapy Arthroscopic surgery of the medial femorotibial joint is helpful to determine the extent of the injury and to debride damaged tissue from the MM or cranial meniscal ligaments that incite further inflammation.[4–6,8] In most horses with meniscal lesions, the tear begins approximately 1 cm from the axial edge of the horn of the meniscus and the ligament.[4,6,8] The depth (full versus split thickness), length and degree of tissue separation of the lesion will vary (Figs 19.6, 19.7). Debridement of loose and damaged tissue may diminish the stimulus for joint inflammation. Arthroscopy can also be used to monitor or assess healing before returning to work.[4] The surgical findings can also be used to formulate a more accurate prognosis for future athletic soundness. Horses with full-thickness tears that extend caudally under the femoral condyle probably have a poorer prognosis for full return to function due to the potential for persistent stifle instability.[4,6,8] Stall rest for 4–8 weeks will minimize further damage to the MM and associated soft tissue. Systemic (NSAID and chondroprotectives) and/or intra-articular (hyaluronic acid and/or corticosteroids) therapy can be used to control the deleterious effects of synovitis on intra-articular structures. Healing can be assessed with ultrasonography or repeat arthroscopy to determine the optimal time to initiate hand-walking and eventual return to work.

Prognosis Horses with lesions confined to the cranial ligament and cranial horn of the meniscus have a fair to good prognosis for returning to athletic competition following arthroscopic debridement and prolonged rest (6–9 months).[4,8] Athletes with large tears involving the body of the meniscus as it courses under the femoral condyle, complete avulsion of the cranial attachment and concurrent CoL or CrL damage have a poor prognosis for athletic use.[4,8]

Prevention

The same shoeing, conditioning, schooling and judicious retreat from adverse conditions as previously described for CoL injuries.

Etiology and pathophysiology

Meniscal injuries can result from crushing forces when the femur rotates over the menisci with the leg in extension during high-speed athletic activities or a traumatic event such as a fall or kick.[9,10] Meniscal injuries can occur after joint instability caused by cruciate ligament disruptions. Small lesions confined to the cranial horn or ligament of the meniscus may cause minimal stifle instability but the ensuing synovitis from the damaged soft tissue can cause chronic lameness and, if not treated in a timely fashion, shorten an athletic career. Extensive lesions involving the body of the meniscus or those that occur in conjunction with other soft tissue injuries will often end a career due to the resulting stifle instability.

Epidemiology

Meniscal injuries are more common in horses competing in jumping disciplines, participating in galloping events with sudden stops and turns or during a fall or traumatic event during a competition.[9] Poor footing, extreme course difficulty and inadequate conditioning or talent may also be contributory.

Cruciate ligament injuries

- Cranial CrL injuries in horses always have a midbody component.
- Avulsion fractures at the attachments are less common and occur in combination with the midbody injury.
- Caudal CrL injuries are rare and they usually occur after cranial CrL damage.
- These injuries will often end the career in equine athletes.

Horses have paired (cranial and caudal) CrLs that are extrasynovial and located in the septum between the medial and lateral femorotibial joints (Fig. 19.1A). They provide stability to the stifle joint and limit cranial or caudal movements of the tibia or femur during locomotion. The CrLs are loaded maximally during stifle extension and the caudal CrL is axially rotated during stifle flexion.[11] During weight bearing the CrLs will limit rotation and forward displacement of the tibia and stabilize the medial aspect of the femorotibial joint.[11] Cranial CrL injuries are more common in horses and are often accompanied by other soft tissue injuries (CoL or MM).[8,12] Caudal CrL injuries are often accompanied by cranial CrL injuries but can occur independently.[13]

Recognition

History and presenting complaint Horses with a cranial CrL injury present with an acute onset of moderate to severe lameness and often have a history of a fall, loss of footing with a sudden forceful attempt to regain it or colliding with an immovable object.[9]

Physical examination There is moderate to severe lameness characterized by non-weight bearing or toe-touching gait on the affected limb immediately following the injury. Over time the lameness may improve but the horse will remain reluctant to flex the stifle during the swing phase and will not completely load the tibia during the stance phase of the stride.[9] Effusion of the femorotibial joints is readily discernible. Flexion of the stifle will often be vigorously objected and will worsen the lameness.[9] Stifle instability and worsening of the lameness may be noted if the tibia is repeatedly rocked caudally while the horse is weight bearing (cruciate test). Crepitus or periarticular thickening is uncommon. Atrophy of the thigh and gluteal musculature is common in chronic cases with marked lameness.

Special examination Because the septum that separates the two joints is usually torn, the cruciate ligaments will then be intrasynovial so that anesthesia of the medial and/or lateral femorotibial joint will often improve the lameness considerably.[8,12] However, there will be a residual mechanical instability of the gait with complete disruptions of the cranial CrL. In acute cases, intra-articular anesthesia is rarely necessary. Radiographs are often non-diagnostic because avulsion fractures at the attachments are rare.[14] An avulsion fracture of the intercondylar eminence of the tibia may be observed infrequently with cranial CrL injuries (Fig. 19.8).[14–16] If a weight-bearing lateromedial projection can be obtained, cranial displacement of the proximal tibia relative to the distal femur may be present after complete cranial CrL disruptions. In chronic cases of CrL disruptions, radiographic evidence of degenerative joint disease will be present and mineralization of the damaged CrL may be seen.

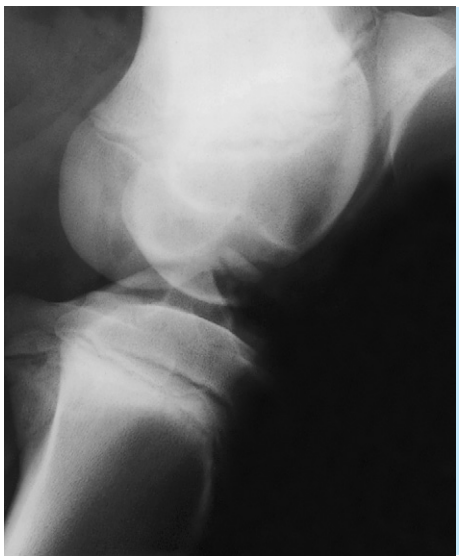


Fig. 19.8 Avulsion fracture of the intercondylar eminence of the tibia.

Ultrasonographic imaging of a cranial CrL tear can be performed in the standing horse by directing a 5 or 7.5 MHz linear or curvilinear probe parallel and between the medial and middle patellar ligaments with the stifle fully flexed.[2,3] This requires sedation and/or articular analgesia as many horses with CrL injuries resent this manipulation. Discontinuity of the fiber pattern or size of the structure is suggestive of injury to the cranial CrL. The caudal CrL may be imaged ultrasonographically from the caudal aspect of the femorotibial joint. Arthroscopic surgery will enable accurate evaluation of the CrL and other intra-articular structures.[6] Magnetic resonance imaging or computed tomography would be ideally suited for the diagnosis and quantification of intra-articular soft tissue injuries of the equine stifle.

Necropsy examination At necropsy, variable disruption of the cranial CrL and other articular soft tissue or bony structures is present with synovitis and hemorrhage. Depending on the duration, there may be evidence of secondary degenerative changes within the joint.

Diagnostic confirmation The differential diagnoses include stifle fractures, soft tissue injuries (CrL, MM), hemorrhage or sepsis. Horses with cranial CrL disruptions are usually very lame. The degree of instability and the arthroscopic and ultrasonographic findings are usually diagnostic.[6,8] Arthroscopic findings may include a variable amount of fiber disruption in the cranial and/or caudal CrL, tearing of the septum between the femorotibial joints, widening of the femorotibial joint space, avulsion fractures of the intercondylar eminence of the tibia and meniscal injuries.[6,8]

Treatment and prognosis

Therapeutic aims Minimize further damage to the CrL with rest and control inflammation to allow soft tissue healing. Physical therapy is used to re-establish joint mobility and tissue strength.

Therapy There are no effective surgical procedures available to reinforce or reconstruct the cranial CrL in horses, as

there are in humans, dogs or cattle, due to anatomic differences, biomechanical demands and expectations for eventual outcome. In addition, horses with complete cranial CrL tears have other intra-articular soft tissue injuries that make any attempt at stabilization unrewarding. A medial, cranial and/or lateral arthroscopic approach to the femorotibial joint will allow visualization of the CrL, articular septum and menisci.[4–6] Arthroscopic debridement of loose soft tissue associated with partial cranial CrL injuries and lavage to remove protein debris and inflammatory mediators may be effective in minimizing the deleterious effects of synovitis and enable some athletes to return to work. Small fracture fragments from the intercondylar eminence of the tibia can be removed but care must be taken to avoid further damage to the CrL or its attachment.[15] Larger fragments involving the insertion of the cranial CrL can be secured to the parent bone using cortical screws.[16] Lag screw technique may be contraindicated as it could weaken the fragment, causing it to shatter when the implant is tightened.

Concurrent use of systemic and intra-articular anti-inflammatory or chondroprotective therapy after surgery is indicated. Complete rest (6–9 months) may increase the strength of the repair tissue in the cranial CrL.[8] Hand-walking immediately after surgery is detrimental if any degree of instability is present. Swimming after 4–6 weeks of stall rest will allow the soft tissues to gain strength and increase the range of motion of the joint without loading the healing structures and exacerbating the instability.

Prognosis The prognosis for future athletic soundness is guarded to poor due to the considerable stifle instability that results from CrL injuries. This will restrict pain-free locomotion and will eventually lead to osteoarthritis. Horses with partial injuries without additional soft tissue injuries may return to light work, but return to more demanding disciplines like eventing, jumping or polo may not be a realistic expectation unless the degree of CrL fiber disruption is minimal and stifle stability is not affected.[4] Horses that require constant analgesic or anti-inflammatory medication to remain in work should be retired from competition. Complete CrL tears usually carry a poor prognosis for even a sedentary pain-free life and euthanasia is a humane option.

Prevention

The training and equestrian competition guidelines mentioned for preventing CoL and MM injuries should be applicable in minimizing the occurrence of these injuries.

Etiology and pathophysiology

The cranial CrL is loaded maximally during stifle extension. Most cranial CrL injuries occur when the stifle is impacted or twisted during weight bearing, causing hyperextension.[9] During a fall, internal rotation of the tibia with the stifle fully flexed can exert enough force to tear the cranial CrL. Once disrupted, the stability of the stifle is adversely affected, making precise alignment of the femur and tibia impossible, leading to painful ambulation and degenerative joint disease. Since the CrLs are loaded maximally during stifle extension, most CrL injuries are midbody tears.[11]

Epidemiology

Cranial CrL injuries can occur in any horse involved in athletic competition at high speeds or those that require jumping, sudden turns or body contact that can precipitate a fall.

Osteochondrosis of the stifle

- The stifle is a very common site for osteochondrosis in the horse.
- The lateral trochlear ridge of the femur is the most frequently affected site in the femoropatellar joint.
- The medial femoral condyle is the most frequently affected site in the femorotibial joint.
- The onset of lameness is variable depending on the size and location of the lesion and age and use of the horse.

Osteochondrosis can affect multiple joints in the horse and in the stifle manifests as osteochondrosis dessicans lesions with loose cartilage flaps or subchondral bone cysts with poor-quality subchondral bone for articular cartilage support. These lesions may actually represent the response to exercise-induced trauma after normal pressures are applied to a joint with an abnormal or immature subchondral bone.

Recognition

History and presenting complaint Horses affected with osteochondrosis dissecans (OCD) of the trochlear ridges or patella will usually present with an obvious rear limb lameness that can be localized to the stifle(s) by gait evaluation, limb manipulation and intrasynovial anesthesia. These horses are often younger than 1 year of age and have obvious femoropatellar joint effusion representative of the more severe nature of the lesions. Horses with less extensive lesions may not present until they are older than 2 years of age and the onset and severity of the lameness may not be as obvious. These horses may become increasingly lame with more rigorous work schedules and the degree of femoropatellar joint effusion may be subtle.

Lameness caused by subchondral bone cysts (SC) of the femoral condyle(s) is usually diagnosed in young athletes (2–4 years of age) but can often affect horses as young as 6–9 months of age. It is frequently the cause of a rear limb lameness that becomes evident when affected horses are first placed into work. The lameness is unilateral or bilateral and the severity is largely dependent on the size of the lesion(s) and type of work the horse is performing. The lameness will vary in severity but will often worsen with work and improve after rest. Horses participating in more strenuous athletic disciplines will present earlier than those involved in less active routines (pleasure). Horses will rarely present with both types of stifle osteochondrosis simultaneously.

Physical examination Affected horses have a characteristic gait common to horses with stifle disease (see previous sec-

tions) and will respond similarly to limb manipulations and change in surface incline. Careful attention to limb movements and gait is necessary because the disease is bilateral in approximately 60% of horses,[17] so that the gluteal rise and change in stride dynamics may not be as obvious as in a horse with disease of only one stifle. Horses with OCD of the trochlear ridges or patella have obvious effusion of the femoropatellar joint and those with SC will have effusion of the medial femorotibial joint. Occasionally horses with simultaneous shoulder and stifle OCD will present with a very stilted, shortened gait (walking on egg shells) and kyphosis of the lumbar spine.

Special examination Intra-articular anesthesia of the affected joint will usually result in a dramatic improvement in the lameness. This may not be necessary in horses with marked lameness and effusion of the stifle, but simultaneous OCD of the shoulder joint(s) is not uncommon and it may be necessary to improve the rear leg lameness to allow careful observation of the thoracic limbs.

Radiographs of the stifle are usually diagnostic for the condition. However, there are horses with OC of the stifle that have normal-appearing radiographs that present with effusion of the stifle and a lameness that can be localized to the joint. The lesions in these horses are limited to the articular cartilage and do not extend deep into the subchondral bone, hence the normal-appearing radiographs. These patients will often require arthroscopy of the affected joint for diagnosis and treatment. Ultrasonographic examination of the cartilage of the dorsal aspect of the trochlear ridges with a 5–7.5 MHz probe positioned between the patellar ligaments may reveal cartilage defects in the femoropatellar joint not visible radiographically.

Both stifles should be radiographed, as the condition is commonly bilateral,[17] even though the clinical signs or radiographic changes may be more obvious or severe on one limb. The lateromedial and oblique views are best suited to evaluate lesions of the lateral (most common) or medial trochlear ridge of the distal femur or rarely the patella (Figs 19.9, 19.10). There may be subchondral lucencies or flattening of the subchondral bone, most commonly on the mid to distal aspect of the lateral trochlear ridge but they can occur anywhere on either ridge (Figs 19.9, 19.10).[18–20] Mineralized or ossified cartilage fragments that are attached or loose can also be present along the articular margin of the trochlear ridges, trochlear groove or patella, either within the articular defects or loose at the bottom of the joint.[18–20] The radiographic appearance of these lesions will usually underestimate the severity of the lesions encountered at surgery.[18–20] The caudocranial view will usually reveal the central location of the subchondral cyst of the medial femoral condyle (Figs 19.11, 19.12), and large cysts can often be seen on the oblique and lateromedial views.[21] These cysts can be quite large (Fig. 19.12), have a variable degree of subchondral bone lucency and most will have sclerotic bone surrounding the cyst cavity.[21] In long-standing cases of stifle OC there may be radiographic evidence of degenerative joint disease (DJD) along the articular joint margins. Adequate radiographic technique and equipment is necessary to adequately image the stifle in an adult horse and is especially important in identifying SC. Nuclear scintigraphy is not accurate in identifying SC lesions due to their relative avascularity.

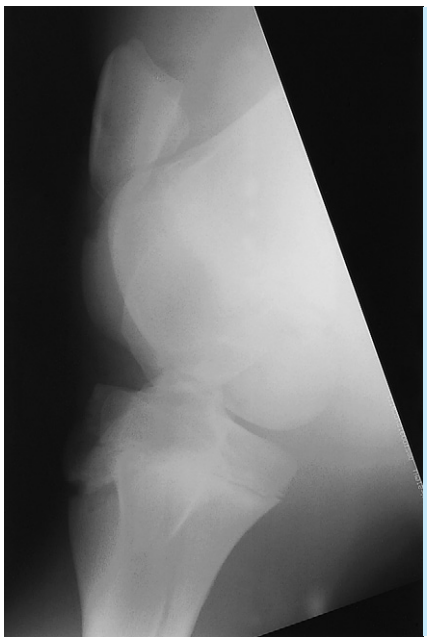


Fig. 19.9 Osteochondrosis dissecans of the lateral trochlear ridge of the femur in a 2-year-old Thoroughbred colt.

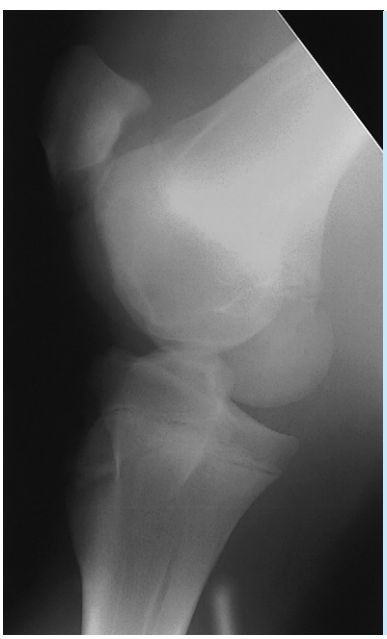


Fig. 19.10 Osteochondrosis dissecans of the medial trochlear ridge of the femur in a 2-year-old Thoroughbred filly.

Necropsy examination Variable amounts of articular cartilage erosion and fibrillation are seen with areas of normal-appearing hyaline cartilage detached or inadequately supported by subchondral bone. The subchondral bone bed may be necrotic or filled with granulation or fibrous tissue or fibrocartilage. Chronic cases may have variable amounts of DJD with thinning of the articular cartilage and the presence of wear lines.

Diagnostic confirmation Osteochondrosis of the stifle is differentiated from other causes of stifle lameness by the

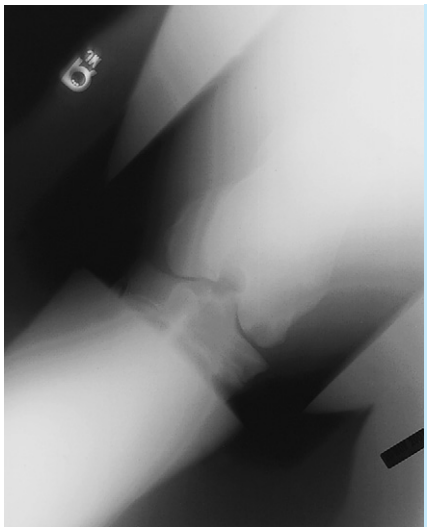


Fig. 19.11
Subchondral bone cyst of the medial femoral condyle of the femur in a 3-year-old Quarter Horse colt.

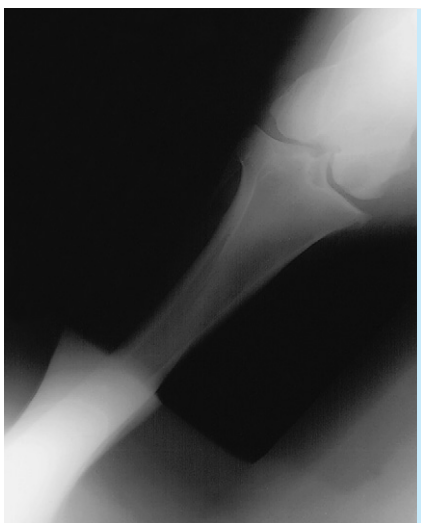


Fig. 19.12
Subchondral bone cyst of the medial femoral condyle of the femur in a 5-year-old Quarter Horse gelding.

gradual onset of the condition and the characteristic radiographic or arthroscopic appearance.

Treatment and prognosis

Therapeutic aims Debride loose cartilage or osteochondral fragments and remove all avascular and unsupported subchondral bone. Allow enough time for the affected articular surfaces to be resurfaced with fibrocartilage.

Therapy The treatment of choice is arthroscopic debridement of the lesions via standard approaches to the femoropatellar or medial femorotibial joint. Trochlear ridge lesions are ideally visualized through an arthroscopic approach between the middle and lateral patellar ligaments with the instrument portal between the middle and medial or lateral patellar ligaments.[17–20] Copious lavage should be used during surgery to remove all cartilage and bone fragments to reduce the inflammatory effects of this debris. If both stifles are affected they should be operated on simultaneously to limit the progression of the disease in the other joint, minimize the anesthetic risk of two surgeries and speed recovery in horses intended for athletic use.

The arthroscopic appearance of OCD lesions in the femoropatellar joint is usually more extensive than the radiographic appearance would indicate and some very distal trochlear ridge or patellar lesions may be surgically challenging. A lateral or cranial arthroscopic approach to the medial femorotibial joint can be used to debride SC lesions of the medial femoral condyle.[6,21,22] The SC lesions will often appear as a subtle dimple of the articular cartilage on the condyle (Fig. 19.13A), which after debridement and forage of all unsupported cartilage and subchondral bone can become rather large defects (Fig. 19.13B).[21,22] These defects may eventually become radiographically indistinguishable or remain as a persistent radiographic defect after the surgery in some relatively sound patients.

Fig. 19.13
(A) Arthroscopic view of a subchondral cyst of the medial femoral condyle.
(B) Arthroscopic appearance of the subchondral cyst in (A) after surgical debridement.

Postoperative pain may be significant in horses with large lesions operated on bilaterally. Use of intra-articular mepivacaine or narcotics (morphine sulfate, 6–15 mg) at the conclusion of surgery will reduce articular pain and often will improve recovery from general anesthesia. Epidural analgesics in the immediate postoperative period may make pain management more effective. Stall confinement for 4–6 weeks after surgery is necessary and a gradual reintroduction to hand-walking started 10–14 days after surgery. Gradual return to exercise after 5 months may be an option for horses with smaller lesions while those with extensive lesions may require 6–9 months of rest. Postoperative use of anti-inflammatory and chondroprotective agents will decrease discomfort and may maximize the quality and quantity of repair tissue in the defect.

Osteochondral grafts harvested from a non-weight bearing area of the joint, autologous, compacted cancellous bone grafts and pluripotential stem cells transformed into cartilage-producing cells prior to implantation into SC have had variable results in improving the quality of tissue that resurfaces these defects in horses.[23–27] Some methods appear promising but are not used at this time due to the morbidity of additional articular defects, the need for multiple surgeries and the unpredictable nature of the results. Improving the quality of repair tissue for articular defects in horses would greatly improve the quality and longevity of many athletic careers.

Conservative treatment of stifle osteochondrosis may be suitable for small OCD lesions and some SC that demonstrate only flattening of the condyle. Horses with OCD of the lateral trochlear ridge or large SC cysts will have a better prognosis for return to athletic function if they are treated surgically with arthroscopy early in the disease process.[18–22] Horses treated conservatively should be rested for 6–8 months with frequent radiographic monitoring for progression of healing. Radiographic resolution of the lesions is usually very slow and incomplete. Often the initiation of exercise will exacerbate the lameness, requiring more aggressive surgical treatment. Conservative therapy may result in loss of the early part of an athletic career if, after a prolonged lay-off, there is no radiographic or clinical improvement and surgery is then required.

Prognosis Stifle OC carries a fair to good prognosis for return to athletic activity in most horses with small to moderate defects.[18–22] Younger horses may benefit from early surgical intervention to curtail progression of the lesion and minimize degenerative articular changes from chronic inflammation.[18–21] Young animals with severe lameness due to stifle OC that is left untreated will spend long periods in recumbency, leading to marked limb deformities and flexural contractions. These horses should be treated surgically early in the disease process to avoid these serious and career-ending complications. The unique biochemical and structural arrangement of hyaline (articular) cartilage makes it capable of withstanding the stresses and loads of vigorous athletic competition. However, articular cartilage defects in older horses do not have the capacity to regenerate hyaline cartilage. These defects are predictably resurfaced with fibrocartilage that does not have the biomechanical capability to withstand the rigors of a strenuous and prolonged athletic career. Horses younger than 2 years of age may have the capability of regenerating some hyaline cartilage, so early surgical intervention may improve the quality of the repair tissue and the integrity of the joint surface. Horses with OCD of the femoropatellar joint may have a better prognosis since the lesions are on a gliding articular surface, in contrast to the usual central weight-bearing surface of the medial femoral condyle where SCs develop. Horses intended for elite athletic use having large femoral SC lesions may not fare as well.

Prevention

Since the disease is multifactorial, complete prevention is unlikely. Maintaining balanced mineral (copper, zinc, calcium and phosphorus) levels in the diet and not overfeeding grain (excess phosphorus) is recommended. Delaying rigorous training may reduce the incidence in horses that are skeletally immature and predisposed to traumatically induced subchondral bone damage and the development of growth cartilage defects.

Etiology and pathophysiology

Osteochondrosis is a developmental disease characterized by disorders of the growing cartilage in the epiphysis and growth plates. This complex biologic mechanism is termed endochondral ossification and it allows for longitudinal bone growth and provides subchondral bone support for all joint surfaces. When this developmental disorder affects the integrity of the articular cartilage due to loss of joint surface support, it will cause joint inflammation (osteochondritis). Other manifestations of this disorder of cartilage development include angular limb deformities, physitis, cervical vertebral malformations and SC.

The disease is multifactorial with genetic (growth rate), nutritional (copper deficiency, calcium and phosphorus imbalance from feeding excess grain), metabolic (vitamin D deficiency) and endocrine (hypothyroidism) influences.[28–31] The predictable locations of many osteochondral articular lesions in the horse are sites where the developing articular cartilage or growth plates are thick, the vascular supply is tenuous but the biomechanical loads are high.[28–31] Therefore, vascular and traumatic insults in these locations are probably very important in the expression of this disease in horses.[21,29–31] The ultimate expression of the disease is unpredictable but controlling some of these factors may help reduce the incidence of the disease in a particular area or farm.

Epidemiology

The disease has worldwide distribution and varied breed predilection. The incidence of the disease may vary from one farm to another and between geographical areas, highlighting the multifactorial nature of the disease. It is a disease of young horses and is reported frequently in breeds used for

speed events such as Standardbreds, Thoroughbreds, Warmbloods and Quarter Horses. Exercise in these breeds at a young age in conjunction with genetic or nutritional predispositions may account for its expression.

Patellar luxation

- Patellar luxations in adult horses are usually the result of severe impact trauma from a fall or collision.
- Lateral luxations are more frequent.
- Affected horses will present with severe lameness and an inability to fix their stifles in extension.
- Radiographs are necessary for diagnosis and to rule out a concurrent patellar fracture.

Horses have three patellar ligaments (medial, middle and lateral). These attach the distal aspect of the patella to the proximal aspect of the tibia (Fig. 19.1A). The medial patellar ligament will be pulled over the medial trochlear ridge of the femur when the stifle is locked in extension. Lateral patellar luxations are more common in horses because the large medial trochlear ridge, particularly in adults, usually prevents medial dislocation. Most luxations are congenital or hereditary and seen in miniature horse or pony foals. In adults or young horses, luxation is secondary to trauma or severe hypoplasia of the lateral trochlear ridge due to osteochondrosis.

Recognition

History and presenting complaint Patellar luxations in adult horses present as an acute onset of severe lameness and swelling of the stifle following a traumatic episode.

Physical examination There is a severe lameness with marked swelling of the involved stifle. Any attempt to fully bear weight on the leg will lead to an inability to fix the stifle in extension. The patella can usually be palpated laterally or may be displaced distally if the attachments of the quadriceps muscle have become detached from the proximal patella.[3,2] The horse will usually resent any attempt at limb manipulation or ambulation.

Special examination Radiographs are usually diagnostic and will reveal the direction of the dislocation.[1] The caudocranial, lateromedial or oblique views are diagnostic for either the more common lateral luxation or the infrequent distal luxation by evaluating the patella in relation to its normal anatomic position in the trochlear groove on the cranial aspect of the femur. A skyline (dorsoproximal to dorsodistal) view of the cranial distal femur will confirm the presence of an empty trochlear groove and the location of the displaced patella.[1] This view may be hard to obtain in a horse with an acute luxation that resists stifle manipulation. The radiographs should be closely evaluated for the presence of any patellar fragmentation, fractures or avulsions that can accompany the luxation. An attempt should be made to evaluate the integrity of the patellar ligaments and medial aspect of the stifle ultrasonographically.

Necropsy examination At necropsy, there is displacement of the patella out of the trochlear groove with variable amounts of hemorrhage, soft tissue swelling, bony fragmentation of the patella or trochlear groove and disruption of the patellar ligaments. In cases secondary to severe OC of the lateral trochlear groove, there will be marked degenerative joint disease, periarticular soft tissue fibrosis, an atrophied trochlear groove and ridge and a variably sized patella in an abnormal lateral location.

Diagnostic confirmation The differential diagnosis for acute onset of stifle swelling and severe lameness includes disruption of intra-articular soft tissue structures (CrL, menisci, CoL), fractures, hemorrhage, sepsis and cellulitis. The radiographic and physical examination findings are diagnostic for patellar luxation.

Treatment and prognosis

Therapeutic aims Replace the luxated patella to its normal anatomic location (trochlear groove) and prevent recurrence.

Therapy Using heavy sedation and possibly a caudal epidural analgesic, the laterally luxated patella should be reduced manually by manipulating it proximally and medially with the horse standing. The manipulation may be difficult and if the horse is attempting to flex the limb while movement of the patella is being attempted, it will make reduction of the lateral luxation impossible. Reduction of the luxation under general anesthesia is generally easier but it will usually re-luxate when the horse attempts to stand and flexes the leg or contracts the quadriceps forcefully. If the luxation can be reduced standing, the horse should be cross-tied for 4–6 weeks to prevent recumbency and extreme joint flexion. Systemically administered analgesics and NSAIDs will help control discomfort and inflammation. Gradual introduction to hand-walking is instituted for another 12–16 weeks, allowing the extracapsular and patellar soft tissue support to adequately fibrose. Ultrasonographic and radiographic imaging should be performed before initiating work to insure complete healing of all the involved structures.

Prognosis The prognosis for soundness is good if there are minimal concurrent injuries to the intra-articular soft tissue structures and the collateral or patellar ligaments. Marked periarticular fibrosis will worsen the prognosis for return to function and luxations accompanied by significant patellar fractures may be difficult to manage to achieve a successful outcome.[3,2]

Prevention

These injuries are usually unforeseen and generally not preventable. However, proper shoeing, schooling and conditioning and avoiding precarious footing conditions may help minimize their occurrence.

Etiology and pathophysiology

These injures are traumatically induced and are usually the result of a fall, collision with a solid object or a kick. A sudden forceful contraction of the quadriceps muscle group during

strenuous activity may lead to disruption of their attachments to the proximal patella, predisposing to distal or lateral luxation.[32]

Epidemiology

This disease occurs infrequently and there are few predisposing factors.

Patellar ligament desmitis

- Horses have three patellar ligaments: medial, middle and lateral.
- The patellar ligaments, particularly the medial, are part of the stay apparatus of the hindlimb.
- Desmitis or tearing of the patellar ligaments in horses is infrequent.
- Avulsion fractures of the distal patella often have a patellar ligament injury associated with them.

Recognition

History and presenting complaint Horses with patellar ligament desmitis will present with an acute or chronic lameness of variable severity.[33] There may be a history of a fall or blunt or sharp trauma.[9]

Physical examination There is usually mild effusion of the femoropatellar joint and palpable thickening of the affected ligament or surrounding soft tissues. The lameness will usually become worse after stifle flexion.

Special examination Intra-articular anesthesia of the femoropatellar joint may improve the lameness slightly due to diffusion of anesthetic around the ligament. The response is more dramatic if fragmentation of the distal patella accompanies the injury. Local infiltration of the area of the ligament with mepivacaine may also improve the lameness to some degree. Fragmentation of the distal patella will be evident radiographically on survey films and mineralization of the ligaments may be evident with chronic injuries. Ultrasonographically, desmitis of the ligaments will appear as hypoechoic or hyperechoic areas with fiber disruption, depending on the stage of the disease. The ligaments may be thickened due to edema or scar tissue or have very reflective areas consistent with mineralization. Ultrasonographic evaluations should be performed with the horse weight bearing and the scans compared to the contralateral limb for ligament size and fiber uniformity.[2,3]

Diagnostic confirmation Patellar ligament desmitis must be differentiated from other causes of acute or chronic stifle lameness. Palpation of thickened or painful patellar ligaments, incomplete response to intra-articular anesthesia and the ultrasonographic appearance of patellar ligament disruption or desmitis are diagnostic.[2,3]

Treatment and prognosis

Therapeutic aims Arthroscopic removal of intra-articular avulsion fragments is indicated if there is a significant response to femoropatellar joint anesthesia and the fragments are radiographically evident.[34] Care must be taken at surgery not to create further damage to the ligament by attempting to extract small but well-embedded fragments that may have little clinical importance.[34] An extracapsular approach for non-articular fragments can be used, but there must be unequivocal presurgical evidence that the fragments are actually the cause of lameness and care must be taken to avoid further damage to the patellar ligament during the procedure.

Rest and systemic anti-inflammatory therapy are indicated for cases of desmitis without bony fragmentation. Usually 8–12 weeks of rest with a gradual return to work will suffice. Horses that had surgery or more severe injuries may require longer rest periods. Healing of the ligament should be monitored ultrasonographically and return to work recommendations made on the basis of these findings.

Prognosis Horses with desmitis, partial tears or small avulsion fractures of the patella have a good prognosis for return to working soundness.[33,34] Complete avulsion or tearing of the middle patellar ligament causes marked stifle instability and is generally unresponsive to treatment, making the prognosis for athletic soundness poor.[32,33]

Prevention

These injuries are infrequent and prevention is difficult.

Etiology and pathophysiology

Blunt or sharp trauma to the patellar ligaments can cause patellar ligament desmitis and a sudden forceful contraction of the quadriceps during a fall or with the stifle in full extension may also lead to these injuries. With a complete tear or avulsion of the middle patellar ligament, marked stifle instability and severe pain will result during ambulation. The patella can be fragmented as a direct result of the impact or from an avulsion of all or part of the attachment of the ligament at the distal border of the patella. Chronic desmitis, intra-articular fragmentation with synovitis and periarticular fibrosis can all lead to persistent lameness in athletes that sustain these injuries.

Epidemiology

Patellar ligament injuries may be more common in horses that event, hunt or steeplechase due to the stresses placed on the structures during jumping or from striking crossrails or obstacles while competing.[9]

Upward fixation and chondromalacia of the patella

- Upward fixation of the patella is usually intermittent but can become persistent.
- Fixation occurs when the medial patellar ligament remains engaged on the medial trochlear ridge during the swing phase of the stride.
- It is more common in younger horses and those with upright conformation.

- Poor quadriceps tone, due to disuse atrophy from injury, inactivity or neurological disease, predisposes to the condition.
- Chondromalacia of the patella can result from instability or weakness of the quadriceps mechanism or patellar ligaments.

Recognition

History and presenting complaint The presenting complaint and history may entail only a change in gait with an exaggerated action to the cranial phase of the stride or complete inability to move the limb with the affected leg fixed in extension. In some routinely active athletes there may be a history of a decline or cessation of their work schedule due to an injury or illness, leading to loss of muscle conditioning that will precipitate the condition once a higher level of activity is resumed. Horses with chondromalacia will present with a rear limb lameness of variable duration and severity.

Physical examination Horses with persistent upward fixation of the patella will present with the affected limb(s) fixed in extension, with an inability to flex their stifle or hock.[33] The distal limb joints can still be flexed. The condition will impede locomotion if bilateral and if unilateral, the horse may advance the affected limb by dragging it in extension. In some horses excessive wearing of the toe in the affected limb(s) will be apparent. In some cases backing the horse, manual pressure on the patella or light sedation may disengage the patella. In many cases it will recur within a short time. Most cases present as intermittent upward fixation with a prolonged posterior stance phase of the stride and a shortened or exaggerated swing phase which can be evident at every stride or only at variable intervals, depending on surface, incline or duration of exercise. Femoropatellar effusion and response to stifle manipulation and a favorable response to intra-articular anesthesia will be evident in horses with chondromalacia of the patella.

Special examination The clinical presentation and history are usually diagnostic in most horses. Limb manipulation, intra-articular anesthesia or radiographs are usually unrewarding. If there is an obvious loss of muscle mass associated with the quadriceps or rear limbs, further diagnostic testing for neuromuscular diseases such as equine lower motor neuron disease, shivers, polysaccharide storage disease or equine protozoal myelitis would be warranted. Young horses with intermittent upward fixation of the patella that present with an upright conformation, flexural contracture or stifle effusion should be evaluated radiographically to determine if there is an underlying developmental orthopedic disease predisposing to the condition.[35] Horses with intermittent upward fixation of the patella may have radiographic evidence of chondromalacia of the patella. Chondromalacia may be the cause or result of upward fixation of the patella and may be a response to chronic inflammation or repeated trauma to the articular cartilage of the patella.[35] The patella may have areas of radiographic lucency or bony proliferation. There may be radiographic evidence of distal medial patellar fragmentation if medial patellar ligament desmotomy was used for treatment of intermittent upward fixation of the patella.

Diagnostic confirmation The principal differential diagnoses include stringhalt, fibrotic myopathy and shivers. Horses with stringhalt will usually have exaggerated hock and stifle flexion that is consistently present at every step and can be severe enough to cause the horse to hit the ventral aspect of the abdomen with the distal limb during walking.[36] The stance phase of the stride in horses with stringhalt is usually normal or shortened. Stringhalt may be unilateral or bilateral, can occur as a herd outbreak and may be related to exposure to certain weeds (*Hypochaeris radicata*; dandelions), trauma or disease of the sciatic or peroneal nerves.[36] Horses with fibrotic myopathy have a pronounced and consistent interruption of the cranial or swing phase of the stride marked by a rapid caudal movement of the affected limb before it makes contact with the ground. The gait in this condition is characteristic and palpation of the semitendinosus and semimembranosus muscles will reveal the fibrotic component of these muscles that will not be apparent in horses with upward fixation of the patella.[35] Shivers will usually present as an exaggerated flexion of the rear limb and flagging or quivering of the tail when the rear limbs are picked up or the horse is backing up or turning in a tight circle. It is often not so obvious when the horse is moving forward in a straight line and may be more common in draft-type horses.[35]

Treatment and prognosis

Therapeutic aims The condition should be differentiated from the previously discussed diseases and the patient thoroughly evaluated for conformational, neurological or orthopedic diseases that may predispose to the condition. If there is an underlying cause, then its removal or treatment will help recovery or resolution of the upward fixation. In cases with marked atrophy of the quadriceps muscle due to neurological disease, identification and resolution of the neurological disease are necessary to restore muscle function and resolve the condition.

Therapy When a lack of muscle tone is present due to inactivity or reduced training schedule, these horses will usually benefit from a gradual reintroduction to work coupled with an increase in the intensity and frequency of exercise until the condition is no longer apparent. For severe cases, exercise regimens that include swimming, underwater treadmill or backing up will increase the strength of the quadriceps muscle group and minimize periods of complete weight bearing that often lead to upward fixation of the patella. As the horse improves, walking up and down a slope will further strengthen the muscles that control patellar movements.

Injection of sclerosing agents such as iodine into or surrounding the patellar ligaments or distal quadriceps has been used clinically to create an inflammatory response in the soft tissue, resulting in fibrosis or 'tightening' of the periarticular connective tissue in an attempt to reduce the occurrence of patellar fixation.[37] Injection of 2% iodine or ethanolamine oleate into the medial or middle patellar ligament in horses

resulted in a significant accumulation of inflammatory cells and fibroplasia of the ligaments.[38] This fibrous reaction may result in contraction and stiffening of the ligaments and may be responsible for the clinical improvement observed when used in cases of intermittent upward fixation of the patella.[38]

Routine desmotomy of the medial patellar ligament for intermittent upward fixation of the patella is not recommended as the practice may lead to chondromalacia and fragmentation of the distal patella when high-speed exercise resumes.[39] Rarely, when the fixation is permanent and cannot be reduced by manipulation or sedation, then a medial patellar ligament desmotomy may be indicated. The procedure is performed in sedated standing horses under local anesthesia.[35] These horses should not be actively exercised for 8–12 weeks to reduce the occurrence of distal patellar fragmentation or chondromalacia. In spite of these precautions, these complications may occur due to chronic trauma to the patella induced by the desmotomy. These horses may require arthroscopic surgery of the femoropatellar joint to remove patellar fragments and any diseased articular cartilage from the patella.[34] Use of anti-inflammatory and chondroprotective drugs in these horses may be of benefit.

Prognosis The prognosis for most athletes with this condition is excellent for resolution if any underlying cause can be identified and treated and the degree of conditioning improved. Horses treated with a medial patellar ligament desmotomy for upward fixation of the patella may develop patellar fragmentation or chondromalacia of the patella. These horses will often present with femoropatellar synovial effusion and lameness. The prognosis for athletic soundness in these horses is guarded.

Prevention

There is no general recommendation on preventing this condition in horses. Maintaining a consistent exercise program of adequate rigor for the particular discipline being pursued is usually all that is required. If predisposed athletes have been removed from training or active exercise for a period of time, an incremental approach to training will be helpful in limiting the disruption caused by this gait abnormality. Reducing or eliminating exercise in horses with a weak quadriceps mechanism and avoiding the indiscriminate use of medial patellar ligament desmotomy may prevent chondromalacia of the patella.

Etiology and pathophysiology

An upright conformation and developmental or orthopedic diseases causing pain during stifle flexion can precipitate the condition. Disuse atrophy or neurological dysfunction of the quadriceps muscle group, limiting the ability to disengage the patella from the medial trochlear ridge as the horse moves, is probably the most common cause for this condition. The condition will affect athletic performance by interfering with the normal range of motion of the stifle joint during locomotion.

Chronic trauma to the posterior aspect of the patella caused by stifle instability (idiopathic or iatrogenic) may lead to chondromalacia of the patella.

Epidemiology

The condition can affect any age and use of horse. It may be more common in younger horses or those with decreased quadriceps tone due to underlying disease or inactivity.

Stifle fractures

- Stifle fractures in adult horses are challenging to treat and often have a guarded prognosis for return to athletic use.
- The patella is the sesamoid bone of the quadriceps muscle group insertion on the proximal tibia.
- Patellar, tibial tuberosity, incomplete distal femoral and condylar fragmentation may all be amenable to treatment, thereby improving the prognosis for return to function.
- These injuries will often have concurrent articular soft tissue or ligament injuries that will make diagnosis, treatment and rehabilitation very challenging.
- Prompt recognition, adequate case selection and excellent clinical therapy are important aspects of managing these injuries in adult horses to restore joint stability and function.

Recognition

History and presenting complaint There is a history of an acute onset of severe lameness of a rear limb after a fall or impact. There may be a complaint of marked swelling, pain or crepitus over the stifle or proximal tibia of the affected limb or an inability to fix the stifle in extension.

Physical examination There is usually a marked degree of lameness present on the affected limb marked by a toe-touching attempt to bear weight or complete non-weight bearing. There may be a variable amount of soft tissue swelling or crepitus centered on the patella or cranial aspect of the tibia. In horses with complete transverse patellar fractures, there may be an inability to maintain the stifle in extension during any attempt at weight bearing, with an obvious protrusion of the distal femoral trochlear ridges.[40] Any attempt to manipulate the stifle will cause marked discomfort and palpation of the periarticular structures will reveal crepitation. There may be obvious soft tissue defects or contusions if the injury resulted from direct impact trauma. These soft tissue injuries need to be completely evaluated to determine if the soft tissues are viable and if communication with the underlying bone or joint is present. Open fractures with devitalized soft tissues will complicate therapy, minimize options and worsen the prognosis.[40] If the fracture has an intra-articular component the degree of femoropatellar and/or femorotibial effusion or hemorrhage will be readily palpable. Horses with distal patellar fragmentation usually present with less severe lameness, femoropatellar effusion and soft tissue swelling.[9,39,41,42]

Special examination Intra-articular anesthesia or limb manipulations are not necessary in horses with complete sagittal, transverse or comminuted patellar fractures or those with tibial tuberosity or distal femoral fractures. The clinical presentation will usually localize the lameness to the stifle. Horses with distal patellar fragmentation or stress fractures will have a less obvious clinical presentation and intra-articular anesthesia or limb manipulations will be necessary.[9,42]

Radiographs of the stifle are necessary to make an accurate diagnosis, formulate a therapeutic plan and determine a prognosis. Transverse or comminuted patellar fractures are imaged on standard lateromedial, caudocranial and flexed lateromedial views. When sagittal patellar or medial patellar avulsion fractures are suspected, the dorsoproximal to dorsodistal (skyline) view (Fig. 19.14) is ideal for imaging the size of the fragments and the location of the fracture line.[42] The caudomedial to craniolateral and caudolateral to craniomedial oblique views are necessary to visualize bony fragments associated with distal patellar avulsions or fragmentation. Distomedial patellar fragmentation may be evident in horses after medial patellar ligament desmotomy was performed for treatment of intermittent upward fixation of the patella.[39,43] The flexed lateromedial or skyline view may be hard to obtain in painful horses. Sedation (detomidine 0.01–0.02 mg/kg i.v. and/or butorphanol 0.01–0.02 mg/kg i.v.) or intra-articular anesthesia may facilitate the manipulations necessary to obtain adequate images. Radiographic quality and completeness will affect preoperative planning and formulation of a prognosis. Tibial tuberosity or distal femoral fractures can be imaged on the lateromedial, caudocranial or oblique views. These radiographs should be carefully evaluated for any intra-articular component or fracture line propagation. Tibial tuberosity fractures may be confused with the active tibial tuberosity physis present in horses up to 3 or 4 years of age and in these cases the lateromedial radiograph of the opposite tibia should be used for comparison.[44,45]

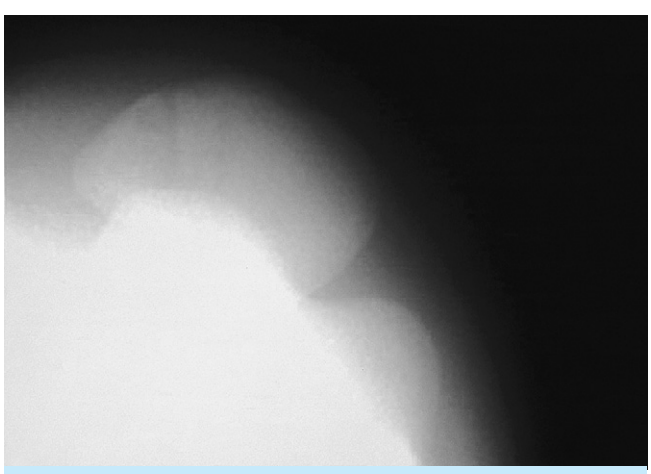


Fig. 19.14
Axial patellar fracture imaged on a dorsoproximal to dorsodistal radiographic projection (skyline) of the patella.

Ultrasonography of the patellar ligaments and the CoL is indicated for all horses with patellar, tibial tuberosity or distal femoral fractures. These scans can be performed standing using a 7.5 or 10.0 MHz linear probe positioned directly over each structure. It is not uncommon to sustain concurrent ligament (patellar, CoL and CrL) or intra-articular soft tissue (MM and articular cartilage) injuries with these fractures.[42,46] Nuclear scintigraphy may be helpful in the diagnosis of incomplete stress fractures or traumatically induced osteitis of the patella, distal femur or proximal tibia.

Diagnostic confirmation The clinical presentation and lameness evaluation will localize the source of lameness to the stifle. Diagnosis of these injuries is dependent on adequate and detailed radiographic studies of the stifle. Special views (skyline) are necessary when unusual fracture configurations are suspected (Fig. 19.14). Ultrasonographic evaluation will reveal concurrent soft tissue injuries. Accurate imaging is imperative to permit optimal therapeutic selection and prognosis.

Treatment and prognosis

Therapeutic aims Before any therapy is attempted, a precise and accurate diagnosis of all affected bony or soft tissue structures is imperative. These injuries adversely affect stifle function and there is no room for tentative or delayed therapeutic efforts that may further compromise function and irreversibly prevent any chance at rehabilitation. When the injuries are severe enough to make repair and rehabilitation unlikely, these horses should be euthanized for humane reasons.

The therapeutic aim is to stabilize fractures that are amenable to internal fixation, remove any intra-articular fragments that cannot be reduced and stabilized but contribute little to joint stability and debride or remove any damaged soft tissues that can promote inflammation.[40,42,47–51] After surgery, every effort must be made to assist the horse during the anesthetic recovery and enforce the required rest periods necessary to insure adequate bony or soft tissue healing. Rehabilitation of joint function is an important therapeutic component for these injuries.

Therapy Patellar fractures are usually treated surgically with internal fixation to re-establish joint stability, articular congruency and quadriceps function.[40,42,47–51] Conservative treatment of patellar fractures with disruption of the quadriceps mechanism (transverse or comminuted) will invariably fail and lead to persistent pain, osteoarthritis and joint fibrosis with contralateral limb breakdown. Sagittal patellar fractures should be treated surgically when there is a palpable fracture line present in the patellar fascia, a fracture gap of greater than 5 mm evident on the skyline view or significant fragmentation of the distomedial aspect of the patella indicating the presence of significant articular disruption.[40] Surgical intervention involves an approach over the patella through the peripatellar fascia and quadriceps muscles with reduction and debridement of the affected tissues.[40] Separate approaches to the medial and lateral aspect of the

femoropatellar joint may be necessary to adequately reduce the fracture. The fracture is maintained in reduction with 4.5 or 5.5 mm cortical or 6.5 mm cancellous screws.[40,49,51] Small axial fractures or distomedial fragments that are too small or comminuted to allow secure internal fixation can be removed (partial patellectomy) with arthroscopy of the femoropatellar joint.[34,39,41,42] Placement of the arthroscope laterally between the middle and lateral patellar ligament will improve visualization of the distomedial aspect of the patella where most of these fragments are located.[34]

Not all distomedial patellar fragments are intra-articular. If their location is determined to be extracapsular due to absence of effusion, lack of lameness or response to intra-articular anesthesia, they should not be removed because the periarticular soft tissue or ligament disruption may cause long-term clinical problems.[34] If there is any doubt as to their intra-articular location, arthroscopic evaluation is preferable to liberal incisions and extensive tissue dissection in an effort to remove the fragments. Non-displaced sagittal fractures (no palpable peripatellar fascial gap or radiographic fracture gap less than 5 mm) will usually heal with a fibrous union after 60–90 days of stall rest.[40] Follow-up radiographs may reveal persistent lucency of the fracture in horses with minimal joint effusion or lameness, indicating fracture stability and adequate joint resurfacing.[40]

Transverse or comminuted patellar fractures must be treated surgically due to complete disruption of the quadriceps mechanism with distraction of the fracture fragments and inability to fix the stifle in extension.[40,49,50] Transverse fractures can be stabilized using 5.5 mm cortical or 6.5 mm cancellous lag screws reinforced with a tension band of 16 or 18 gauge orthopedic wire to neutralize the pull of the quadriceps apparatus.[49] Comminuted fractures are repaired using a combination of lag screws, tension band wiring and removal of small fragments.[40] The aim of any surgical procedure is to restore continuity of the quadriceps mechanism and re-establish congruency of the joint surface.

Arthroscopic approaches to the femoropatellar joint for treatment of patellar fractures are preferable to arthrotomies that are prone to incisional dehiscence due to suture line tension from joint effusion, soft tissue swelling and joint motion.[34,41,42] Every attempt should be made to eliminate all dead space during closure of the incision to minimize incisional complications and implant sepsis. Disruption of the muscular or ligament attachments to the patella will complicate the ensuing instability and place added or abnormal loads on the orthopedic implants and fracture repair. Full limb casts or bandages are contraindicated for managing these injuries as a substitute for surgery or as coaptation after surgery as they will actually increase the distractive forces across the injured tissues.[40]

Assisted and controlled recovery from anesthesia is imperative to minimize disruption of the internal fixation, incisional dehiscence or lateral patellar luxation following partial patellectomy caused by a sudden forceful contraction of the quadriceps muscle. After surgery, cross-tying the patient for 4–6 weeks will prevent recumbency and minimize incisional or orthopedic implant failure.

Administration of NSAIDs and stent bandages of the surgical incision is important to control swelling. The degree of soft tissue damage, presence of closed suction drains, duration of surgery and rigidity of the fracture repair will determine the duration of broad-spectrum antimicrobial drug administration. Patellar fractures will require 5–6 months for adequate bony and soft tissue healing. Atrophy and fibrosis of the articular and periarticular soft tissues are common and physical therapy (swimming) to re-establish range of motion and strength of soft tissues is imperative before a return to riding may resume at 9–12 months. Healing may be delayed due to the constant tension created by the pull of the quadriceps muscle group on the injured tissues. Serial radiographic evaluation for fracture healing and implant positioning should be used as a guide to changes in activity levels during the postoperative period. Patellar fractures may heal with a fibrous union that will be radiographically apparent.[40] Lack of effusion and resolution of the lameness should be used as indicators of healing and guide increasing activity levels.[40]

Tibial tuberosity fractures may be intra-articular if the depth and angle of fracture propagation are steep enough.[44,45] The pull of the quadriceps through the middle patellar ligament will concentrate the distractive forces on the tuberosity during stifle flexion and further displace an existing fracture.[9,44,45]

Non-displaced fractures may be diagnosed radiographically or with scintigraphy and can be treated conservatively with stall rest and cross-tying for 3–6 weeks. They should be serially radiographed to insure that the pull of the quadriceps does not displace the fracture during convalescence. Displaced fractures and those with an intra-articular component should be surgically repaired using a tension band principle to offset the pull of the quadriceps muscle through the middle patellar ligament.[44,45,52,53] The same biomechanical principle may make surgical therapy of non-displaced fractures ideal to speed healing.

Large fractures with an intra-articular component can be repaired using a 4.5 mm broad dynamic compression plate (DCP) with 4.5 or 5.5 mm cortical screws.[44,45,52,53] The 5.5 mm screws have greater holding power and the broad DCP with the staggered screw hole configuration will reduce the probability of inducing horizontal fissures through the fractured tuberosity.[44,52] However, the 4.5 mm narrow DCP is easily contoured to the cranial aspect of the tibia, thereby avoiding placement of the screws in one plane.[45,53] When the plate is secured with 4.5 mm cortical screws it should provide adequate stability for these fractures.[45,53] Alternatively, 4.5 or 5.5 mm cortical lag screws can be used with 16 or 18 gauge orthopedic wire in a tension band principle to secure smaller fractures.[44] Small non-displaced fragments can be left alone to minimize disruption of the attachment of the middle patellar ligament to the tibia during attempts at surgical removal or the fragments can be carefully removed if they are unstable or causing lameness.[45] After surgery horses should be assisted during the recovery and confined to a stall for 6–8 weeks.[44,45,52] Hand-walking or exercise can be gradually introduced after radiographic evaluations of complete fracture healing.

Adult athletes with comminuted or over-riding distal femoral fractures that involve the diaphysis, metaphysis or femoral condyle(s) should be humanely destroyed.[54] The small or comminuted distal fragments are not usually large enough to permit secure fixation with orthopedic implants. Non-displaced distal femoral Salter-Harris physeal fractures that occur in young (18–20 months) horses (Fig. 19.15) will generally respond to conservative treatment and will usually heal in 8–12 weeks.[55] Femoral condylar fragments that involve less than 25% of the caudal aspect of the condyle in an adult horse can be removed surgically via a caudal arthrotomy or arthroscopic approach.[56,57]

Prognosis The prognosis for horses with patellar fractures that can be adequately reduced and secured with implants or have intra-articular fragments removed arthroscopically is favorable for return to athletic competition.[34,40–42,48] Re-establishment of articular congruency and the integrity and function of the periarticular soft tissues will improve the eventual outcome. Horses with partial patellectomies at the proximal or distomedial aspect of the patella have a favorable prognosis if the fragment is small and soft tissue disruption is minimized at surgery.[34,42] Horses with significant comminution of the patella have a worse prognosis due to difficulty in re-establishment of joint congruity.[40]

Horses with tibial tuberosity fractures that are non-displaced or displaced fractures that can be adequately reduced and secured at surgery have a favorable prognosis for return to athletic function if the implants and soft tissues remain intact during the recovery and early postoperative period.[44,45,52,53] Horses in which significant disruption of either occurs postoperatively will have a poor prognosis for use or pain-free ambulation.[44,45,52]

Adult horses with femoral condylar fractures involving less than 25% of the condyle treated surgically (fragment removal) have a good prognosis for return to athletic use.[56] Those with non-displaced distal femoral physeal fractures have an excellent prognosis for full return to function if displacement or limb contracture does not occur.

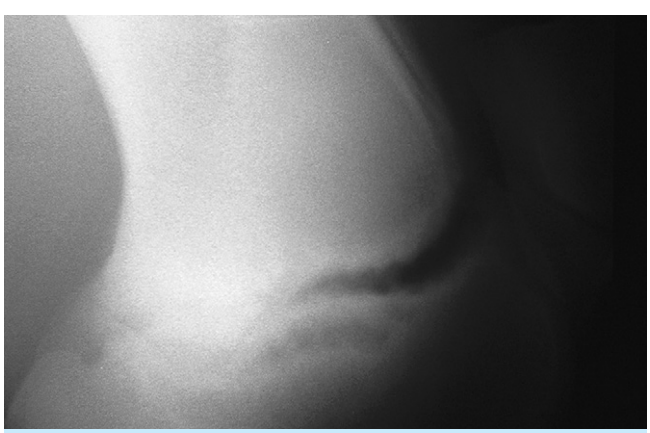


Fig. 19.15
Non-displaced, incomplete Salter-Harris fracture of the distal femur in a 2-year-old Thoroughbred colt.

Prevention

There is no effective way to prevent these athletic injuries. Attention to footing, conditioning and level of training in light of the degree of difficulty of the endeavor may reduce the possibility of an accident causing one of these injuries.

Etiology and pathophysiology

Patellar fractures in adult horses occur infrequently and are the result of a kick or collision with a fence or crossrail while jumping.[9] When the stifle is flexed (as in jumping) the patella is fixed in the trochlear groove, concentrating the force of the impact on the patella.[9]

Tibial tuberosity fractures are caused by blunt or impact trauma to the cranial aspect of the dorsal tibia, which has little soft tissue coverage to dissipate any disruptive force applied directly to it.[45] The physis of the tibial tuberosity does not completely ossify and fuse with the proximal tibial epiphysis until 2–3 years of age.[44] The quadriceps muscle group attaches to the tibial tuberosity through the middle patellar ligament. This attachment may concentrate distractive forces during contraction or loading of the quadriceps apparatus.[45,52,53] If the fracture line is deep into the tibial cortex and propagates caudally at a steep angle, the fracture will be intra-articular.[44,52]

Distal femoral fractures in adult horses are rare and traumatically induced after a kick or collision. There is often a marked amount of soft tissue trauma associated with these injuries.

Epidemiology

These injuries can occur in any type of athletic horse involved in a discipline in which a sudden loss of footing at high speed can occur or full-speed exercise around or over immovable objects is undertaken.

Tarsus

The equine tarsus has high-motion (tarsocrural) and low-motion (sustentaculocalcaneal, tarsometatarsal, distal and proximal intertarsal) joints. The distal tibia articulates with the medial and lateral trochlear ridges and trochlear groove of the talus (Fig. 19.16). This articulation provides for hock flexion and extension during locomotion. The talus articulates with the flattened central tarsal bone distally and the calcaneus on the plantar aspect of the tarsus (Fig. 19.16). The articulations of the calcaneus with the plantar surface of the talus and the proximal surface of the fourth tarsal bone are low-motion joints. The proximoplantar aspect of the calcaneus projects plantar to the tibia and serves as the attachment of the gastrocnemius tendon (GT), which contributes to hock movement and is part of the reciprocal apparatus of the hindlimb. The superficial digital flexor (SDF) tendon courses over the calcaneus and GT on the plantar surface of the hock

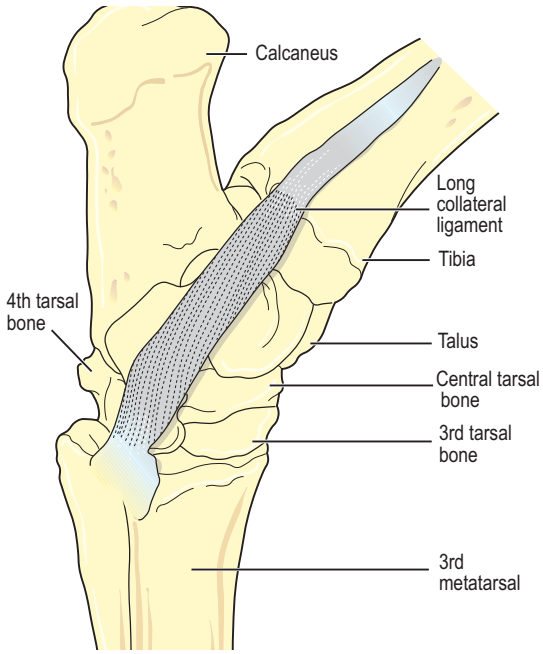


Fig. 19.16
Lateral view of the right equine tarsus.

and eventually attaches to the plantar surface of the proximal and middle phalanx. The medial and lateral edges of the SDF have firm fascial attachments to the calcaneus to maintain its central position over the calcaneus. A bursa separates it from the GT, allowing it to glide over the calcaneus during tarsocrural joint motion. The deep digital flexor (DDF) tendon is encased in the tarsal sheath as it courses medially in the tarsal canal formed by the plantar and distomedial borders of the talus and calcaneus, respectively. The distomedial projection of the calcaneus that encases the DDF plantar to the talus is the sustentaculum tali. Distally, the talus and calcaneus articulate with the central tarsal bone and the proximal aspect of the fourth tarsal bone to form the proximal intertarsal joint (Fig. 19.16). The central tarsal bone articulates distally with the third and fused first and second tarsal bones to form the distal intertarsal joint. The tarsometatarsal joint is the collective articulation of the fused first and second, third and fourth tarsal bones with the second, third and fourth metacarpal bones, respectively (Fig. 19.16). These distal joints are primarily low motion–high impact joints subjected to shear stress, compression and torsion during athletic activity in horses.

This complex bony arrangement is held together by a system of collateral ligaments and fascia that alternately tighten or loosen during flexion and extension to maintain precise bony alignment.[58] The *long lateral* collateral ligament (CoL) originates proximally on the lateral tibial malleolus and courses distally to insert on to the calcaneus, fourth tarsal bone, talus and the fourth and third metacarpal bones (Fig. 19.16). The *long lateral* CoL is loose in flexion and taut during extension of the tarsus. The *short lateral* CoL mechanism is composed of three (superficial, middle and deep) ligaments (Figs 19.17, 19.18). All three originate proximally on the lateral tibial malleolus and insert distally on the calcaneus (superficial) and talus (middle and deep). The *lateral short* CoLs are variably tight or loose during flexion or extension of the tarsus. The *medial long* CoL originates proximally at the medial tibial malleolus and inserts distally on the fused first and second tarsal bones and on the talus, central and third tarsal bones by two separate fiber bundles (Fig. 19.19). It is loose during tarsocrural joint flexion and tight during extension. The *short medial* CoL is made up of the superficial, middle and deep *short medial* CoLs (Figs 19.20, 19.21, 19.22). They originate proximally on the medial tibial malleolus and insert distally on the deep fascia, fibrous joint capsule, sustentaculum tali and central tarsal bone. The *medial short* CoLs are variably tight or loose during flexion or extension of the tarsus, with the majority of the deep component remaining tight during the entire range of motion of the tarsocrural joint.[58]

The tarsocrural joint communicates with the proximal intertarsal joint in most horses. Communication between the distal intertarsal and tarsometatarsal joints has been reported to occur in 26%,[59] 35%,[60] or 38%[61] of horses when the tarsometatarsal joint is injected first. Following the same injection, 3–4% of tarsometatarsal joints would be expected to communicate with the proximal intertarsal and tarsometatarsal joint.[59,60] Increasing the volume or pressure of injection of liquid agents does not increase the probability of communication, but will increase the amount of subcutaneous leakage of fluid.[61] The tarsometatarsal and distal intertarsal joints may also communicate with the tarsal

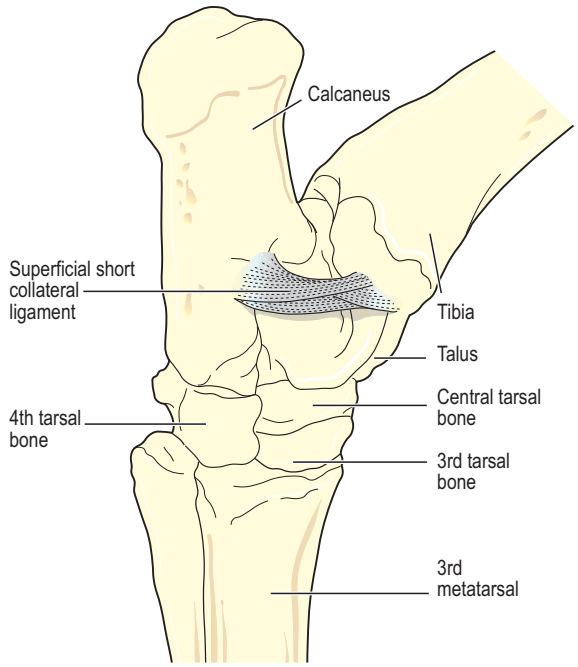


Fig. 19.17
Lateral view of the right equine tarsus demonstrating the superficial short lateral collateral ligament (SSCoL).

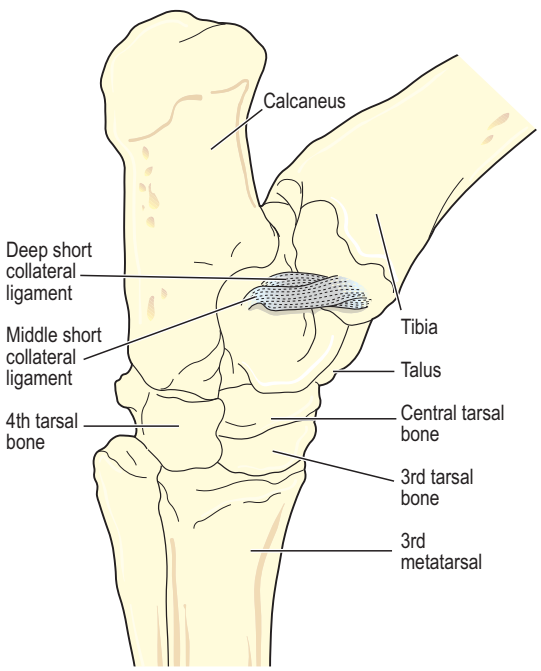


Fig. 19.18
Lateral view of the right equine tarsus demonstrating the middle short lateral collateral ligament (MSCoL) and deep short lateral collateral ligament (DSCoL).

sheath, tendon of the tibialis cranialis and the subtarsal tissues near the origin of the suspensory ligament at the plantar surface of the third metacarpal bone.[60,61] Due to this variable communication between synovial structures of the tarsus, intrasynovial anesthesia or medication of the distal intertarsal or tarsometatarsal joint cannot be accurately predicted to affect more than a single compartment and may have an extrasynovial effect on the suspensory ligament. In addition, any substance placed into one of these joints could diffuse into the tarsal sheath or tarsocrural joint.[60]

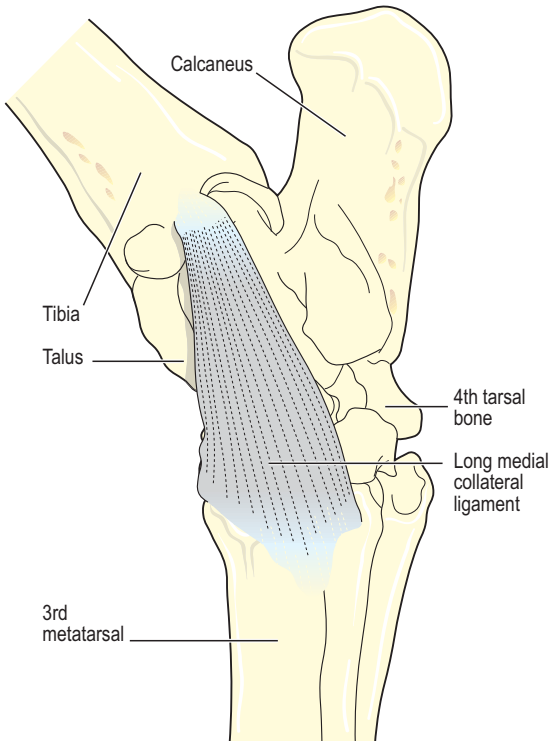


Fig. 19.19
Medial view of the right equine tarsus demonstrating the long medial collateral ligament (LMCoL).

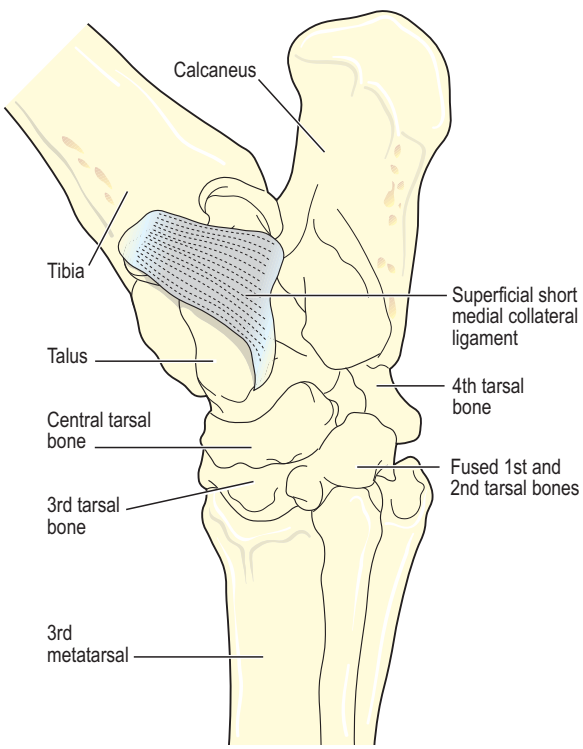


Fig. 19.20
Medial view of the right equine tarsus demonstrating the superficial short medial collateral ligament (SSMCoL).

Osteochondrosis of the tarsus

- The tarsus and stifle joints are the most frequently affected with osteochondrosis in horses.
- Standardbreds, Warmbloods and draft horses are more frequently affected.
- Osteochondrosis of the distal intermediate ridge of the tibia is the most common lesion in the tarsocrural joint.

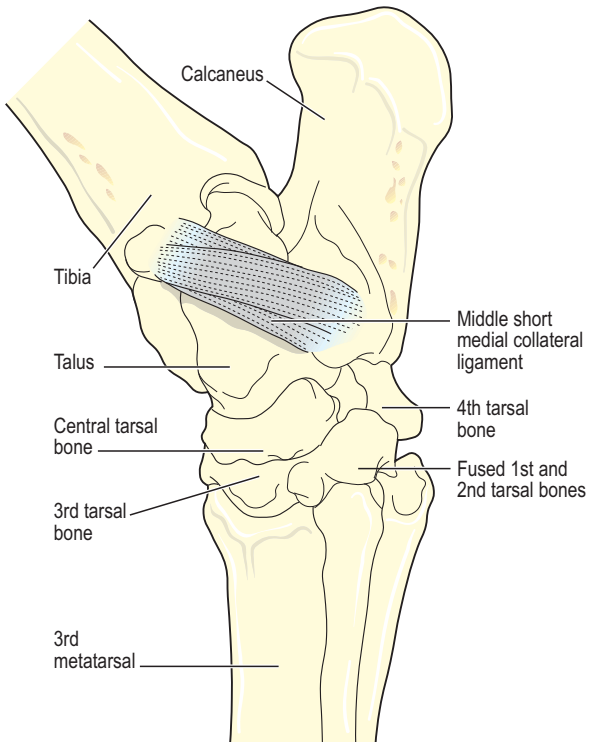


Fig. 19.21
Medial view of the right equine tarsus demonstrating the middle short medial collateral ligament (MSMCoL).

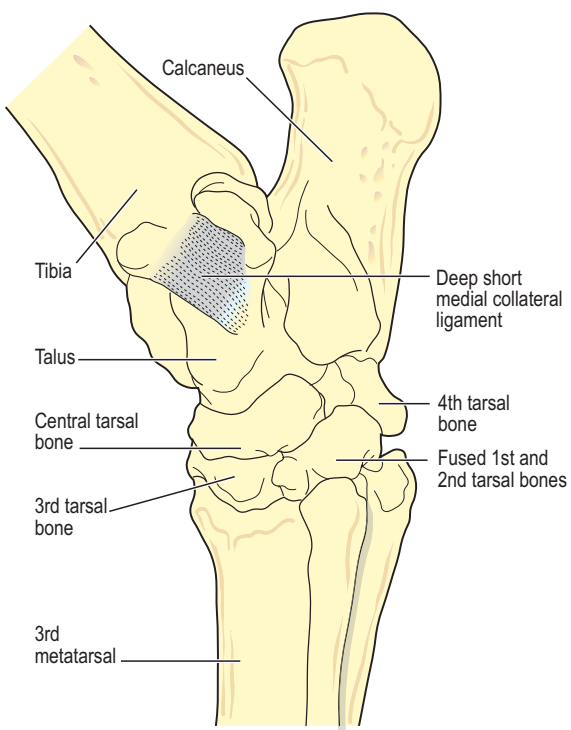


Fig. 19.22
Medial view of the right equine tarsus demonstrating the deep short medial collateral ligament (DSMCoL).

- The lateral trochlear ridge of the talus and medial malleolus of the tibia are the next most frequently affected sites in the tarsocrural joint.
- The degree of effusion and lameness is variable depending on the age and use of the horse.
- In equine athletes that are lame, surgical treatment will minimize the deleterious effects of synovitis on articular cartilage.
- Osteoarthritis and collapse of the intertarsal or tarsometatarsal joints in young athletes is seen with osteochondrosis of these joints.

Recognition

History and presenting complaint The history and clinical presentation of horses with osteochondrosis (OC) of the tarsus is variable. There are mature athletic horses (older than 2 years of age) in which there is no lameness or effusion associated with an OC lesion that is considered an incidental finding on routine tarsal radiographs. There are young horses (less than 12 months of age) that have marked effusion of one or both tarsocrural joints. In most horses of this age group, there is usually no complaint of lameness or the degree of lameness is very subtle. Horses with OC of the tarsus that is affecting athletic performance are usually in training or racing (2–3 year olds). These horses will present with a mild to moderate degree of lameness associated with effusion of the tarsocrural joint.

Physical examination Horses that are symptomatic for OC of the tarsus will present with effusion of the tarsocrural joint. The distension can be subtle or obvious and in horses with marked effusion it can be tight if the distension developed recently after rigorous exercise was initiated or soft if the distension is chronic. In most horses, the degree of lameness varies from mild to moderate and they are rarely markedly lame. A fracture of a tibial malleolus may be mistaken for an OC lesion radiographically, but fractures have an acute onset of swelling and marked lameness associated with them. The lameness is characterized by reduced flexion of the hock during the swing (anterior) phase of the stride. The duration of the weight-bearing or stance phase is usually normal but the horse may drag the toe of the affected limb(s) at a walk or trot. Due to this shortened gait, extended high-speed exercise or collected work where optimal hock flexion is required becomes more difficult for the athlete to perform adequately. Affected Standardbreds may break gait at high speeds, lean on the shafts of the cart during high-speed exercise or pull away from the affected side, making it difficult to keep the horse in a straight line. Since the degree of lameness is often mild, there is usually no gluteal rise accompanying the lameness. Upper limb flexion will exacerbate the lameness in most horses, the duration and severity of the effect being variable. Horses with OC of the small tarsal joints may have severe degenerative joint disease of the distal intertarsal or tarsometatarsal joints. They usually present with a marked lameness with a shortened swing and stance phase, a prominent gluteal rise and a positive response to upper limb flexion.

Special examination Perineural analgesia of the peroneal and tibial nerves should be expected to improve lameness caused by tarsal OC. Horses with osteoarthritis of the intertarsal or tarsometatarsal joint secondary to OC would be expected to improve after this block. Perineural analgesia is usually not required for cases of tarsocrural OC as the degree of effusion raises the index of suspicion for that joint. Intra-articular analgesia of the tarsocrural, intertarsal or tarsometatarsal joints will improve a lameness originating from these joints if they are affected with OC. The use of intrasynovial anesthesia may be of particular value in determining if a radiographically evident OC lesion is the cause of lameness, especially in cases where the degree of effusion is minimal. This may help decide which horses are likely to benefit from surgery to debride the OC lesion. Horses with OC of the small tarsal joints would be expected to improve after intrasynovial anesthesia of the affected joint(s). If the small intertarsal joints are collapsed, it may be difficult to perform the arthrocentesis to effectively block the joint.

Complete radiographic evaluation of the tarsus should be performed in affected horses and these should be obtained bilaterally even if only one tarsus appears to be clinically affected. These include the dorsoplantar, lateromedial, dorsolateral-plantaromedial and dorsomedial-plantarolateral obliques and a flexed lateral view.[62] Osteoarthritis and collapse of the tarsometatarsal and intertarsal joints due to tarsal OC will be evident on all views, but often more obvious on the lateromedial and dorsolateral-plantaromedial oblique.[62] The OC lesion of the distal intermediate ridge of the tibia, lateral trochlear ridge of the talus and medial tibial malleolus are often best imaged on the oblique views (Figs 19.23, 19.24). However, the lesions are also evident on the dorsoplantar and lateromedial views if the radiographic positioning and technique are adequate (Fig. 19.25). Lesions of the distal intermediate ridge and medial malleolus of the tibia consist of variably sized osteochondral fragments still attached to the parent bone (Figs 19.23, 19.24).[63] Lateral trochlear ridge lesions are usually lucent areas on the distal aspect of the ridge accompanied by overlying, variably sized osteochondral flaps (Fig. 19.26).[63] The lesions can vary in size and depth and in some horses marked distal trochlear ridge osteochondral fragmentation may be the predominant radiographic finding. Horses may have radiographically inapparent OC lesions of the trochlear ridges causing lameness and effusion. These may be imaged by ultrasonographic evaluation of the articular cartilage of the trochlear ridges of the talus.[64]

Young horses used in speed events may present with a marked lameness that appears to localize to one tarsus, with minimal effusion of the tarsocrural joint, a radiographically evident OC lesion of the intermediate ridge of the tibia and no radiographic evidence of osteoarthritis of the small tarsal joints. These horses may improve considerably but not completely after intrasynovial anesthesia of the tarsocrural joint. They may have a stress fracture of the distal tibia or talus (see fracture section) that communicates with the tarsocrural joint and the OC lesion is often an incidental finding. The marked lameness of one limb, minimal effusion and partial

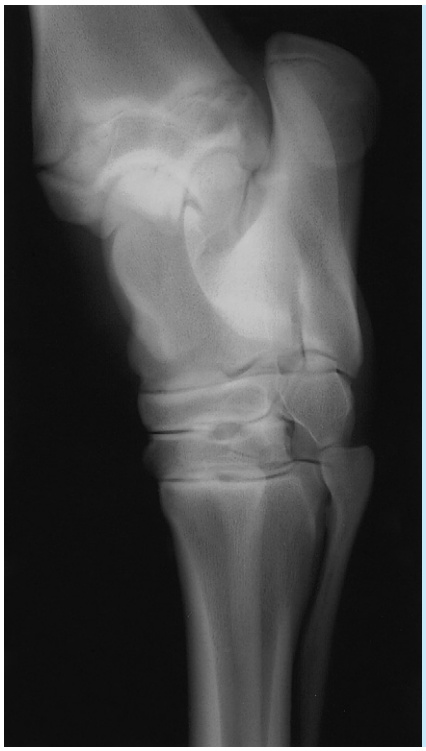


Fig. 19.23 Dorsolateral to plantaromedial radiographic view of the tarsus with an osteochondrosis lesion of the distal intermediate ridge of the tibia.

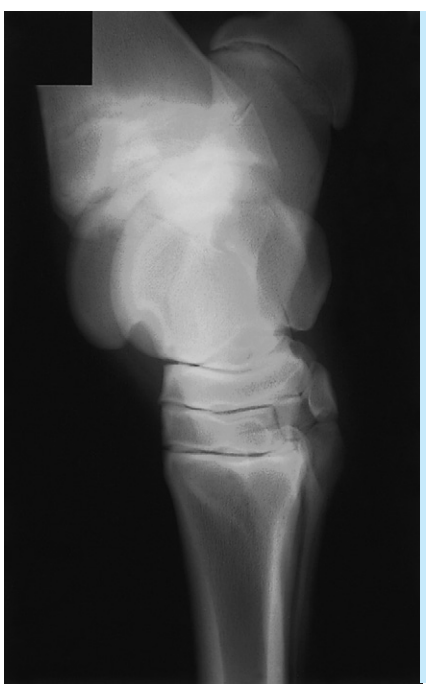


Fig. 19.24 Dorsomedial to plantarolateral radiographic view of the tarsus with an osteochondrosis lesion of the lateral malleolus of the tibia.

response to intrasynovial anesthesia should raise the index of suspicion for an additional cause for the lameness. Surgical therapy for the OC lesion will not address the source of lameness, may predispose to a catastrophic failure of the affected bone during anesthetic recovery and may lead to premature reintroduction to high-speed work before the stress fracture has healed. To determine the significance of the OC lesion and

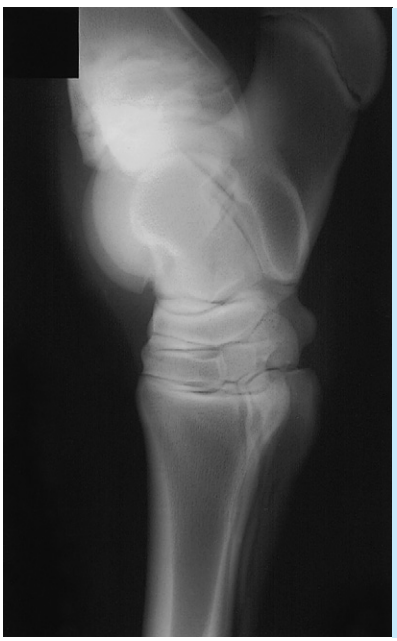


Fig. 19.25 Lateromedial radiographic view of the tarsus with an osteochondrosis lesion of the distal intermediate ridge of the tibia.

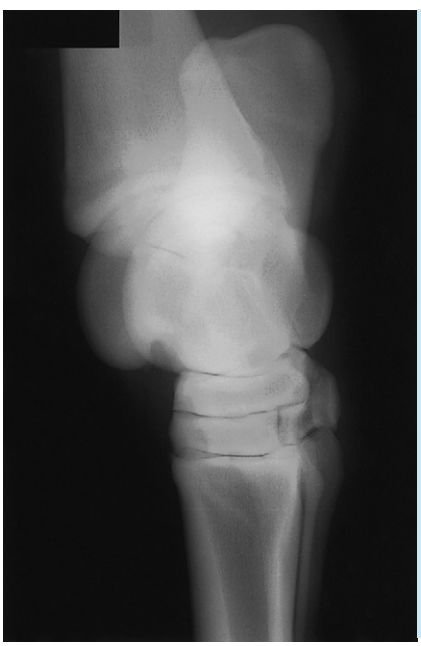


Fig. 19.26 Dorsomedial to plantarolateral radiographic view of the tarsus with an osteochondrosis lesion of the distal aspect of the lateral trochlear ridge of the talus.

if a stress fracture is present, nuclear scintigraphy and/or high-quality radiography is recommended.

Laboratory examination No special laboratory examination is necessary. If there is a doubt as to the etiology for the effusion, cytological evaluation of a synovial sample may help. Horses with osteochondrosis have synovial fluid nucleated cell counts of 1000–5000 cells/μL and protein levels close to or below 2.5 g/dL indicative of a mild synovitis.[65] Horses with traumatically induced synovitis or moderate to severe osteoarthritis have synovial fluid nucleated cell counts between 5000 and 25 000 cells/μL and protein levels of 2.5–4.0 g/dL. Severe inflammation such as occurs with sepsis will result in synovial fluid protein levels greater

than 4.0 g/dL and nucleated cell counts in excess of 30 000 cells/μL.[65]

Diagnostic confirmation Diagnosis is confirmed by the radiographic appearance of the lesions. However, not all horses with radiographically evident tarsocrural OC lesions are clinically affected. Therefore, correlation of the radiographic images with a thorough evaluation of the history, clinical evaluation and lameness examination is necessary to determine the clinical significance of a radiographic finding of tarsocrural OC in young horses. In addition, some horses with radiographically inapparent cartilage lesions may have effusion and synovitis and be clinically lame. Ultrasonography of the articular cartilage of the trochlear ridges of the hock may reveal defects not apparent on radiographs.[64]

Treatment and prognosis

Therapeutic aims The aim of treatment in horses that require therapy is to remove the involved tissue and debride the surrounding area of all loose and unattached cartilage.[63,66] This will remove the stimulus for synovitis and minimize the continued trauma to the affected area during high-speed exercise. In horses treated conservatively with rest or a reduction in the exercise schedule, the aim is to minimize disruption of the OC lesion to allow healing by completion of endochondral ossification with increasing skeletal maturity or by fibrous attachment of the affected area to the parent bone.[67] This will increase stability of the lesion and minimize the development and progression of synovitis. It is difficult to predict how long it will take for conservative therapy to work and how effectively the lesion is ossified or anchored, as radiographic monitoring will usually reveal persistence of the lesion. Return to high-speed exercise may cause a recrudescence of the lameness, necessitating surgical therapy or a more prolonged rest period.[67]

Therapy The preferred therapy for OC of the tarsocrural joint that is causing lameness and effusion is arthroscopic surgery to debride and remove loose osteochondral fragments and cartilage flaps.[63] Since articular cartilage lesions that are radiographically inapparent can perpetuate synovitis, surgical exploration of the joint may be warranted in promising athletes.

Under general anesthesia and with the horse positioned in dorsal recumbency, lesions of the distal intermediate ridge of the tibia are best approached using a dorsomedial arthroscopic portal and a dorsolateral instrument portal.[68] Lesions on the lateral trochlear ridge of the tibia can be approached similarly with the instrument portal placed slightly more laterally to improve access to the lesion.[68] In horses with marked effusion or joint capsule thickening, dorsolateral arthroscopic and instrument portals may be necessary. For surgery on lesions on the medial malleolus of the tibia, the instrument and arthroscope portals are usually reversed.[68] Bandaging and stall rest are continued for 2–3 weeks after surgery. Hand-walking can be started 10–14 days after surgery with limited turnout (paddock) initiated after 30–45 days, depending on the location of the OC and extent of articular cartilage involvement. Horses with uncomplicated distal intermediate ridge lesions usually have a shorter convalescent time. Training is resumed after 90–120 days for most tarsocrural OC. Horses with extensive articular cartilage fibrillation or synovitis will usually benefit from an extended (5–6 months) interruption of strenuous activity. Single-dose intra-articular hyaluronic acid and corticosteroids may be beneficial in decreasing synovitis and reducing the catabolic effects of inflammation on the articular cartilage.

Conservative treatment entails rest or reduction in the exercise schedule for a variable period of time. Younger horses with lesions causing mild lameness and that can be taken out of a rigorous training program may benefit from conservative therapy. The length of the rest period is somewhat arbitrary, but will be at least 60–120 days. The disadvantage of this approach is that if the lameness recurs when high-speed exercise is reinstated then surgery will be required, thereby doubling the lay-off or time away from competition. If performance is being adversely affected (lameness) and the stage of the athletic career will not permit a prolonged lay-off time, then surgery should be recommended. Intra-articular anti-inflammatory medications to control synovitis and lameness will usually result in a clinical improvement, but repeated and frequent use of this approach alone will likely result in a shortened athletic career. The medications may permit pain-free high-speed exercise, but this level of activity will likely further traumatize the lesions causing the lameness, creating more severe synovitis and articular cartilage damage elsewhere in the joint.

Horses with tarsometatarsal or intertarsal osteoarthritis may benefit from intra-articular medications such as hyaluronic acid and/or corticosteroids to improve clinical function. Phenylbutazone (NSAID) can be used to reduce the level of lameness during periods of heavy work. There are regulatory issues with the use of this class of drug and in some jurisdictions and athletic competitions its use is banned. Prolonged use may lead to debilitating gastrointestinal or renal side effects. There may be a therapeutic benefit from the use of parenterally administered polysulfated glycosaminoglycans to decrease articular cartilage degradation and synovitis and promote the production of endogenous hyaluronic acid. These therapeutic regimens may have a limited clinical effect, depending largely on the degree of tarsal bone involvement and joint collapse present. Horses with marked OC of the small tarsal joints that develop severe osteoarthritis may not be able to maintain the level of soundness required to participate in elite athletic competition.[69,70] Surgical and chemical arthrodesis of these joints may be an option and will be discussed later in this chapter.

Prognosis The prognosis for horses with OC of the tarsocrural joint is excellent if there is a favorable response to either surgical or conservative treatment. Horses treated conservatively may be less likely to have a prolonged athletic career, but the performance is usually comparable to unaffected horses while they are actually competing.[63] Horses treated conservatively or surgically are likely to race as successfully as unaffected horses of the same age, breed and use.[63,66,67] The size of the lesion or resolution of the effusion

after surgery do not appear to be as reliable prognostic indicators for horses that undergo arthroscopic surgery for OC of the distal intermediate ridge or medial malleolus of the tibia or the lateral trochlear ridge of the talus. Horses that have erosive articular cartilage lesions at the time of surgery have a guarded prognosis for athletic soundness.

Horses with severe osteoarthritis of the intertarsal or tarsometatarsal joints secondary to OC of these joints have a guarded prognosis for elite athletic use.

Prevention

Osteochondrosis is a multifactorial disease so complete prevention is unlikely. Feeding diets with balanced mineral (copper, zinc, calcium and phosphorus) levels and not overfeeding grain (excess phosphorus) are recommended. Delaying rigorous training until horses have reached skeletal maturity may reduce the incidence of traumatically induced subchondral bone damage and the development of defects during endochondral ossification. Genetic selection away from breeding lines predisposed to OC is controversial because superior racing stock in some breeds may have a genetic predisposition for the disease. In cases of tarsocrural OC, the prognosis for racing performance with treatment is good, making removal of these animals from the breeding pool unrealistic in light of the fact that the disease is multifactorial.

Etiology and pathophysiology

Osteochondrosis is a developmental disease characterized by disorders of the growing cartilage in the epiphysis and growth plates. This complex biologic mechanism is termed endochondral ossification and it allows for longitudinal bone growth and provides subchondral bone support for all joint surfaces. When this developmental disorder affects the integrity of the articular cartilage due to loss of joint surface support, it will cause joint inflammation (osteochondritis). Other manifestations of this disorder of cartilage development include angular limb deformities, physitis, cervical vertebral malformations and SC. The disease is multifactorial with genetic, nutritional (copper deficiency or zinc excess, calcium and phosphorus imbalance from feeding excess grain), metabolic (vitamin D deficiency) and endocrine (hypothyroidism) influences.[28–31] The predictable locations of many osteochondral articular lesions in the horse are sites where the developing articular cartilage or growth plates are thick, the vascular supply is tenuous but the biomechanical loads are high.[28–31] Therefore, vascular and traumatic insults in these locations are probably very important in the expression of this disease in horses.[21,29–31] The ultimate expression of the disease is unpredictable but controlling some of these factors may help reduce the incidence of the disease in a particular area or farm.

Epidemiology

Tarsocrural osteochondrosis is widely distributed and is reported to occur in Standardbreds, Warmbloods, Thoroughbreds, Quarter Horses and draft breeds, among others, with Standardbreds being over-represented. The incidence of the disease may vary from one farm to another and between geographical areas, highlighting the multifactorial nature of the disease. Exercise in these breeds at a young age in conjunction with genetic or nutritional predispositions may account for its expression.

Collateral ligament injuries and tarsal luxations

- Collateral ligament (CoL) injuries of the tarsocrural joint can be treated successfully and affected horses returned to athletic use.
- Radiography, nuclear scintigraphy and ultrasonography may all be necessary to accurately diagnose these injuries.
- Tarsal luxations can occur at the tarsocrural, intertarsal or tarsometatarsal joints.
- Horses with tarsal luxations can be salvaged and restored to light use if they are treated early and aggressively.

Recognition

History and presenting complaint Horses with tarsal luxations will usually present with an acute onset of severe lameness and swelling of the tarsus. There may be a wound associated with the tarsal luxation or it may be a closed injury. There may be a history of a traumatic event such as a kick from another horse, a fall or an accident (collision or fall) while engaged in an athletic competition.

Horses with CoL desmitis will present with a history of rear limb lameness of variable duration and severity depending on the inciting cause and degree of ligament involvement. There may be historical information (fall, kick or slip during competition) that may provide useful details as to the probable etiology. There may have been an initial response to treatment (reduction in lameness with rest and/or medication) only to have a residual component that may be static or progressively deteriorating with prolonged exercise. Standardbred pacers will present with a rear limb lameness of variable severity and increased tarsocrural joint effusion.

Physical examination Horses with tarsocrural luxations will have marked periarticular swelling, crepitus and an obvious angular (valgus or varus) and rotational deformity of the tarsus at presentation.[71–74] Once the distal tibia luxates off the trochlear ridges of the talus, it will remain in this position until it is surgically reduced even if the collateral ligaments are severely damaged or stretched.[73] Open tarsal luxations usually involve the synovial cavity of the affected joint and the articular cartilage can often be visualized through the wound. Damage to the flexor or extensor tendons and major vasculature supply may also accompany these injuries. The limb should be carefully evaluated for concomitant structure involvement before proceeding with attempts at reduction and stabilization as the prognosis worsens with extensive soft tissue damage. Horses with intertarsal or tarsometatarsal luxations may also present with an open

wound, which makes the diagnosis straightforward. Since these joints are flat, horses with closed luxations do not have an obvious angular deformity because the luxation usually propagates from the cranial edge of the joint in a plantar direction.[71,74]

These horses are usually toe touching the limb to the ground and the injury may not be readily apparent except for the obvious swelling around the tarsus. As the limb is manipulated or the horse moves the limb spontaneously, the cranial to caudal instability is easily appreciated. The calcaneus, reciprocal apparatus and suspensory ligament on the plantar surface of the limb limit these luxations to a cranial caudal plane. As the soft tissue swelling increases within hours of the injury, it will stabilize some of the laxity and the swinging movement may not be as appreciable. A high index of suspicion for a tarsal luxation is warranted for any horse with a sudden onset of severe lameness and swelling of the tarsus without a wound, especially if there are few or subtle bony changes radiographically to explain the degree of lameness.

Athletes with tarsal CoL injuries will present with a rear limb lameness of variable severity that worsens with exercise and can usually be markedly exacerbated by upper limb flexion.[75–77] There may be palpable swelling, thickening and pain of the soft tissues surrounding the affected structure. Effusion of the tarsocrural joint or tarsal sheath may be obvious. Tarsocrural joint effusion has been reported as a consistent finding in Standardbred pacers with long CoL injuries.[76]

Special examination Radiographs should be obtained on all horses presenting with an acute onset of severe tarsal swelling, even if a tarsal luxation is obvious.[72,73] Significant concomitant fractures of the tarsus will complicate treatment and markedly reduce the prognosis. In cases of tarsocrural luxations, the radiographic appearance is typical with the trochlear ridges of the talus no longer articulating with the distal tibia.[72,73] The luxation may be in a medial, lateral or dorsal direction. The calcaneus, SDF and CT may limit the development of plantar luxations.

Tarsal radiographs of horses with intertarsal or tarsometatarsal luxations may reveal a widened joint space dorsally at the affected site during the acute phase (Fig. 19.27).[71,74] If the radiographs are taken with the foot on the ground or the soft tissue swelling has stabilized the joint (luxation is reduced), the radiographic diagnosis may not be obvious. Therefore, a stressed lateromedial radiographic view is recommended to identify this injury. The foot is lifted slightly off the ground by an assistant and pulled in a plantar direction to 'open' the affected articulation dorsally and obtain an adequate image of the luxation (Fig. 19.27). The patient will often resent this manipulation, necessitating adequate restraint (sedation and/or lip chain).

Ultrasonography of the CoLs is usually not performed in cases of tarsal luxation due to the swelling present and the fact that significant disruption or stretching of the major supporting soft tissues of the hock occurs with these injuries.

In horses with desmitis of the CoL tarsal radiographs may reveal enthesiophytes at the attachments of the CoL to the parent bone (see previous section).[75–77] There may be dystrophic mineralization of the tissue evident in chronic cases and degenerative joint disease or collapse of the joint space(s) if there is long-standing instability present due to the CoL injury. Ultrasonography of the CoLs of the hock in horses is possible and disruptions of the long components of the medial or lateral CoL are more readily imaged.[78] The more superficial areas of the short portions of the CoLs and long plantar ligament can be adequately imaged.[78] Ultrasonographically there will be disruption of the fiber pattern, hypoechoic fluid accumulation within the ligament or hyperechoic deposition of fibrous or mineralized soft tissue, depending on the stage and extent of the injury. Pronounced periarticular soft tissue swelling may interfere with ultrasonographic imaging of these structures.

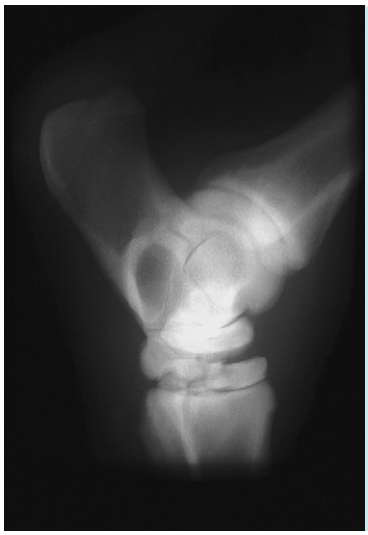


Fig. 19.27 Stress lateromedial radiograph of the tarsus of a horse with a luxation of the intertarsal joint, demonstrating widening of the joint space.

Perineural analgesia of the peroneal and tibial nerve should improve most lameness associated with CoL injuries of the tarsus. Nuclear scintigraphy in horses with tarsal CoL injuries will reveal a pattern of increased radioisotope uptake at the attachment of the CoL to the bone (Fig. 19.28).[76] The pattern of uptake and its location will help identify the structure involved (long versus short CoL) and the degree of involvement (single versus multiple areas).[76] Scintigraphy is especially useful in horses with a subtle lameness localized to the hock where radiographic studies are inconclusive. Magnetic resonance imaging would be ideally suited for the diagnosis of CoL injuries of the tarsus in horses.[79]

Laboratory examination If there is effusion of the tarsocrural joint or tarsal sheath and the radiographic diagnosis is equivocal, arthrocentesis of the affected synovial compartment and cytological analysis of the fluid should confirm the traumatic etiology of the effusion.

Necropsy examination At necropsy, there will be disruption of the soft tissue covering of the tarsus in open luxations with exposure of the articular surface and a variable amount of damage to the articular cartilage. There is usually significant disruption of all the supporting soft tissue structures of the hock with these injuries. There may also be significant bony injuries present.

In horses with closed luxations, there will be subcutaneous hemorrhage and edema associated with the injury and

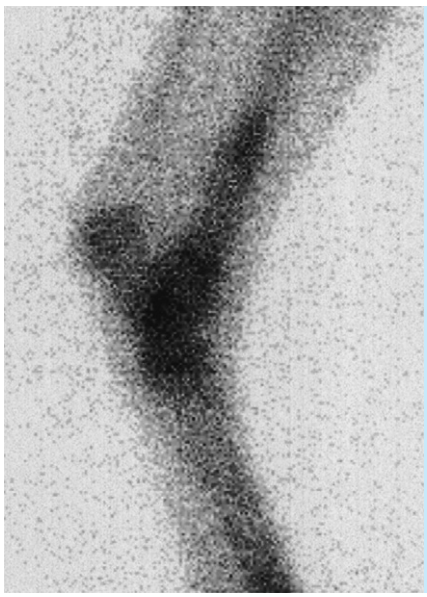


Fig. 19.28
Nuclear scan of the tarsus in a horse revealing increased isotope uptake at the attachment of the collateral ligament on the talus.

disruption of the supporting structures of the tarsal joints (CoLs, fibrous joint capsule). There may be associated bony injuries ranging from small avulsion fractures at the attachments of the CoLs to significant fractures of the talus, calcaneus, tarsal bones or distal tibia.

Horses with desmitis of the CoLs will have variable degrees of fiber disruption or thickening and fibrous proliferation or mineralization of the affected structure(s), depending on the duration of the condition.

Treatment and prognosis

Therapeutic aims The therapeutic aim for horses with any type of tarsal luxation is to reduce the luxation and immobilize the tarsus.[71–74] Major bony injuries are addressed at this time and internal fixation performed when indicated. An adequate period of coaptation and rest must be provided to allow all soft tissue and bony injuries to heal adequately. Most tarsometatarsal or intertarsal luxations treated successfully will result in arthrodesis of these joints. Physical therapy after prolonged coaptation will be important to regain as much as possible of the articular range of motion and supporting soft tissue structure elasticity that is lost due to fibrosis and disuse.

Therapy Horses with open luxations and significant fractures should be carefully evaluated before pursuing treatment. Devitalized soft tissues and septic synovial structures will complicate treatment, increase expense of therapy and worsen the prognosis. In addition, these injuries are difficult to manage effectively when external coaptation is used. Due to the poor prognosis for horses with complicated, exposed and infected tarsal luxations, euthanasia may be considered.

Horses with tarsocrural or tarsometatarsal luxations are reduced with the patient anesthetized. Tarsocrural luxations are difficult to reduce and an adequate plane of anesthesia to create muscle relaxation, limb distraction and patience are often required to achieve reduction. The marked disruption of the supporting structures (CoLs, fibrous joint capsule and fascial sheaths) makes reduction difficult and if accomplished, maintenance of the reduction is unlikely. Intertarsal and tarsometatarsal luxations are usually easy to reduce but maintaining reduction while placing the limb in a cast may be more challenging.

Once reduced, the tarsus should be radiographed to insure that proper alignment was achieved before applying a full-limb fiberglass cast from the foot to the proximal aspect of the tibia (Fig. 19.29). Adequate padding is necessary to minimize the development of cast sores. Particular areas that need adequate protection are the cranial tibial tuberosity, calcaneus and the proximal sesamoids. Excessive padding will compress during ambulation, eventually leading to cast loosening and the development of pressure sores. The limb should be cast with the hock angle near maximal extension appropriate for weight bearing (Fig. 19.29). Care must be taken during cast application to limit moving the tarsus and either losing the reduction on the luxation or creating an unwanted degree of tarsal flexion that will make it difficult for the horse to ambulate in the cast because it will make the affected leg 'shorter' than the contralateral limb. Placement of a frog support on the opposite hindlimb while the horse is anesthetized may help prevent contralateral limb laminitis during the convalescent period. Incorporating a walking bar (aluminum rod) into the cast may be necessary for larger horses to increase the strength of the construct. Smaller patients (ponies and miniature horses) may require only a full-limb Robert-Jones bandage with splints or bars cranially and caudally to achieve effective immobilization. In cases of tarsometatarsal or intertarsal luxation, placement of orthopedic implants to secure the reduced luxation or stabilize large fragments has been described. Implants include lag screw fixation, arthrodesis of the distal tarsal or tarsometatarsal joint(s) with a plate(s) or lag screws. The technique used will vary and depends on the extent and location of the bony injury.

Horses with full-limb casts must be assisted to stand after anesthesia and careful monitoring during the perioperative

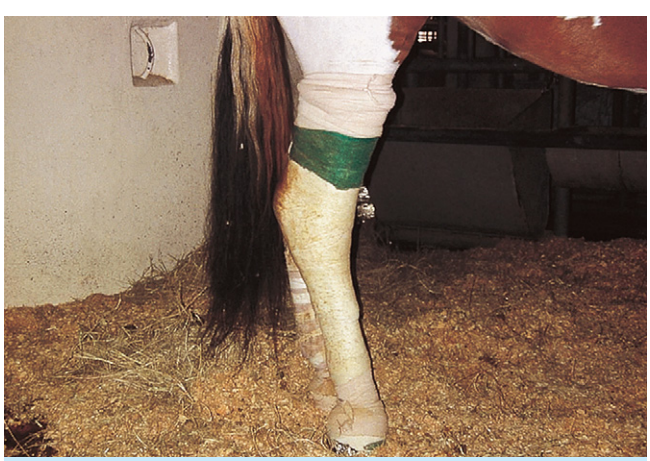


Fig. 19.29
The horse in Fig. 19.27 after coaptation in a full-limb cast.

period is required. Some horses adapt very quickly to this form of coaptation, but some will panic and become uncooperative. It will be difficult or impossible for horses to rise if they lie down with the cast limb down. In horses with closed luxations that may have difficulty accepting the cast, placing them in a full-limb bandage overnight and delaying the reduction may be of benefit to allow them to accept the immobilization. Cast sores are a problem with full-limb casts of the rear limb. They should be monitored for exudate, heat or reluctance to bear weight. Any of these is a signal for immediate replacement. These casts will loosen significantly after 10–14 days as the swelling subsides and muscle atrophy ensues, so they need to be changed at that time. Stall rest and casting should be maintained for 4–6 weeks and then a Robert-Jones bandage used for another 4–6 weeks. Hand-walking can be initiated after 90 days and turnout in a paddock after 6 months. Swimming may help restore range of motion and elasticity of the soft tissues and improve tarsocrural joint function. Arthrodesis of the intertarsal or tarsometatarsal joints will usually occur during convalescence from these luxations. Light exercise on flat ground may resume after 9–12 months if the horses are relatively sound and radiographic evaluation reveals minimal degenerative changes in the tarsocrural joint or adequate arthrodesis of the intertarsal or tarsometatarsal spaces.

Horses with desmitis of the CoL need to be rested to allow the collagen in the ligament to be replaced and to organize along the lines of stress.[75,76] Rest should entail stall rest for the first 14–21 days after the injury, with a gradual resumption of hand-walking only (5–10 minutes twice a day) after that time. Systemic NSAID therapy, cold compresses or hydrotherapy and leg wraps are helpful in eliminating soft tissue swelling and restoring adequate circulation to the injured area. Continued activity with further ligament disruption will generate a pronounced fibrovascular response that will eventually fibrose in a very disorganized manner, resulting in an architecturally weakened structure with little elasticity and poor function. This will interfere with joint movement and create a persistent mechanical or painful disruption of the gait.[76] These horses should be monitored ultrasonographically and with nuclear scintigraphy during their convalescence to evaluate ligament healing. When a significant reduction in the size of the original injury coupled with an increased tissue organization has occurred, then a gradual increase in activity is warranted to restore full function. This usually requires 3–6 months of rest. Swimming these patients may be beneficial before starting flat work to increase the strength of the tissues without loading them.

Prognosis The prognosis for horses with tarsocrural luxations of any kind is guarded to poor for athletic performance and life. Open luxations or those associated with significant fractures have a very poor prognosis for life or athletic use. Horses with closed tarsometatarsal or intertarsal luxations without significant fractures of the small tarsal bones may be able to return successfully to rigorous athletic competition or participate in disciplines not requiring frequent stops and turns or collected work (flat racing, trail riding, fox hunting). If a significant amount of soft tissue disruption occurred on the dorsal surface of the hock, the ensuing fibrosis may limit joint motion and prevent a full recovery.

Patients with CoL injuries can return to full athletic use if these injuries are diagnosed early, treated aggressively and rehabilitated properly. Standardbred pacers have a good prognosis for racing as well or better after diagnosis (scintigraphy) and treatment (rest) of long CoL injuries.[76] However, horses with extensive disruption that involves most of the cross or longitudinal section of the ligament(s) will usually not be able to return to rigorous athletic use, especially if mineralization or osteophyte production eventually interferes with joint function.[76]

Prevention

Prevention of these injuries is difficult since they are traumatic in nature. Paying attention to footing and terrain conditions (ice or mud) during strenuous athletic activity may help avoid situations (fall or collision) that may precipitate these injuries. Separating horses likely to fight will reduce the likelihood of kicking injuries. Close attention to tack, shoeing, conditioning and schooling, and matching the difficulty of the athletic competition to the abilities of the horse and rider will all increase the safety of athletic competition.

Preventing lateral CoL desmitis in Standardbred pacers may require not using shoes with lateral trailers that may exacerbate the strain placed on the lateral side of the tarsus when pacing at high speeds. Treating any front limb lameness that may be forcing the horse to shift more weight on the rear limbs to get off the front leg(s) and maintaining a reasonable work/training schedule in light of the athlete's age and level of conditioning may help reduce the frequency of these injuries.

Etiology and pathophysiology

Tarsal luxations and CoL injuries occur in horses after a forceful blow to the tarsus (kick or collision), hyperextension of the hock during a fall or rotation of the tibia while the distal limb is immobilized or rotating in the opposite direction during a sudden or explosive change in direction.

Tarsal CoL injuries in athletes can be caused by the accumulation of microtrauma in these structures during training or competition at high speeds, particularly breeds (Standardbreds) that place maximum stress on their hocks during high-speed racing in a collected gait (pacing).

Epidemiology

Tarsal luxations and CoL injuries can occur in any age, breed and use of horse. It does not appear that horses involved in any specific type of strenuous athletic activity are predisposed to tarsal luxations. However, long or short lateral CoL injuries of the tarsus may be more common in Standardbred horses, especially pacers.[76]

Tarsal fractures or osteitis of the calcaneus or talus

- Fractures of the lateral tibial malleolus are seen frequently in horses and are much more common than medial fractures.
- Lateral tibial malleolar fractures will usually involve some part of the attachment or body of the lateral CoL.
- Distal tibial stress fractures can occur in young Thoroughbred and Standardbred race horses.
- Traumatic soft tissue defects or wounds often accompany fragmentation of the talus and calcaneus in horses.
- Proximoplantar to distoplantar (skyline) and flexed lateral radiographic views are often necessary to adequately visualize these fractures.
- Slab fractures of the central or third tarsal bone occur frequently in young horses during high-speed training or racing.
- Stress fractures of the talus have been documented as a cause of lameness in Standardbred race horses.
- Fractures of the fused first and second or the fourth tarsal bone are rare.

Horses can sustain fractures of the distal tibia or tarsus that can be comminuted, displaced or open. These types of injuries are straightforward to diagnose but challenging and often unrewarding to treat. They will not be discussed in this section. Only the types of tarsus fractures seen more frequently in athletes and that are amenable to treatment or can be diagnostically challenging will be discussed.

Recognition

History and presenting complaint Depending on the inciting cause, location and size of the fracture, there will be a sudden onset of a moderate to severe lameness following a traumatic episode (fall, kick or collision) or high-speed exercise. The location and size of the fracture will determine the degree and location of any observed synovial effusion or periarticular swelling. Horses with the more common non-displaced fractures of the tarsus will usually exhibit a significant improvement in the degree of lameness at a walk or slow jog within a few days of the injury. Horses treated with NSAIDs may show an even more dramatic improvement while on the medication. Some horses with effusion of the tarsal sheath or calcaneal bursa may have a draining tract associated with the synovial structure.

Physical examination Horses with fractures of the malleolus, talus or calcaneus will often present with a moderate to severe lameness depending on the size of the fragment(s), duration of the condition and degree of synovial effusion of the tarsocrural joint, tarsal sheath or calcaneal bursa. The lameness is characterized by decreased hock flexion (reduced arc during the swing phase), shortened stance phase (weight bearing) and a gluteal rise on the affected side. The lameness is always exacerbated by manipulation and flexion of the upper limb.

There is usually some degree of soft tissue swelling, pain and crepitus localized over the area of the fracture. Horses with slab fractures of the central or third tarsal bone are usually very lame immediately after the injury, but improve considerably after a few days.[80,81] There is minimal swelling, crepitus or effusion associated with third tarsal bone fractures at presentation, but there may be effusion of the tarsocrural joint in horses with central tarsal bone fractures.[81] A painful response can often be elicited by deep palpation over the cranial or lateral surface of the affected joint.[81]

Horses with fractures of the calcaneus or talus will usually present with effusion of the tarsal sheath and/or calcaneal bursa. There may be a wound near the calcaneus that can discharge clear synovial fluid or purulent material. The degree of lameness is variable depending on the location of the injury. Horses with osteomyelitis of the calcaneus, sustentaculum tali and/or sepsis of the tarsal sheath are usually very lame.[82,83]

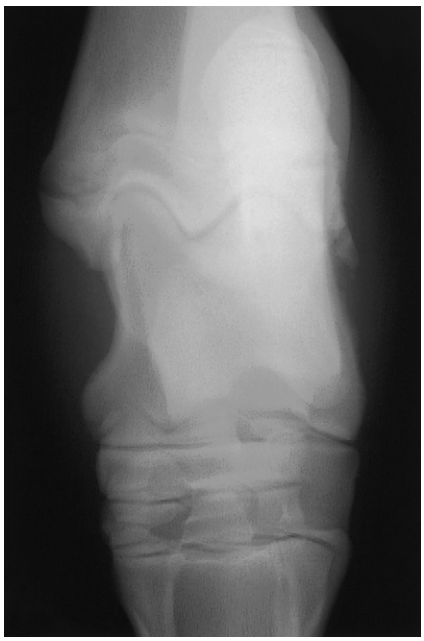
Horses with stress fractures of the talus will usually present with a mild to moderate but persistent lameness of variable duration that worsens with high-speed exercise (pacing or trotting). Tibiotarsal joint effusion is usually present but not dramatic. Upper limb flexion will exacerbate the lameness and analgesia of the joint will relieve it considerably.

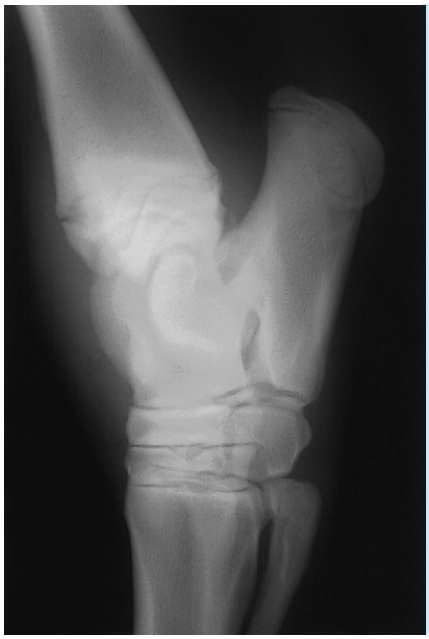
Special examination Intrasynovial or intra-articular anesthesia or tibial and peroneal nerve analgesia should provide considerable improvement in affected horses with most types of non-displaced tarsal fractures. This must be done with caution, because the fracture could become displaced or comminuted while the horse is exercised after the block. Any equine athlete that presents for a lameness evaluation with a history of an acute onset of a severe lameness after work, with or without synovial effusion and having no obvious soft tissue swelling or crepitus on the limb, should be assumed to have a stress or non-displaced fracture that could be aggravated by an extended lameness examination. Radiographic imaging of suspect or frequently involved areas and nuclear scintigraphy (after 3–5 days) may be preferable to avoid further damage to an injured osseous structure(s), which could mean a treatable condition becoming the end of an athletic career.

Lateral malleolus fractures are readily seen on the dorsoplantar and dorsomedial to plantarolateral oblique radiographic views of the tarsus (Figs 19.30, 19.31).[84] The fragments are variably sized and the degree of surrounding osseous reaction is an indicator of duration.[84]

Most slab fractures of the third or central tarsal bone are located in a frontal plane or on the craniolateral edge of the bone. Therefore, they are best imaged on the lateromedial or dorsomedial to plantarolateral oblique radiographic views.[80,81] Most are non-displaced and there is minimal dorsal or medial distraction of the slab. They can be 4–8 mm thick and variably wide.[81]

Fragmentation of the calcaneus or sustentaculum tali can be difficult to image on conventional radiographic views if they are small and located on the dorsal, distal or axial surface of the bone. Those on the proximal, caudal and





Figs 19.30, 19.31
Dorsoplantar and dorsolateral to plantaromedial radiographs of the tarsus in a horse with a fracture of the lateral malleolus.

lateral surfaces are easier to identify on conventional views. If axial or distal fragmentation of the calcaneus is suspected or there is distension of the tarsal sheath associated with a wound, a skyline (dorsoplantar to distoplantar) view of the plantar aspect of the tarsus should be obtained (Fig. 19.32). Radiographically there may be marked lysis of the calcaneus or sustentaculum tali associated with bony fragments in horses with osteomyelitis and/or sequestrum formation (Figs 19.33, 19.34). In horses with effusion of the tarsal sheath accompanied by bony proliferation of the sustentaculum tali, contrast radiography of the tarsal sheath can help differentiate between effusion caused by the exostosis and the passive effusion associated with thoroughpin.[85,86] The technique requires aseptic injection of 5–8 mL of a positive contrast agent followed by air (40–45 mL). Horses with passive effusion of the tarsal sheath generally have a smooth outline of the tarsal sheath and associated soft tissue structures evident without the filling defects or soft tissue masses seen with adhesions of the tendon or tarsal sheath frequently identified in horses with chronic tenosynovitis secondary to bony involvement of the sustentaculum tali.

Transverse fractures of the calcaneus are readily apparent on the lateromedial and oblique radiographic projections. These fractures are rare and will have a similar presentation

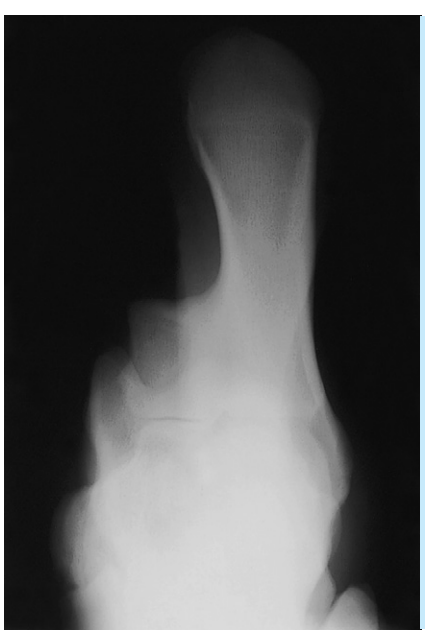


Fig. 19.32
Skyline (dorsoplantar to distoplantar) view of the calcaneus.

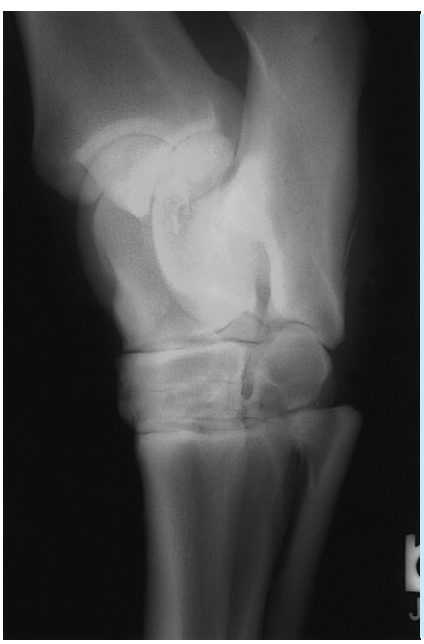


Fig. 19.33
Radiographs of the tarsus of a horse with a sequestrum of the calcaneus associated with a draining tract on the caudal aspect of the tarsus.

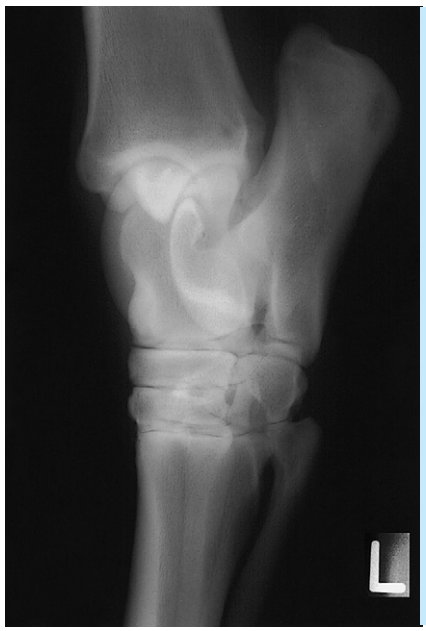
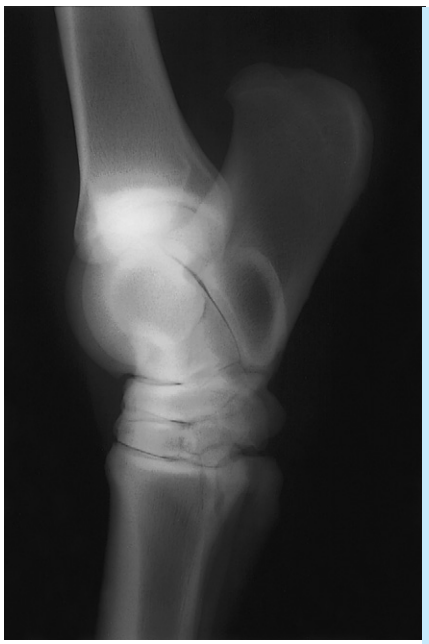
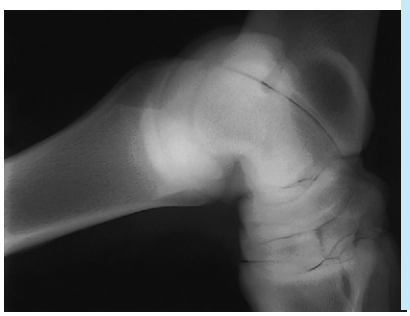


Fig. 19.34 Lytic area on the calcaneus of a horse associated with distension of the tarsal sheath and marked lameness.





Figs 19.35, 19.36 Lateromedial and flexed lateromedial radiographs of the tarsus in a Standardbred race horse with stress remodeling of the talus evidenced by subchondral sclerosis of the talus.

to a horse with disruption of the reciprocal apparatus (dropped hock and hyperflexion of the limb during attempts at weight bearing).

Osseous disruption of the talus can usually be seen on the conventional views of the tarsus. Large fractures are readily apparent but distomedial fragments may be visible only on a skyline view of the plantar tarsus and there will be bony lysis when a septic process accompanies the injury within the tarsal sheath. Fractures affecting the trochlear ridges of the talus may be small and located distally on the ridge(s) or groove or they can involve a large portion of the articular surface with marked joint instability, pain and effusion.

Standardbred horses with remodeling or stress fracture of the talus will often have a sclerotic area in the center of the talus, best projected on the weight-bearing lateromedial or flexed lateromedial view of the tarsus (Figs 19.35, 19.36). The degree of sclerosis will depend on the duration and severity of the injury. Nuclear scintigraphy will reveal a very intense but focal area of radioisotope uptake in the talus on the lateromedial, flexed lateromedial and plantar views of the tarsus (Figs 19.37, 19.38). Arthroscopic evaluation of the plantar aspect of the tarsocrural joint will often reveal mild proliferative synovitis, roughening of the distal plantar surface of the tibia and/or mild fibrillation or wear lines in the articular cartilage of the plantar surface of the trochlear ridges or groove of the talus.

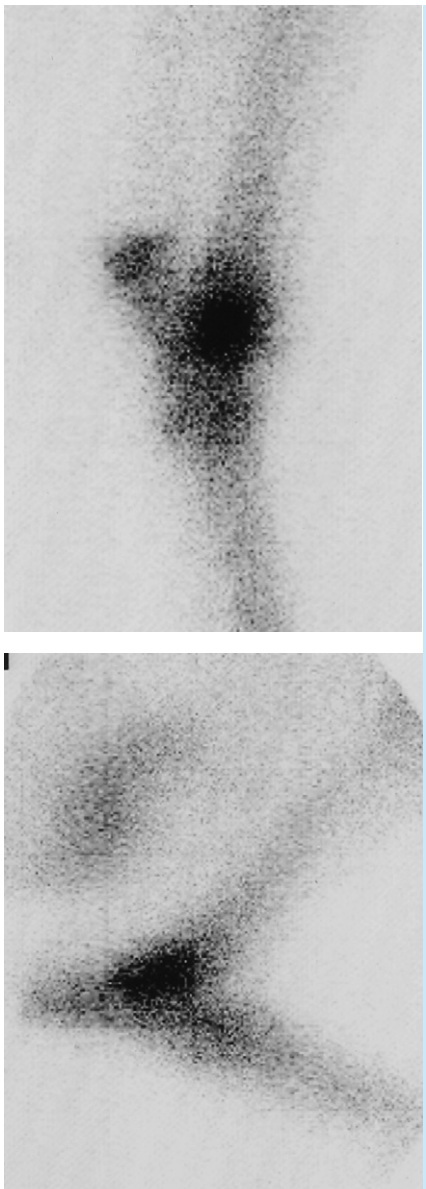
More complex fractures of the talus or fractures of the fused first and second or fourth tarsal bone can be readily imaged on routine radiographic projections. Flexed lateromedial views will allow the calcaneus and sustentaculum tali to rotate distally, permitting better visualization of the proximoplantar aspect of the talus (Fig. 19.36).

Laboratory examination Cytologic evaluation of synovial effusions associated with tarsal fragmentation may help determine if there is a developmental (nucleated cell count (NCC) less than 5000 cells/μL and protein levels (PL) less than 2.5 g/dL), traumatic (NCC of 5000 to 25 000 cells/μL and PL less than 4.0 g/dL) or septic (NCC greater than 30 000 cells/μL and PL greater than 4.0 g/dL) etiology.[65]

Necropsy examination At necropsy there will be variable amounts of soft tissue and bony disruption, hemorrhage and instability, depending on the involved structures and duration. In chronic cases with significant soft tissue or bony involvement, there may be evidence of fibrosis of the soft tissues, articular cartilage degeneration and proliferative or lytic bone depending on the etiology.

Diagnostic confirmation The diagnosis is confirmed by the specific clinical and radiographic appearance of each condition. In horses with remodeling or stress fractures of the talus, the scintigraphic appearance will confirm the diagnosis. Synovial fluid analysis may help determine a definitive diagnosis in horses with tarsal disease that have synovial effusion with equivocal radiographic or clinical findings (see Laboratory examination).

Lateral tibial malleolus and distal trochlear ridge of the talus fractures must be differentiated from OC lesions of the distal tibia or the talus, respectively. Unlike OC, fractures have an acute onset of lameness with effusion and swelling of the tarsus. In addition, there is usually a history of a traumatic episode or onset of lameness after exercise.[84] Ultrasonographic examina-



Figs 19.37, 19.38 Lateromedial and flexed lateromedial nuclear scans of the tarsus of a Standardbred race horse with stress remodeling of the talus.

tion of the long lateral CoL of the tarsus may reveal disruption of the architecture of the ligament, which would be rare in a horse with OC.[78] Fragmentation of the distal aspect of the trochlear ridges of the talus may have a similar radiographic appearance to OC of the talus, but with the fractures there is usually more bony disruption, effusion and lameness.

Treatment and prognosis

Therapeutic aims The therapeutic goal is to stabilize unstable structures, remove loose or devitalized bone or soft tissues, rid tissues of any infectious organisms and provide adequate rest and support to allow adequate healing. Serial monitoring with radiographs or nuclear scintigraphy may be required to critically evaluate the rate and quality of the repair process.

Therapy Slab fractures of the third or central tarsal bone in race horses can be repaired with lag screw internal fixation when return to racing is contemplated.[81,87] Displaced central or third tarsal bone fractures are uncommon, but when they occur and future athletic performance is expected, these fractures should be stabilized surgically. Horses that are treated conservatively (stall rest) may develop osteoarthritis of the affected joint that will adversely affect athletic soundness or return to racing.[80,87] Any residual instability and joint incongruency present will make natural arthrodesis slow and unlikely to provide long-term relief.[80]

Conservative treatment (stall rest) of third tarsal bone slab fractures in race horses appears to have a better prognosis (77%) than in those with central tarsal bone fractures treated similarly (29%).[88] A total of 64% of race horses with central or third tarsal bone fractures treated conservatively returned to their previous level of activity, but a significantly higher proportion (71%) of these were Standardbred or Quarter Horse race horses when compared to Thoroughbred horses with the same injuries.[88] Internal fixation may be more important in Thoroughbred race horses when return to racing is contemplated.

The surgical technique requires general anesthesia and radiographic or fluoroscopic guidance for proper drill and screw placement.[81] These fractures can usually be repaired with a single 3.5 or 4.5 mm cortical screw or a cannulated screw system. The head of the cortical screw is usually not countersunk to reduce the probability of the fragment shattering when the implant is tightened. An incision over the affected joint to identify the center of the fragment and proximal and distal margins of the joint for proper screw placement will expedite surgery. It should minimize the risk of damage to the dorsal tarsal vessels that can occur when the surgery is done with needle guidance through stab incisions. The horses are assisted for the recovery and confined to a stall for 4–6 weeks. Gradual introduction to hand-walking can begin at that time and return to training can occur 4–8 months after repair. Radiographic evaluation may be the best guide for increasing activity levels.

Lateral malleolus fractures should be treated surgically, especially in horses with synovial effusion and lameness.[84] Arthroscopic visualization will allow a thorough evaluation of the entire joint to assess the articular surface for damage, look for and remove any loose osteochondral fragments, inspect the fractured malleolus and flush proteinaceous and tissue debris out of the joint. The fracture fragment(s) can be removed arthroscopically, but it may be difficult to dissect the pieces from under the long lateral CoL and will often require a dorsal and caudal approach. Alternatively, the fragment can be removed quickly and effectively through a dorsal arthrotomy centered over the fragment.[84] Careful dissection will prevent further damage to the long lateral CoL. If the fragment is large enough, where a considerable portion of the attachment of the long lateral CoL is involved, reduction and fixation with a lag screw (4.5 or 5.5 mm cortical screw) will be necessary. Removing these large fragments will cause further damage to the CoL and would perpetuate tarsocrural instability. An adequately centered and securely closed dorsal

arthrotomy of the tarsocrural joint will have little impact on the future athletic performance of horses.[84] Assisted recovery should be used with these horses to limit further damage to the CoL and avoid tarsal luxation. Postoperatively, the limb is kept bandaged for 2–4 weeks to control swelling and reduce the effusion. In some horses, a residual amount of effusion will remain that appears to be inconsequential to future performance. Hand-walking can be initiated at 2–3 weeks after surgery and turnout in 4–6 weeks. Training can resume in 90–120 days depending on the resolution of the majority of the effusion and lameness and the degree of pre-existing damage to the long lateral CoL. If a lag screw fixation was performed, 6–8 months of rest will be required before resuming exercise to insure healing of the malleolus and CoL. Radiographs can be used to assess bony healing.

Fractures of the calcaneus can be treated conservatively or surgically. Fragmentation of the calcaneus or sustentaculum tali is usually accompanied by a soft tissue defect over the lesion and/or marked effusion of the tarsal sheath. Secondary sepsis of the tissue will be manifested as osteomyelitis of the calcaneus and/or sepsis of the tarsal sheath or calcaneal bursa, depending on the location of the wound or bony lesion.[89,90] These cases should be treated aggressively by surgical debridement, antibiotic regional limb perfusion, drain(s), lavage and systemically and/or locally administered specific antibiotic regimen or combination based on culture and sensitivity results of deep tissue (synovial or osseous tissue) gathered at surgery. Removal of devitalized and infected tissue is necessary to speed recovery and minimize the development of deep-seated synovial or osseous infections that will promote periarticular and synovial sheath adhesions that will adversely affect athletic performance.[83,90] Releasing the tarsal retinaculum of the tarsal sheath and transecting adhesions between the DDF and the sheath may reduce swelling and improve mobility.[82] A midtarsal tenotomy of the DDF will decrease motion of the tendon within the sheath, reducing pain and mechanical disruption of healing tissue.[82] This is considered a salvage procedure and athletic performance after its use is unlikely.

Endoscopic approaches to the tarsal sheath and calcaneal bursa have been described and can be used to effectively debride infected tissue and remove osseous fragmentation within these synovial structures to minimize dissection.[91,92] Endoscopic approaches may limit postoperative adhesion formation and restrictive scar tissue deposition.

After complete transverse fractures of the calcaneus, the attachment of the gastrocnemius tendon will displace the proximal fragment with luxation of the SDF, disabling the reciprocal apparatus of the hindlimb. These horses must be treated surgically with a tension band repair on the caudal aspect of the calcaneus to counteract the distractive forces of the pull of the gastrocnemius on the calcaneus. Plates, screws and/or wires can all be used depending on the size and location of the fragments. If the SDF is luxated, it is repaired simultaneously.[93,94] The repair is protected with a full-limb cast during recovery and the first 2–4 weeks following surgery, and full-limb bandages to limit hock flexion used for another 4–6 weeks. Casting alone is insufficient to neutralize the pull of the gastrocnemius and SDF. Radiographic monitoring for healing is recommended. Due to the extensive soft tissue attachments to the calcaneus, implant removal may be necessary as soon as bony healing occurs to limit fibrosis and interference with normal function. Even with uncomplicated healing, the ensuing fibrous scar tissue from the trauma and surgical exposure will often limit joint mobility, thereby adversely affecting future athletic performance.

Fractures of the talus may be confined to the dorsal or plantar articular surfaces of the trochlear ridges. These fragments are best removed arthroscopically or via an arthrotomy, depending on size and location. Stress fracture or remodeling of the talus as seen in pacing or trotting race horses will respond to rest. Return to training recommendations are based on repeat scintigraphic evaluations with resolution of the inflammatory focus. Non-displaced fractures of the talus can be repaired with lag screw fixation if the articular surface is minimally disrupted and there are pieces large enough where one or two cortical screws will adequately reduce and secure the fracture. The size of the implants and surgical approach are dictated by the location and configuration of the fracture. Comminuted fractures with complete collapse of the tarsocrural joint are not amenable to repair and these patients should be humanely destroyed. Casting may be necessary during recovery and the immediate postoperative period, but if the repair is well secured then assisted recovery should suffice. Removal of the implants is usually not necessary, but the return to athletic use will be influenced by the degree of articular involvement or damage to soft tissue structures such as the collateral or plantar ligaments. Sufficient bone, articular cartilage and soft tissue healing to allow return to work may require 4–8 months. Limited activity (hand-walking or turnout) can begin after 4–6 weeks of stall rest.

Fractures of the fused first and second or fourth tarsal bone are rare. Choice of therapy (conservative or surgical) will depend on the size of the fragment, location and articular involvement. Fractures or fragments that are minimally displaced will usually heal without surgical intervention. These tarsal bones are not subjected to the compressive forces that the third and central tarsal bones experience and conservative therapy may be sufficient for adequate healing. This approach may not be suitable for performance horses because a fibrous union with articular or periarticular degenerative changes could result in residual lameness during high-speed or rigorous exercise. Larger fragments may have to be removed or secured with lag screws. If the fracture is unstable or the articulation of the bone with the splint bone, central tarsal bone or talus is compromised, then an attempt at surgical repair is justified. Approach and choice of implant is determined by the size and location of the fragment(s). Convalescence and return to work are as described before.

Rehabilitation of the soft tissues as soon as possible after surgery will restore range of motion to the joint and decrease the morbidity associated with disuse and fibrosis. This may be as important as surgical therapies in bringing these athletes back to work. Range of motion exercises

with the joint and swimming may be useful adjuncts to exercise regimens to rehabilitate periarticular soft tissues.

Prognosis Establishing a prognosis for these tarsal fractures is challenging. In order to have a realistic expectation for return to athletic performance, a thorough assessment of the ligamentous, synovial cavity, articular and bony involvement is important. Horses with extensive damage to the CoL, SDF, fibrous joint capsule or articular cartilage have a very guarded prognosis for athletic use, even if a surgical procedure successfully removed fragmentation, secured loose fractures or resolved sepsis. Horses with fragmentation of the dorsodistal or very plantar aspect of the trochlear ridges, fractures of the lateral malleolus, slab fractures of the central or third tarsal bone and stress fractures of the talus will have a good prognosis for return to function with proper therapy.[81,84] Standardbred race horses with slab fractures of the third tarsal bone treated surgically or conservatively appear to have a good prognosis for return to racing.[81,88] Thoroughbred race horses or other racing breeds may not fare as well with central tarsal bone fractures treated conservatively.[88] In other retrospective studies, the outcome of conservative treatment of central or third tarsal bone fractures in race horses has been unfavorable.[80,87] Horses with more complex injuries (transverse calcaneal or complete talus fractures) have a poor prospect for returning to high-level athletic activity.

Involvement of the tarsal sheath or calcaneal bursa secondary to a proliferative bony response after a fracture or osteomyelitis carries a good to guarded prognosis for athletes.[85,89] If soft tissue fibrosis restricts motion and obliterates the synovial lining of these cavities necessary to allow unrestricted movement of tendons or ligaments, the prognosis is unfavorable. If treated early and aggressively, horses with osteomyelitis of the sustentaculum tali and tarsal sheath effusion may return to athletic competition.[82,90]

Early and consistent physical therapy may improve the prognosis and shorten the convalescent period for these athletes.

Prevention

There are no definitive recommendations that can be made to prevent these tarsal injuries. Most are traumatically induced from a sudden internal or external application of force that is difficult to predict or avoid. Good horsemanship and avoiding conditions that could predispose to these injuries is adequate. Stress fractures in young race horses often result from accumulated stresses (loads) and non-adaptive bone modeling or remodeling in response to strenuous exercise. Varying exercise regimens by reducing distance work in favor of speed work may decrease the accumulation of microtrauma that can cause these injuries.

Etiology and pathophysiology

The etiology of these injuries is accumulated microtrauma (stress fractures in race horses) or single event application of external (kick or collision) or internal (fall or slip) torque sufficient to disrupt the osseous and soft tissue structures.

Thoroughbred or other performance horses that have a wedge-shaped conformation of the craniolateral aspect of the third tarsal bone may be predisposed to sustaining a slab fracture of this bone during high-speed training or racing,[95] by presumably concentrating compressive forces along the trough in the wedge.

These injuries will adversely affect performance by disrupting the function of the tarsus during joint movement and weight bearing, and by causing marked discomfort. Residual articular cartilage erosions in weight-bearing areas, instability, tarsal sheath adhesions, calcaneal bursa fibrosis or osteoarthritis that persists or develops after therapy will adversely affect athletic performance due to pain and loss of motion.

Epidemiology

These injuries can affect any breed, age or use of horse. It appears that stress fractures of the talus, slab fractures of the central or third tarsal bones and lateral malleolar fractures are more common in young Thoroughbreds and Standardbreds in training or racing.

Osteoarthritis or inflammation of the intertarsal, tarsometatarsal and talocalcaneal joints

- The tarsometatarsal and distal intertarsal joints of a wide range of equine athletes are commonly affected by osteoarthritis.
- Horses involved in activities that increase stress on the tarsus are predisposed to osteoarthritis of the small joints.
- Disciplines commonly affected include three-day event horses, jumpers, Standardbred race horses, barrel racers, reining and dressage horses.
- The clinical presentation and therapeutic approach are variable and will largely depend on the age, use and severity of the condition.
- Talocalcaneal osteoarthritis is rare, traumatically induced and usually ends the career.

Recognition

History and presenting complaint Osteoarthritis of the tarsus can affect athletes at a young age (in training) or at later stages of their athletic careers. They will present with a rear limb(s) lameness of variable severity and duration that may improve with rest, only to recrudesce when placed back in work. Affected athletes can sometimes warm out of the lameness after a short period of work or will get worse when they are forced to work vigorously with their rear limbs while in a collected posture (dressage or approaches to obstacles for jumping). This disease is often insidious in onset and some chronically affected horses will refuse to perform certain movements under tack and may even object vigorously by tail

swishing, bucking, refusals at jumps and an unwillingness to take or stay in a particular leg lead.

Horses with talocalcaneal degenerative joint disease will commonly have a history of trauma preceding the lameness.

Physical examination There is usually no external soft tissue swelling or effusion evident on the rear limb(s) and affected horses may have straight-legged (post-legged) or a tarsal valgus or varus (cow or sickled hocks) conformation. The medial aspect of the intertarsal and tarsometatarsal joints may appear thickened or have a boxed appearance in some horses.

The severity of the presenting lameness will vary dramatically but generally these athletes have decreased hock flexion (reduced arc during the swing phase), a shortened stance phase (weight bearing) and a shortened gluteal rise on the affected side. The lameness can be variable but sometimes imperceptibly exacerbated by flexion of the upper limb (hock flexion) or inward pressure on the second metacarpal bone (15–30 seconds) followed by trotting (Churchill test). When ridden in a collected fashion, the lameness will often become more apparent than when being trotted in hand or lunged.

Special examination Perineural analgesia of the tibial and peroneal nerve or intra-articular anesthesia of the tarsocrural, tarsometatarsal or intertarsal joint(s) will usually improve the lameness and reduce the response to upper limb flexion. Intra-articular anesthesia of the intertarsal and tarsometatarsal joint is not always specific for that compartment. The middle and bottom joints communicate in approximately 26–35% of horses and anesthetic can also diffuse into the tarsal sheath or proximal intertarsal or tarsocrural joint after injection into the tarsometatarsal joint space.[59–61] The plantar extension of the synovial sac of the tarsometatarsal joint may cover the origin of the suspensory ligament so that substances injected into this joint can affect this structure by diffusion also.[60] Care must be taken when evaluating the horse in a straight line in hand after perineural or intra-articular analgesia. If the lameness was worse when lunged or ridden in a collected fashion, then the evaluation after the blocks should be performed during lunging or riding.

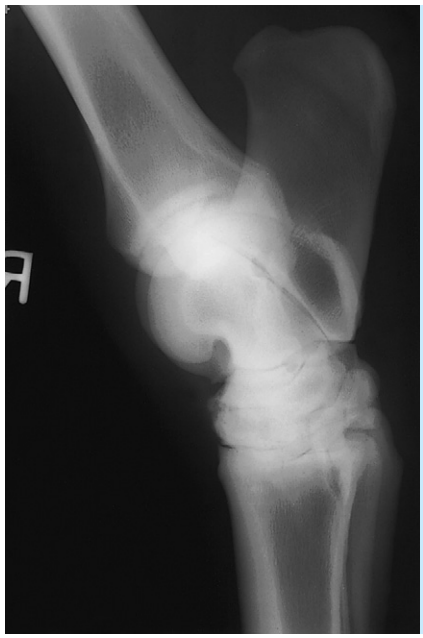
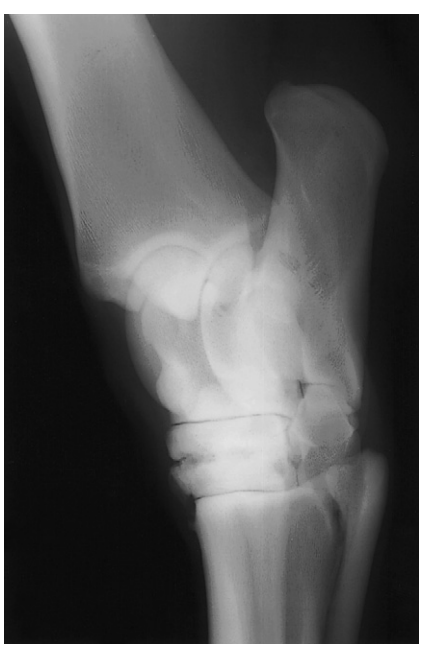
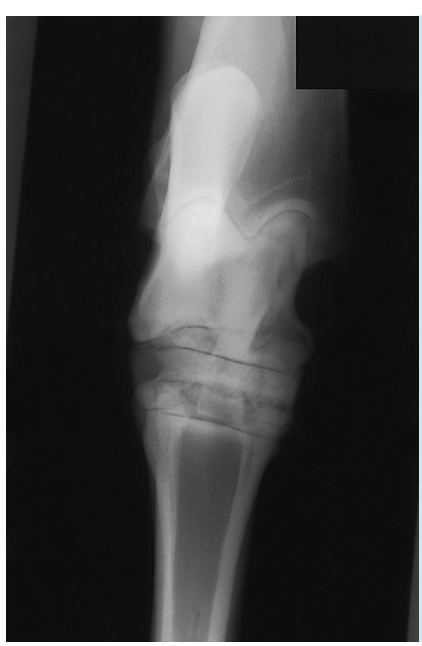


Fig. 19.39 Periarticular osteophytes in a horse with osteoarthritis of the intertarsal joint.

Standard radiographic views of the tarsus in horses affected with osteoarthritis of the small tarsal joints will demonstrate some degree of joint space collapse, periarticular osteophyte production (Fig. 19.39) or bony lysis (Figs 19.40, 19.41). The disease often begins on the dorsomedial surface of the joint(s). The radiographic changes, when present, are consistently seen on the lateromedial and dorsolateral to plantaromedial oblique projections. However, there are many young horses that participate in activities in which excessive strain is placed on the hocks that will have a



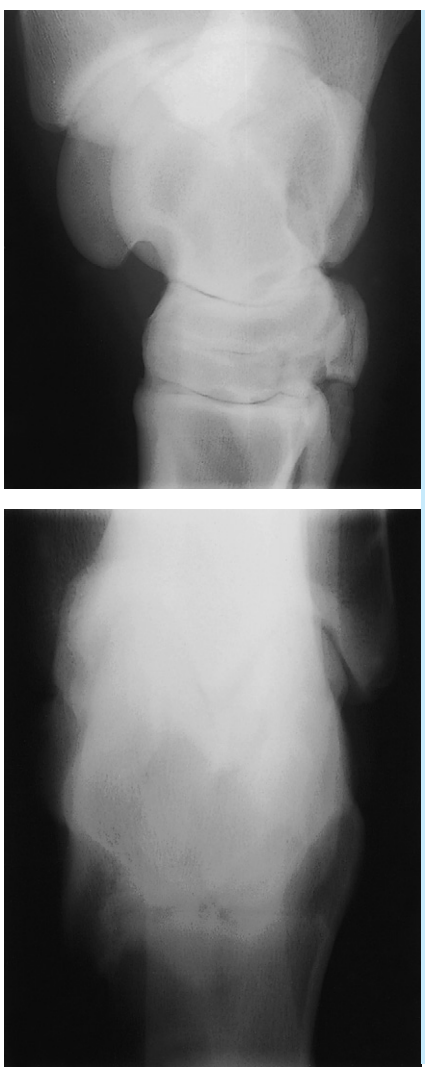


Figs 19.40, 19.41 Oblique and dorsoplantar views of the tarsus in a horse with osteoarthritis and lysis of the distal intertarsal joint.

tarsal lameness localized to one or both distal joints but have normal-appearing radiographs. This is seen frequently in Standardbred race horses and some young horses used for dressage and jumping disciplines. This is presumably because the disease is early and affecting only the articular cartilage or periarticular soft tissues which are indistinguishable radiographically. Horses in which this clinical presentation is common include Standardbred race horses, Quarter Horses participating in reining or roping and young dressage, jumping or Western pleasure athletes of any breed.

Race horses and other athletes that participate in jumping disciplines with inflammation of the small tarsal joints that do not have evidence of osteoarthritis radiographically will often have increased uptake of the isotope in one or both affected tarsi when nuclear scintigraphy is performed.[96,97] Any horse with involvement of the intertarsal or tarsometatarsal joint(s) with normal-appearing radiographs would likely benefit from this diagnostic tool.

Horses with degenerative joint disease of the talocalcaneal joint will have radiographic evidence of bony lysis and sclerosis at the normally smooth contour of the articulation between the talus and calcaneus (Figs 19.42, 19.43).



Figs 19.42, 19.43 Oblique and skyline radiographs of the tarsus in a horse with osteoarthritis of the talocalcaneal joint.

Diagnostic confirmation Horses with proximal suspensory ligament disease may appear clinically similar to horses with tarsal disease, have a positive response to upper limb flexion and may also respond favorably to anesthesia of the tarsometatarsal joint.[60] Care must be taken when interpreting the response to this block and during the clinical assessment because these horses are often unilaterally involved whereas distal tarsal joint involvement is usually bilateral. Careful palpation and ultrasonographic and/or radiographic or scintigraphic examination of the attachment of the proximal suspensory ligament will reveal an area of ligament disruption, cortical bone discontinuity or radioisotope uptake typical of this condition.

The radiographic appearance and clinical examination are usually diagnostic. Horses with radiographically normal tarsi should be evaluated with scintigraphy. There will usually be a diffuse pattern of radioisotope uptake in the tarsometatarsal and/or intertarsal joints.

Treatment and prognosis

Therapeutic aims The aim of therapy is to reduce intra-articular inflammation and the discomfort associated with motion and compression of these joints. Reducing or eliminating articular pain should permit adequate joint movement and loading and this should provide joint flexion and propulsion. The therapeutic aims are either medical or surgical. Medical therapy is directed at minimizing inflammation and includes intra-articular or systemically administered anti-inflammatory medications. Surgical therapy is aimed at creating a stable arthrodesis of the affected joint to eliminate movement and provide for pain-free ambulation. The choice of therapy is determined by the use, age and extent of articular involvement in the individual patient and owner expectations.

Therapy Medical therapy for horses with osteoarthritis of the tarsus includes intra-articular or parenterally administered drugs. Parenteral NSAIDs (phenylbutazone) to reduce inflammation and pain are commonly used for managing this disease. The dosage (2.2–4.4 mg/kg, daily) is often tailored to the individual horse depending on the severity of the disease and the patient's training or competitive schedule. A tapering 2–3 week dosing schedule is often used in an attempt to reduce the discomfort and inflammation while the work schedule is maintained at a reduced level until the horse can sustain an adequate work schedule while being comfortable. Regulatory bodies governing competitive sport often restrict the use of NSAIDs or any other medication, either banning their use completely or allowing them only under very strict guidelines.

Intra-articular corticosteroids (methylprednisolone, betamethasone, triamcinolone) or chondroprotective agents (hyaluronic acid) alone or in combination can be used successfully to reduce inflammation and the catabolic effects of the inflammatory cascade on articular cartilage. This will often permit the patient to return successfully to athletic activity for a variable period of time. These joints should be injected aseptically and the horses are routinely rested for 3–7 days after the injection to allow any soft tissue damage from the arthro-

centesis or hemorrhage to subside. The duration of relief can vary from days or weeks to months. It appears that horses with advanced osteoarthritis and marked radiographic degenerative changes may not respond as favorably or for as long as less severely affected horses. In addition, horses that have had repeated intra-articular injections at decreasing intervals with a marginal response will often not have a favorable or prolonged response to this form of therapy.

The decision to use this form of therapy will depend on clinical impression, radiographic findings, success of previous therapies, duration of the condition and use of the horse. It is probably more suitable for a horse with mild to moderate disease (clinically and/or radiographically) that has been infrequently treated by this route. Horses with severe disease, in heavy work and that have not responded favorably (improved lameness or prolonged response) to previous intra-articular injections are less likely to have a favorable long-term outcome with this therapy.

The tarsometatarsal or distal intertarsal joints are the most frequently treated. The degenerative joint disease of the tarsometatarsal joint may contribute to tarsal lameness more often and more severely than the other small tarsal joints. Other joint involvement should be determined by intra-articular anesthesia and radiographic evaluation. If both distal joints are involved, they should be treated separately since communication between joints does not exceed 38% of joints.[59–61] Numerous techniques have been described for injection of these joints and the reader is referred to these descriptions for specific details.[65]

This form of therapy will allow the horse to remain athletically active while the lameness is managed. This is particularly important in young athletes or horses competing in seasonal events where more invasive approaches would limit their use during this time. The goal is to limit joint inflammation. Repeated use of intra-articular corticosteroids will enhance catabolism of the articular cartilage, promoting the degenerative changes. This may explain why many horses that have been treated repeatedly become refractory and develop more advanced forms of the disease with time and use. It is very unlikely that joint collapse and organized arthrodesis will result from this approach and most horses will have persistent joint spaces in spite of numerous intra-articular injections over a prolonged period of time.

Systemic administration of chondroprotective agents such as hyaluronic acid and polysulfated glycosaminoglycans is frequently used alone or in combination with intra-articular medication. Regimens vary using intramuscular (polysulfated glycosaminoglycans) or intravenous (hyaluronic acid) injections at intervals ranging from every week to once a month. Oral administration of chondroitin sulfate or glucosamines is also widely used. The extent of oral absorption of these products may be unpredictable depending on individual patient differences and quality of the preparation. The effectiveness of these forms of therapy is less predictable but there appear to be cases in which they were clinically effective in providing relief for tarsal lameness for a protracted period of time. Removal of the medications or supplements resulted in recrudescence of the lameness.

Adequate heel support to maintain a straight pastern axis and a rolled or squared toe allows easier breakover of the foot, reducing the arc of flight and subsequent concussion of the joint surfaces during high-speed or collected work. The use of heel caulks or trailers may increase the rotational forces placed across the joint surfaces in horses during high-speed exercise, especially in Standardbreds. Avoiding their use may limit development and/or expression of the condition. In horses with sickle or cow hocks, attempts to induce breakover of the medial toe may be of benefit in limiting uneven loading of the joint surfaces.

Acupuncture has been used for many musculoskeletal disorders in horses and may have a therapeutic role in the treatment of tarsal disease in equine athletes. Lack of an appropriate duration or extent of response is an important determinant for continuation of this form of therapy alone or whether an alternative therapeutic regimen is indicated.

Surgical therapy for this disease is aimed at achieving arthrodesis of these joints by various means. Use of stainless steel cylinders to secure a cancellous bone graft in the spaces between joints in an effort to promote an arthrodesis has been successfully described but not widely accepted for clinical use.[98] A diode laser has been used effectively to remove the articular cartilage to arthrodese the distal tarsal joints in equine athletes.[99] The procedure is performed with the horse anesthetized. The joint spaces are localized with needles using radiographic or fluoroscopic guidance. Once the needles are positioned in the desired joint, they are used as cannulas to introduce the laser fiberoptic cable into the joint. Laser energy is used to remove the articular cartilage from the majority of the joint surface.[99] Exposing subchondral bone surfaces in apposition will promote the formation of an arthrodesis and joint stability. These horses are hand-walked for 4–6 weeks after laser treatment. Light flat work is then begun with a gradually incrementing exercise regimen begun after a couple of weeks. Laser arthrodesis may reduce the perioperative morbidity associated with other surgical techniques (drilling) or chemical fusion.[99]

Drilling the joint surfaces in an effort to remove the articular cartilage has also been described as a method to promote arthrodesis.[100] With this technique the tarsometatarsal and distal intertarsal joints are identified with radiographic guidance from the medial aspect of the tarsus. Using three separate 3.5 mm drill passes from an incision on the medial aspect of the joint, the individual joint(s) are then drilled in a fan-shaped manner towards the opposite side (lateral) of the joint. The joints are bandaged and the horse kept in a stall for 7–14 days at which time hand-walking is begun if the patient can tolerate it. Some patients may become very painful after surgery and remain recumbent. Discomfort should be controlled using NSAIDs or epidurally administered analgesics such as morphine or xylazine. Arthrodesis of these joints may take 6–9 months to complete and it is not uncommon for these horses to be out of work for up to 12 months and have a poorly cosmetic bony thickening of the medial aspect of the tarsus.[100] They may have a residual lameness present in spite of the fact that the joint(s) appear to be radiographically

fused. All other causes of lameness must be ruled out before contemplating this surgical procedure in any horse. In addition, it would be best suited for horses in which other forms of medical or surgical therapy have failed and that have radiographic evidence of severe osteoarthritis.

Arthrodesis using internal fixation has been described using a single 4.5 mm cortical lag screw placed from distal to proximal through the third metacarpal bone into the third and central tarsal bone to compress the joints.[100] Application of a fingerplate or a T-plate on the medial aspect of the tarsus with 3.5 or 4.5 mm cortical screws placed into the central and third tarsal and third metatarsal bones to bridge the joints and compress them has also been reported as a suitable alternative to drilling the joint surfaces.[100] It appears that use of a stabilizing implant on the medial aspect of the joint may reduce the number of horses in which failure of arthrodesis occurs when compared to drilling alone but it does not appear to reduce the convalescent period, which may be 6–12 months irrespective of procedure used.[100]

Chemical fusion with sodium monoiodoacetate has been advocated as a therapeutic option for horses with osteoarthritis of these joints.[101,102] This chemical is caustic and extremely chondrotoxic. It will induce arthrodesis by irreversibly damaging the articular cartilage, exposing subchondral bone surfaces. Either single[102] or three injections of 150 mg of filtered chemical administered at 3-week intervals[101] have been used to achieve chemical arthrodesis of the tarsal joints. The joint space must be localized with radiographic guidance prior to injecting this substance into the joint. Contrast arthrography is warranted to make sure there is no communication of these joints with the proximal intertarsal, tarsocrural or tarsal sheath synovial spaces. Movement of the chemical into any of these cavities could be disastrous and prematurely terminate an athletic career. Extra-articular placement of the chemical will cause cellulitis and may lead to tissue necrosis with loss of some soft tissue coverage requiring prolonged wound therapy. Similar to the drilling surgical arthrodesis, these horses may be very uncomfortable for 12–36 hours after the procedure, requiring appropriate analgesia. Hand-walking or light riding can be initiated in 7–10 days after the first injection.[101,102] There will be a radiographically evident collapse of the joint space(s), but there is usually incomplete radiographic evidence of arthrodesis in clinical cases.[102] In normal horses, the radiographically evident arthrodesis approaches 89%.[101] Prolonged swelling, chronic pain and lameness have been reported after its use.[102] Chemical arthrodesis may not be a suitable first choice of therapy for most affected horses.[102]

Few therapeutic choices would be expected to provide relief of lameness in athletes with talocalcaneal degenerative joint disease. Theoretically, arthrodesis of the joint could be attempted but there are no reports of this procedure or long-term follow-up of its use in athletes.

Prognosis The prognosis for athletic performance is good for most horses. Those horses affected with severe degeneration and arthritis of the intertarsal or tarsometatarsal tarsal joints at an early age have a guarded prognosis for maintenance of soundness with medical therapy and surgical options may offer an improvement but for some high-level athletes, the degree of improvement may not be enough to permit a successful athletic career in the more demanding disciplines.

Horses with talocalcaneal degenerative joint disease have a guarded prognosis for use in athletic endeavors.

Prevention

Prevention of this disease in horses is difficult. Delaying heavy work in young athletes may reduce articular damage in those predisposed to the disease. Proper shoeing to provide breakover of the center or medial aspect of the foot may be of benefit. Horses with straight-legged, sickle or cow-hocked conformation are predisposed and selecting away from this type of conformation may be sensible. Indiscriminate use of intra-articular corticosteroids in performance horses that present with rear limb lameness is probably detrimental to the long-term health of these joints and may predispose many athletes to premature development of osteoarthritis of these joints. Adequate localization of the lameness to these joints through diagnostic blocks and radiographic evaluation may limit the number of horses that are treated unnecessarily.

Etiology and pathophysiology

This disease is caused by multiple factors, among them conformation (sickle and cow-hocked and straight-legged), athletic use (dressage, jumping, reining horses, Standardbred race horses), angular limb deformities (valgus or varus) centered on the tarsus,[103] osteochondrosis or juvenile spavin[70] and incomplete ossification of the tarsal bone leading to tarsal bone collapse in foals.[104] These conformational faults or eccentric joint loading due to type of work being performed may contribute to the development of tarsal inflammation and osteoarthritis due to axial loading of the joints and/or shear stresses placed on the distal rows of tarsal bones during competition.

Trauma appears to be the inciting cause of most cases of talocalcaneal degenerative joint disease.

Epidemiology

Degenerative joint disease of the intertarsal or tarsometatarsal joints can affect nearly any breed of horse involved in any athletic endeavor. It is common in horses participating in dressage, jumping, gaited and Western performance disciplines, pacers and trotters.

Gastrocnemius tendon (GT), plantar ligament and superficial digital flexor (SDF) tendon injuries of the tarsus

- Most distal GT injuries present as a tendinitis rather than avulsion fractures or complete disruption.
- The SDF can luxate medially or laterally after disruption of the facial attachments to the calcaneus.
- Desmitis of the plantar ligament is caused by excessive tension on the plantar surface of the tarsus (sprain).
- Moderate or severe GT or SDF injuries carry a poor prognosis for athletic soundness.

Recognition

History and presenting complaint These horses can present with an acute onset of moderate to severe swelling of the caudal aspect of the tarsus or around the calcaneus. Horses with disruption of the caudal portion of the reciprocal apparatus (SDF and gastrocnemius) of the hindlimb will present with an acute onset of severe lameness.[105,106] However, GT or SDF tendinitis or plantar ligament desmitis will more often present with a chronic lameness of variable severity and less obvious swelling on the proximoplantar or plantar aspect of the hock.[107] These injuries can occur after high-speed exercise or after a fall or traumatic episode (collision or impact) during a competition. Tendinitis or dislocation of the SDF, tendinitis of the GT or plantar ligament desmitis can be observed in horses competing in high-speed events or jumping disciplines.[9]

Physical examination Horses with tendinitis or dislocation of the SDF, tendinitis of the GT or plantar ligament desmitis will present with a mild to moderate lameness depending on the severity of the injury and duration of the condition. There may be diffuse swelling over the point of the hock or more discrete thickening of the SDF or GT at the site of injury. The lameness evident at presentation is usually exacerbated by flexion of the upper limb. When luxated, the SDF can be manually luxated and reduced onto the calcaneus but will not stay in its normal anatomic position during ambulation.[93,94] The tendon will luxate to the side opposite to where the retinaculum and ligamentous attachments to the tarsus (calcaneus and talus) are located (if the lateral attachments are torn, the tendon will luxate medially).[93]

Horses with disruption of any part of the caudal portion of the reciprocal apparatus (SDF and gastrocnemius) of the hindlimb will present with an acute onset of severe lameness. In cases with disruption of the stay apparatus, an inability to completely fix the hock in extension during attempts at weight bearing is often present.[105,106] The disruptions in the stay apparatus are usually proximal (distal femur) and there is no swelling or pain around the tarsus. Although the disease appears to involve the hock due to its dropped appearance, there is no disruption of the tarsal structures. Distal GT disruptions, avulsion or transverse fractures of the calcaneus appear similar clinically (dropped hock), but there is obvious swelling of the calcaneus and/or GT.

Special examination Perineural analgesia of the peroneal and tibial nerves above the tarsus will usually improve the degree of lameness in horses with desmitis of the plantar ligament or tendinitis of the SDF or GT proximal to the tarsus.[107] It will usually also eliminate or reduce the positive response to the upper limb flexion. Horses with plantar ligament desmitis may improve after intrasynovial anesthesia of the tarsometatarsal joint space if any of the anesthetic diffuses from the joint to the surrounding ligament. Care must be taken to assess the area on the plantar surface of the tarsus for any swelling or thickening that may be indicative of plantar ligament desmitis before anesthetizing the joint.

Ultrasonographic evaluation of the tendons (SDF or GT) or plantar ligament can be performed standing using a 7.5 MHz probe.[107] Ultrasonographic images will usually reveal variably sized areas of tendon or ligament hypoechogenicity associated with fiber disruption and fluid accumulation (edema and/or hemorrhage).[107] The size of the lesions should be measured sagittally and transversely and as a percentage of the area of the structure and the images recorded. This will serve as a baseline quantification of the original injury for prognostic purposes and allow for comparisons during healing. With chronic desmitis or tendinitis, the ultrasonographic pattern will reveal thickening of the involved structure and a variable amount of hyperechoic tissue characterized by fiber pattern disorganization that is consistent with fibrosis. Ultrasonography of horses with a complete tear of the GT will reveal a total disruption of the GT in a transverse plane and in those with a transverse fracture of the calcaneus, cortical disruption of the calcaneus is also readily apparent.

Ultrasonographic examination of the SDF is not necessary to diagnose luxation of the SDF, but it should be performed to make sure that there are no concurrent extensive tendon defects that may worsen the prognosis.

Routine radiographs of the tarsus (all standard views and a skyline) should be obtained to identify avulsions or fractures of the calcaneus or enthesiophytes at the insertions of these soft tissue structures. Nuclear scintigraphy may be useful in subtle cases with a more chronic duration.

Laboratory examination There are no specific laboratory examinations indicated for these conditions.

Necropsy examination At necropsy, acutely affected horses will have soft tissue swelling with hemorrhage and/or edema. The involved structure (SDF, GT or plantar ligament) will be variably enlarged or disrupted and the defect(s) filled with fresh hemorrhage, clotted blood or granulation tissue. In more chronic cases there will be less peritendinous soft tissue swelling and the affected structure will be thickened by the presence of mature fibrous tissue. The histological appearance of the tissues would be similar in that more acute lesions would be characterized by blood elements and granulation tissue and chronic cases by fibrosis.

Diagnostic confirmation Disruption of the distal portion of the reciprocal apparatus is diagnosed by the clinical appearance and the ultrasonographic and radiographic findings.[105,106] Disruptions of the plantar portion (SDF) of the reciprocal apparatus are usually proximal and do not directly involve the hock. Disruptions of the distal portion of the dorsal part of the reciprocal apparatus (GT) are rare and usually involve the calcaneus but can occur anywhere along the structure.[106] Radiography and/or ultrasonography will identify the affected structure. Luxation of the SDF is diagnosed by the clinical appearance and history.[93]

Tendinitis (SDF or GT) or desmitis (plantar) is diagnosed by clinical appearance, lameness examination, ultrasonography and radiography.[107] These injuries must be differentiated from other causes of tarsal lameness. Horses with plantar ligament desmitis may improve after anesthesia of the tarsometatarsal joint (see previous section). Perineural analgesia (tibial and peroneal) will improve the lameness in cases of tendinitis, but intrasynovial anesthesia will not. This serves to differentiate tarsal conditions from those proximal to the tarsus.

Treatment and prognosis

Therapeutic aims The aim of therapy is to surgically stabilize or repair the affected tissue in cases of SDF luxation or bony calcaneal injuries (see fracture section). In cases with desmitis or tendinitis, the aim is to rest and rehabilitate the patient to allow deposition of collagen in an organized and functional pattern that will allow the affected structure to regain its previous biomechanical function and tissue strength necessary for athletic performance.

Therapy In cases with complete disruption of the dorsal or both portions of the reciprocal apparatus, therapy consists of full-limb coaptation to permit fibrosis of the structure.[105,106] Cases with complete disruption of the reciprocal apparatus will rarely respond to coaptation as the cast will not immobilize the limb completely, leading to cast disease and contralateral limb laminitis before useful fibrosis of the reciprocal apparatus occurs. Partial disruptions may respond better to this form of therapy, as there is still one intact part of the system (SDF or GT) left. Disruptions of the reciprocal apparatus that involve all or part of the calcaneus have been discussed in the previous section.

Cases of desmitis (GT) or tendinitis (SDF) should be rested until healing is complete when evaluated ultrasonographically. This may require up to 6–12 months, since many of these injuries are either quite large or very chronic with significant fibrosis and a poor blood supply. Inadequate or incomplete healing is not uncommon.[107] There are no described surgical procedures available to augment healing and most surgical interventions would probably increase the amount of tissue damage. Medical therapy during the acute stages consists of NSAID administration and regional cold therapy to reduce inflammation. Therapeutic heat, shock waves or ultrasound application (extracorporeal shock wave therapy or therapeutic ultrasound) during the convalescent period may help increase circulation and promote healing. Intralesional administration of medications has not met with universal acceptance due to the unpredictable clinical and histological results when used for tendon or ligament defects. Rehabilitation of the soft tissues should be initiated as soon as there is enough healing to support a controlled increase in activity without disrupting the repair tissue. This early mobilization will improve the reorganization of the tissue and restore soft tissue elasticity. This is particularly important when SDF or GT injuries are located within the calcaneal bursa(s), where deposition of scar tissue and adhesions will adversely affect tarsal function irrespective of the strength or completeness of the repair. Adhesions or diseased tissues within the calcaneal bursa can be debrided and lavaged via an endoscopic approach to minimize further soft tissue trauma.[91] The approach consists of a distal scope (or instrument) portal and a proximal instrument (or scope) portal at the limits of the bursa to converge on the affected area.[91]

Luxation of the SDF is usually treated surgically to reposition the tendon and repair the retinaculum and attachment to the talus/calcaneus.[93,94] The repair is performed in lateral recumbency with a direct incision over the affected side. The tendon is repositioned and the disrupted edges of the retinaculum are sutured with a pre-placed interrupted mattress pattern of one or two absorbable (polidioxanone) or non-absorbable (nylon) monofilament suture. A synthetic mesh (Marlex) has been successfully used to repair a medial SDF luxation in an adult horse that eventually returned to work.[93] These horses should be assisted to stand after surgery. Using some form of external coaptation (cast, Robert-Jones bandage, splints) to prevent hock flexion during the first 4–6 weeks after surgery is important to avoid disruption of the repair and reluxation of the tendon. Once the repair tissue is strong enough to permit removal of the coaptation, hand-walking is initiated to strengthen the repair tissues. Swimming or range of motion exercises will minimize the restrictive effects of the scar tissue and adhesions.

Prognosis Horses with partial or complete disruption of the reciprocal apparatus have a poor prognosis for future athletic performance.[105,106] Even with adequate fibrosis and healing, there will be some residual excessive tarsal flexion remaining that will make athletic competition unlikely.

Tendinitis of the GT carries a guarded prognosis for future athletic performance. These injuries are often chronic when diagnosed and they can affect a significant portion of the tendon.[107] The chronicity, extent and restriction of motion by the scar tissue will all combine to decrease the prognosis for athletic use.[107]

Luxations of the SDF with or without accompanying tendinitis have a guarded prognosis for return to athletic performance, especially those athletes competing in higher level athletic disciplines. Early recognition, surgical repair, limited soft tissue damage and aggressive rehabilitation may all help improve the prognosis in horses with these injuries.

Prevention

There are few specific recommendations that can be made to prevent these injuries. Adequate footing during competition, good horsemanship skills and attention to husbandry may help reduce their occurrence. Early recognition of athletes with GT tendinitis may improve the prognosis by allowing adequate therapy (rest, rehabilitation, extracorporeal shock wave) to be instituted prior to the development of debilitating scar tissue, large defects and adhesions.

Etiology and pathophysiology

These soft tissue injuries of the hock are traumatic in nature and can occur from impact trauma or a fall/slip during athletic competition. The injury results from either externally or internally applied forces (sprain) that exceed the biomechanical load limits of the affected structure.

Epidemiology

These injuries are more likely to occur in athletes participating in strenuous disciplines such as, but not limited to, flat racing, jumping and three-day eventing.

References

1. Harrison L, Edwards G. Radiographic investigation of the equine stifle. Equine Vet Educ 1995; 7(3):16–68.
2. Dik K. Ultrasonography of the stifle. Equine Vet Educ 1995; 7(3):154–160.
3. Cauvin E, Munroe G, Boyd J, et al. Ultrasonographic examination of the femorotibial articulation in horses: imaging of the cranial and caudal aspects. Equine Vet J 1996; 28(4):285–296.
4. Walmsley J. Vertical tears of the cranial horn of the meniscus and its cranial ligament in the equine femorotibial joint: 7 cases and their treatment by arthroscopic surgery. Equine Vet J 1995; 27(1):20–25.
5. McIlwrath C. Diagnostic and surgical arthroscopy of the femoropatellar and femorotibial joint. In: McIlwrath C, ed. Diagnostic and surgical arthroscopy in the horse, 2nd edn. Philadelphia, PA: Lea and Febiger; 1990; 113–153.
6. Peroni J, Stick JA. Evaluation of a cranial arthroscopic approach to the stifle joint for the treatment of femorotibial joint disease in horses: 23 cases (1998–1999). J Am Vet Med Assoc 2002; 220(7):1046–1052.
7. Sanders-Shamis M, Bukowiecki C, Biller D. Cruciate and collateral ligament failure in the equine stifle: seven cases (1975–1985). J Am Vet Med Assoc 1988; 193(5):573–576.
8. Walmsley J. Cruciate, meniscal and meniscal ligament injuries. In: Robinson N, ed. Current therapy in equine medicine, 4th edn. Philadelphia, PA: Saunders; 1997; 84–88.
9. Dyson S. Stifle trauma in the event horse. Equine Vet Educ 1994; 6(5):234–240.
10. Anderson R, Woo S, Kwan M, et al. Viscoelastic shear properties of the equine medial meniscus. J Orthopedic Res 1991; 9(4):550–558.
11. Rich R, Glisson R. In vitro properties and failure mode of the equine (pony) cranial cruciate ligament. Vet Surg 1994; 23(6):257–265.
12. Prades M, Grant B, Turner T, et al. Injuries to the cranial cruciate ligament and associated structures: summary of clinical, radiographic, arthroscopic and pathological findings from 10 horses. Equine Vet J 1989; 21(5):354–357.
13. Baker G, Moustafa M, Boero M, et al. Caudal cruciate ligament function and injury in the horse. Vet Rec 1987; 121:319–321.
14. Edwards R, Nixon A. Avulsion of the cranial cruciate ligament insertion in a horse. Equine Vet J 1996; 28(4): 334–336.
15. Mueller P, Allen D, Watson E, et al. Arthroscopic removal of a fragment from an intercondylar eminence fracture of the tibia in a two-year-old horse. J Am Vet Med Assoc 1994; 204(11):1793–1795.
16. Walmsley J. Fracture of the intercondylar eminence of the tibia treated by arthroscopic internal fixation. Equine Vet J 1997; 29(2):148–150.
17. Folan J, McIlwrath C, Trotter G. Osteochondritis dessicans of the femoropatellar joint: results of treatment with arthroscopic surgery. Equine Vet J 1992; 24(6):419–423.
18. McIlwrath C, Martin G. Arthroscopic surgery for the treatment of osteochondritis dessicans in the equine femoropatellar joint. Vet Surg 1985; 14(2):105–116.
19. Pascoe J, Pool R, Wheat J, et al. Osteochondral defects of the lateral trochlear ridge of the distal femur of the horse: clinical, radiographic and pathological examination and results of surgical treatment. Vet Surg 1984; 13(2):99–110.
20. Dabareiner R, Sullins K, White N. Progression of femoropatellar osteochondrosis in nine young horses: clinical, radiographic and arthroscopic findings. Vet Surg 1993; 22(6):515–523.
21. Baxter G. Subchondral cystic lesions in horses. In: McIlwrath C, Trotter G, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 384–397.
22. Howard R, McIlwrath C, Trotter G. Arthroscopic surgery for subchondral cystic lesions of the medial femoral condyle in horses: 41 cases (1988–1991). J Am Vet Med Assoc 1995; 206(6):842–850.
23. Jackson W, Stick J, Arnoczky S, et al. The effect of compacted cancellous bone grafting on the healing of subchondral bone defects of the medial femoral condyle in horses. Vet Surg 2000; 29(1):8–16.
24. Sullins K. Osteochondral grafts to fill large articular defects in horses. Vet Surg 1989; 18(1):77–80.
25. Kold S, Hickman J. Results of treatment of subchondral bone cysts in the medial condyle of the equine femur with an autogenous cancellous bone graft. Equine Vet J 1984; 16(4):414–418.
26. Vachon A, McIlwrath C, Powers B. Morphologic and biochemical study of sternal cartilage autografts for resurfacing induced osteochondral defects in horses. Am J Vet Res 1992; 53(6):1038–1047.
27. Howard R, McIlwrath C, Trotter G. Long-term fate and effects of exercise on sternal cartilage autografts used for repair of large osteochondral defects in horses. Am J Vet Res 1994; 55(8):1158–1167.
28. van Weeren P, Oldruitenborgh-Oeste S, Barneveld A. The influence of birth weight, rate of gain and final achieved height and sex on the development of osteochondritic lesions in a population of genetically predisposed Warmblood foals. Equine Vet J 1999; 31(1):26–30.
29. van Weeren P, Barneveld A. The effect of exercise on the distribution and manifestation of osteochondritic lesions in the Warmblood foal. Equine Vet J 1999; 31(1):16–25.
30. Dik K, Enzerink E, van Weeren P. Radiographic development of osteochondral abnormalities, in the hock and stifle of Dutch Warmbloods, from age 1 to 11 months. Equine Vet J 1999; 31(1):9–15.
31. Barneveld A, van Weeren P. Conclusions regarding the influence of exercise on the development of the equine musculoskeletal system with special reference to osteochondrosis. Equine Vet J 1999; 31(1):112–119.
32. McIlwrath C. Distal luxation of the patella in a horse. J Am Vet Med Assoc 1982; 19(5):67–69.
33. Dugdale D. Intermittent upward fixation of the patella and disorders of the patellar ligaments. In: Robinson N, ed. Current therapy in equine medicine, 4th edn. Philadelphia, PA: Saunders; 1997; 82–84.
34. Marble G, Sullins KE. Arthroscopic removal of patellar fragments in horses: five cases (1989–1998). J Am Vet Med Assoc 2000; 216(11):1799–1801.
35. Stashak T. Lameness. In: Stashak T, ed. Adams' lameness in horses, 4th edn. Philadelphia, PA: Lea and Febiger; 1987; 486–743.
36. Cahill J, Goulden B, Pearce H. A review and some observations on stringhalt. New Zealand Vet J 1985; 33(1):101–104.
37. Brown M. The effects of an injection of iodine counterirritant into the patellar ligaments of ponies: application to stifle lameness. J Equine Vet Sci 1983; 3:149–153.
38. van Hoogmoed LM, Agnew DW, Whitcomb MB, et al. Ultrasonographic and histologic evaluation of medial and middle patellar ligaments in exercised horses following

injection with ethanolamine oleate and 2% iodine in almond oil. Am J Vet Res 2002; 63(5):738–743.
39. Gibson K, McIlwrath CW, Parks RD, et al. Production of patellar lesions by medial patellar desmotomy in normal horses. Vet Surg 1989; 18(6):466–471.
40. Hance S, Bramlage LR. Fractures of the femur and patella. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 284–293.
41. McIlwrath C. Osteochondral fragmentation of the distal aspect of the patella in horses. Equine Vet J 1990; 22(4):157–163.
42. Dyson S, Wright I, Kold S, et al. Clinical and radiographic features, treatment and outcome in 15 horses with fracture of the medial aspect of the patella. Equine Vet J 1992; 24(4):264–268.
43. Riley C, Yovich JA. Fracture of the patella after medial patellar desmotomy in a horse. Aust Vet J 1991; 68(1):37–39.
44. Smith B, Auer JA, Watkins JP. Surgical repair of tibial tuberosity avulsion fractures in four horses. Vet Surg 1990; 19(2):117–121.
45. Wright I, Montesso F, Kidd LJ. Surgical treatment of fractures of the tibial tuberosity in 6 adult horses. Equine Vet J 1995; 27(2):96–102.
46. Pennick D, Nyland TG, O'Brien TR, et al. Ultrasonography of the equine stifle. Vet Radiol 1990; 31(6):293–298.
47. Pankowski R, White K. Fractures of the patella in horses. Compend Contin Educ Pract Vet 1985; 7(10):S566-S573.
48. Watkins J. Femoral and patellar fractures. In: White NA, Moore JN, eds. Current practice of equine surgery. Philadelphia, PA: JB Lippincott; 1996; 665–671.
49. Hunt R, Baxter GM, Zamos DT. Tension band wiring and lag screw fixation of a transverse, comminuted fracture of a patella in a horse. J Am Vet Med Assoc 1992; 200(6): 819–820.
50. DeBowes R, Grant BD, Chalman JA, et al. Fractured patella in a horse. Equine Pract 1980; 2(5):143–148.
51. Aldrete A, Meagher DM. Lag screw fixation of a patellar fracture in a horse. Vet Surg 1981; 10(2):143–148.
52. Watkins J. Fractures of the tibia. In: Nixon AJ, ed. Equine fracture repair. Philadelphia, PA: Saunders; 1996; 273–283.
53. Eliashar E, Smith RKW, Schramme MC, et al. Preoperative bending and twisting of a dynamic compression plate for the repair of tibial tuberosity fracture in the horse. Equine Vet J 2000; 32(5):447–448.
54. Hance S, Bramlage LR, Schneider RK, et al. Retrospective study of 38 cases of femur fractures in horses less than one year of age. Equine Vet J 1992; 24(5):357–363.
55. Embertson R, Bramlage LR, Gabel AA. Physeal fractures in the horse I: classification and incidence. Vet Surg 1986; 15(3):223–229.
56. Dabareiner R, Sullins KE. Fracture of the caudal medial femoral condyle in a horse. Equine Vet J 1993; 25(1):75–77.
57. Stick J, Borg LA, Nickels FA, et al. Arthroscopic removal of an osteochondral fragment from the caudal pouch of the lateral femorotibial joint in a colt. J Am Vet Med Assoc 1992; 200(11):1695–1697.
58. Updike S. Functional anatomy of the equine tarsocrural collateral ligaments. Am J Vet Res 1984; 45(5):867–874.
59. Bell B, Baker G, Foreman J, et al. In vivo investigation of communication between the distal intertarsal and tarsometatarsal joints in horses and ponies. Vet Surg 1993; 22(4):289–292.
60. Dyson S, Romero J. An investigation of injection techniques for local analgesia of the equine distal tarsus and proximal metatarsus. Equine Vet J 1993; 25(1):30–35.
61. Kraus-Hansen A, Jann H, Kerr D, Fackleman G. Arthrographic analysis of communication between the tarsometatarsal and distal intertarsal joints of the horse. Vet Surg 1992; 21(2):139–144.
62. Schougaard H, Falk Ronne J, Phillipson J. A radiographic survey of tibiotarsal osteochondrosis in a selected population of trotting horses in Denmark and its possible genetic significance. Equine Vet J 1990; 22(4):288–289.
63. McIlwrath C, Foerner J, Davis D. Osteochondrosis dissecans of the tarsocrural joint: results of treatment with arthroscopic surgery. Equine Vet J 1991; 23(3):155–162.
64. Tomlinson J, Redding W, Sage A. Ultrasonographic evaluation of tarsocrural joint cartilage in normal adult horses. Vet Radiol Ultrasound 2000; 41(5):457–460.
65. Trotter G, McIlwrath C. Clinical features and diagnosis of equine joint disease. In: McIlwrath C, Trotter G, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 120–145.
66. Beard W, Bramlage L, Schneider R, et al. Postoperative racing performance in standardbreds and thoroughbreds with osteochondrosis of the tarsocrural joint: 109 cases (1984–1990). J Am Vet Med Assoc 1994; 204(10):1655–1659.
67. Laws E, Richardson D, Ross M, et al. Racing performance of Standardbreds after conservative and surgical treatment for tarsocrural osteochondrosis. Equine Vet J 1993; 25(3):199–202.
68. McIlwrath C, Foerner J. Diagnostic and surgical arthroscopy of the tarsocrural (tibiotarsal) joint. In: McIlwrath C, ed. Diagnostic and surgical arthroscopy in the horse, 2nd edn. Philadelphia, PA: Lea and Febiger; 1990; 161–193.
69. Laverty S, Stover S, Belanger D, et al. Radiographic, high detail radiographic, microangiographic and histological findings of the distal portion of the tarsus in weanlings, young and adult horses. Equine Vet J 1991; 23(6):413–421.
70. Watrous B, Hultgren B, Wagner P. Osteochondrosis and juvenile spavin in equids. Am J Vet Res 1991; 52(4): 607–612.
71. Moll H, Slone D, Humburg J, et al. Traumatic tarsal luxation repaired without internal fixation in three horses and three ponies. J Am Vet Med Assoc 1987; 190(3):297–300.
72. Laing J, Caves S, Rawlinson R. Successful treament of a tarsocrural joint luxation in a pony. Aust Vet J 1992; 69(8):200–201.
73. Reeves M, Trotter G. Tarsocrural joint luxation in a horse. J Am Vet Med Assoc 1991; 199(8):1051–1053.
74. Dowling B, Dart A, Hodgson D. Surgical treatment of tarsometatarsal joint luxation in a miniature horse foal. Aust Vet J 2000; 78(10):683–684.
75. Dik K, Leitch M. Soft tissue injuries of the tarsus. Vet Clin North Am Equine Pract 1995; 11(2):235–247.
76. Boero M, Kneller S, Baker G, et al. Clinical, radiographic, and scintigraphic findings associated with enthesitis of the lateral collateral ligaments of the tarsocrural joint in Standardbred racehorses. Equine Vet J 1988; 6(suppl):53–59.
77. Goodrich L, Trostle S, White N. What is your diagnosis? Avulsion fracture of the calcaneus at the attachment of the long collateral ligament of the tarsus. J Am Vet Med Assoc 1997; 210(9):1277–1278.
78. Dik K. Ulrasonography of the equine tarsus. Vet Radiol Ultrasound 1993; 34(1):36–43.
79. Blaik M, Hanson R, Kincaid S, et al. Low-field magnetic resonance imaging of the equine tarsus: normal anatomy. Vet Radiol Ultrasound 2000; 41(2):131–141.

80. Tulamo R, Bramlage L, Gabel A. Fractures of the central and third tarsal bones in horses. J Am Vet Med Assoc 1983; 182(1):1234–1238.
81. Winberg F, Pettersson H. Outcome and racing performance after internal fixation of third and central tarsal bone slab fractures in horses: a review of 20 cases. Acta Vet Scand 1999; 40(2):173–180.
82. Santschi E, Adams S, Fessler J, et al. Treatment of bacterial tarsal tenosynovitis and osteitis of the sustentaculum tali of the calcaneus in five horses. Equine Vet J 1997; 29(3):244–247.
83. Dart A, Hodgson D. Surgical management of osteomyelitis of the sustentaculum tali in a horse. Aust Vet J 1996; 73(2):73–74.
84. Wright I. Fractures of the lateral malleolus of the tibia in 16 horses. Equine Vet J 1992; 24(6):424–430.
85. Dik K, Merkens H. Unilateral distension of the tarsal sheath in the horse: a report of 11 cases. Equine Vet J 1987; 19(4): 307–313.
86. Dik K, Keg P. The efficacy of contrast radiography to demonstrate 'false thoroughpins' in five horses. Equine Vet J 1990; 22(3):223–225.
87. Lindsay W, McMartin R, McClure J. Management of slab fractures of the third tarsal bone in 5 horses. Equine Vet J 1982; 14(1):55–58.
88. Murphey E, Schneider R, Adams S, et al. Long-term outcome of horses with a slab fracture of the central or third tarsal bone treated conservatively: 25 cases (1976–1993). J Am Vet Med Assoc 2000; 216(12):1949–1954.
89. Welch R, Auer J, Watkins J, et al. Surgical treatment of tarsal sheath effusion associated with an exostosis on the calcaneus of a horse. J Am Vet Med Assoc 1990; 196(12):1992–1994.
90. Hand D, Watkins J, Honnas C, et al. Osteomyelitis of the sustentaculum tali in horses: 10 cases (1992–1998). J Am Vet Med Assoc 2001; 219(3):341–345.
91. Ingle-Fehr J, Baxter G. Endoscopy of the calcaneal bursa in horses. Vet Surg 1998; 27(6):561–567.
92. Cauvin E, Tapprest J, Munroe G, et al. Endoscopic examination of the tarsal sheath of the lateral digital flexor tendon in horses. Equine Vet J 1999; 31(3):219–227.
93. Scott E. Surgical repair of a dislocated superficial digital flexor tendon and fractured fibular tarsal bone in a horse. J Am Vet Med Assoc 1983; 183(3):332–333.
94. Sullins K, Stashak T. An unusual fracture of the tibiotarsal bone in a mare. J Am Vet Med Assoc 1983; 182(12): 1395–1396.
95. Baird D, Pilsworth R. Wedge-shaped conformation of the dorsolateral aspect of the third tarsal bone in the Thoroughbred racehorse is associated with development of slab fractures in this site. Equine Vet J 2001; 33(6):617–630.
96. Ehrlich P, Seeherman H, O'Callaghan M, et al. Results of bone scintigraphy in horses used for show jumping, hunting, or eventing: 141 cases (1988–1994). J Am Vet Med Assoc 1998; 213(10):1460–1467.
97. Ehrlich P, Dohho I, O'Callaghan M. Results of bone scintigraphy in racing standardbred horses: 64 cases (1992–1994). J Am Vet Med Assoc 1999; 215(7):982–991.
98. Archer R, Schneider R, Lindsay W, et al. Arthrodesis of the equine distal tarsal joints by perforated stainless steel cylinders. Equine Vet J 1988; 6(Suppl):125–130.
99. Hague B, Guccione A. Clinical impressions of a new technique utilizing a ND:YAG laser to arthrodese the distal tarsal joints. 35th Annual Scientific Meeting of the American College of Veterinary Surgeons. Arlington, VA, 2000; 35.
100. Wyn-Jones G, May S. Surgical arthrodesis for treatment of osteoarthrosis of the proximal intertarsal, distal intertarsal and tarsometatarsal joints in 30 horses: a comparison of four different techniques. Equine Vet J 1986; 18(1):59–64.
101. Bohanon T, Schneider R, Weisbrode S. Fusion of the distal intertarsal and tarsometatarsal joints in the horse using intraarticular sodium monoiodoacetate. Equine Vet J 1991; 23(4):289–295.
102. Sammut E, Kannegieter N. Use of sodium monoiodoacetate to fuse the distal hock joints in horses. Aust Vet J 1995; 72(1):25–28.
103. Dutton D, Watkins J, Honnas C, et al. Treatment response and athletic outcome of foals with tarsal valgus deformities: 39 cases (1988–1997). J Am Vet Med Assoc 1999; 215(10): 1481–1484.
104. Dutton D, Watkins J, Walker M, et al. Incomplete ossification of the tarsal bones in foals: 22 cases (1988–1996). J Am Vet Med Assoc 1998; 213(11):1590–1594.
105. Shoemaker R, Martin G, Hillman D, et al. Disruption of the caudal component of the reciprocal apparatus in two horses. J Am Vet Med Assoc 1991; 198(1):120–122.
106. Mattoon J, Parker J, Huber M. What is your diagnosis? Avulsion of the origin of the gastrocnemius tendon in a horse. J Am Vet Med Assoc 1999; 214(6):783–784.
107. Dyson S, Kidd L. Five cases of gastrocnemius tendinitis in the horse. Equine Vet J 1992; 24(5):351–356.

CHAPTER 20

Soft tissue injuries: tendinitis and desmitis

Carol Gillis

Introduction

Thirteen percent of equine athletes sustain a soft tissue injury sufficiently severe to require a period of rest each year. Horses at greatest risk are those whose work load is increasing rapidly, for example, horses undertaking work at racing speed prior to their first race or dressage horses training to achieve the next training level.

Tendons and ligaments have a slow metabolic rate of activity and require a period of 8–14 months to return to the normal tensile strength range after damage. Confinement and rehabilitative exercise needed for optimum healing are expensive and time consuming; therefore an accurate diagnosis of all injuries currently affecting the horse is very important to allow for simultaneous treatment. Tendons and ligaments in varying locations respond to treatment and rehabilitation in a relatively similar fashion so even if one is confronted with a new or unusual injury, basic treatment principles apply. Although the published prognosis is fair or even poor for many soft tissue injuries, early diagnosis, good client compliance with repeated clinical and ultrasound examinations and a controlled exercise program tailored to the stage of healing of the injured tendon or ligament have improved the prognosis for most injuries. The prognosis for return to full athletic soundness is often good when using these principles, as long as adequate care and time are provided to allow for complete healing.

Superficial digital flexor tendinitis (bowed tendon)

Recognition

History and presenting complaint

Horses presented for superficial digital flexor (SDF) tendinitis are usually in full athletic use. Affected horses often have a workload that consists primarily of galloping and/or jumping (Fig. 20.1). Most tendon injuries are due to cumulative damage rather than a single event, the exception being a fall or a strike from another limb. Horses often develop clinically apparent pain, swelling and lameness 2–3 days following SDF injury.

Physical examination

Lameness ranges from grade 1 to 3 of 5 and is often transient or intermittent. It often resolves rapidly with the use of ice and anti-inflammatory agents. There may be pain on palpation, heat and swelling at the lesion site. These signs may not be apparent as the lameness resolves. Affected horses frequently exhibit a decrease in performance ability after the initial lameness resolves.[1,2]

Fig. 20.1
Horse competing in the stadium jumping phase of the Rolex Three-Day Event (CCI****).

Luxation of the SDF tendon from its attachment to the calcaneus often presents as an acute injury during exercise, particularly in polo ponies and eventers. An audible pop may be heard, followed by acute lameness. As luxation usually occurs laterally, the tendon can be seen coursing down the lateral aspect of the tarsus. Within a few days, massive swelling of the limb obscures anatomic details if the injury is not treated aggressively for inflammation.

Differential diagnosis for lesions in the metacarpal/metatarsal region is usually limited as the SDF tendon is readily palpated and separated from deeper structures. Carpal sheath synovitis may be associated with proximal SDF tendinitis. Digital sheath synovitis may be associated with SDF tendinitis in the fetlock region. Differential diagnosis in the pastern region includes damage to the sesamoidean ligaments or the collateral ligaments of the proximal

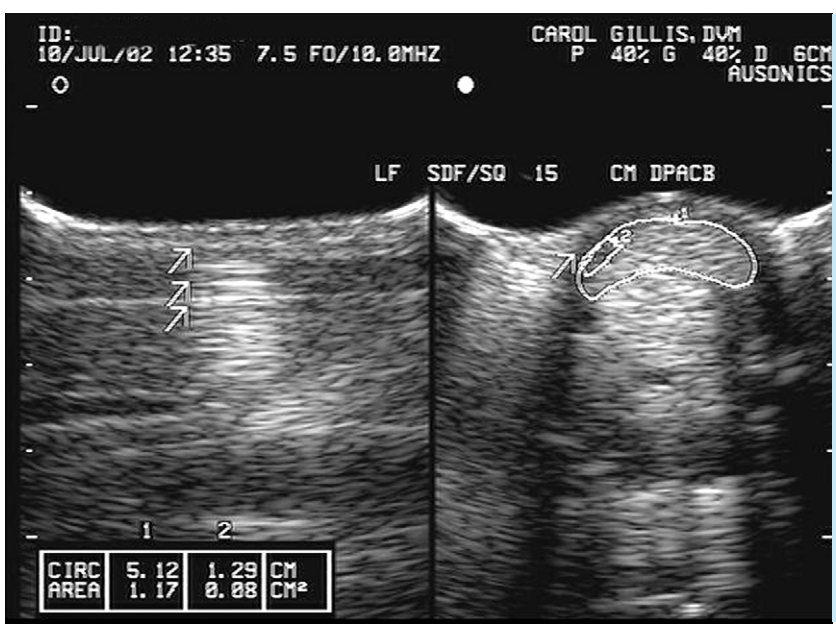


Fig. 20.2
Ultrasonographic image of a SDF tendon core lesion showing a subcutaneous organizing hematoma in the short-axis (right-hand) view as indicated by the arrow.

interphalangeal or distal interphalangeal joints. The foot must always be ruled out as a source of pain.

Special examination

For SDF branch lesions, a low palmar digital nerve block generally provides analgesia. For SDF lesions in the metacarpal/metatarsal region, a high palmar nerve block resolves the lameness.[3]

Increased size of the affected tendon region combined with loss of echogenicity and normal parallel linear fiber pattern observed with diagnostic ultrasonography provides the definitive diagnosis (Figs 20.2, 20.3, 20.4).[1,4–10]

Tenoscopy of the carpal and digital sheaths can provide additional diagnostic information as well as further treatment options. For example, under arthroscopic guidance debridement of frayed tendon fibers and resection of proliferative synovium and adhesions may be performed.[11,12]

Treatment and prognosis

Therapeutic aims

Control inflammation and prevent further tendon injury either directly, through reducing tendon fiber swelling and

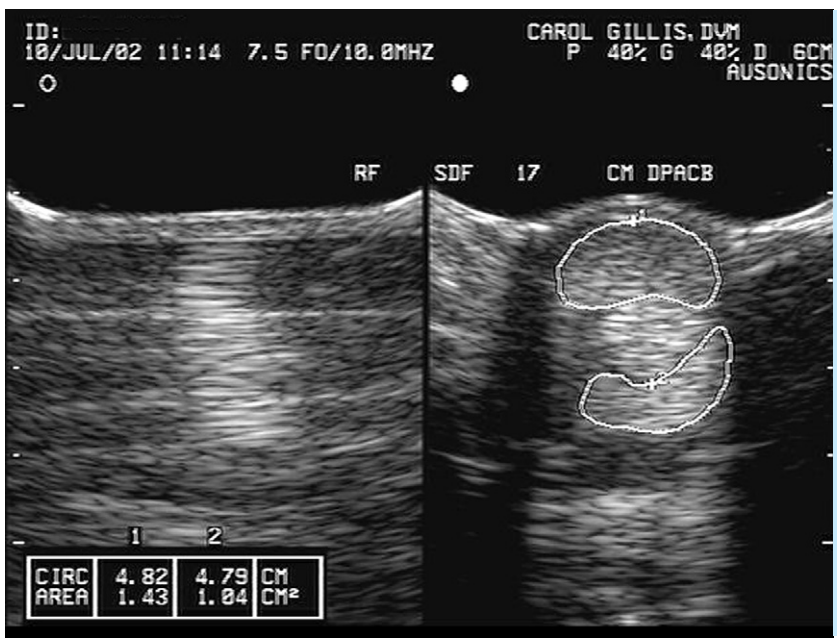


Fig. 20.3
Ultrasonographic image of chronic, generalized SDF tendinitis in the metacarpal region. The tendon is enlarged, hypoechoic and has a fair fiber pattern.

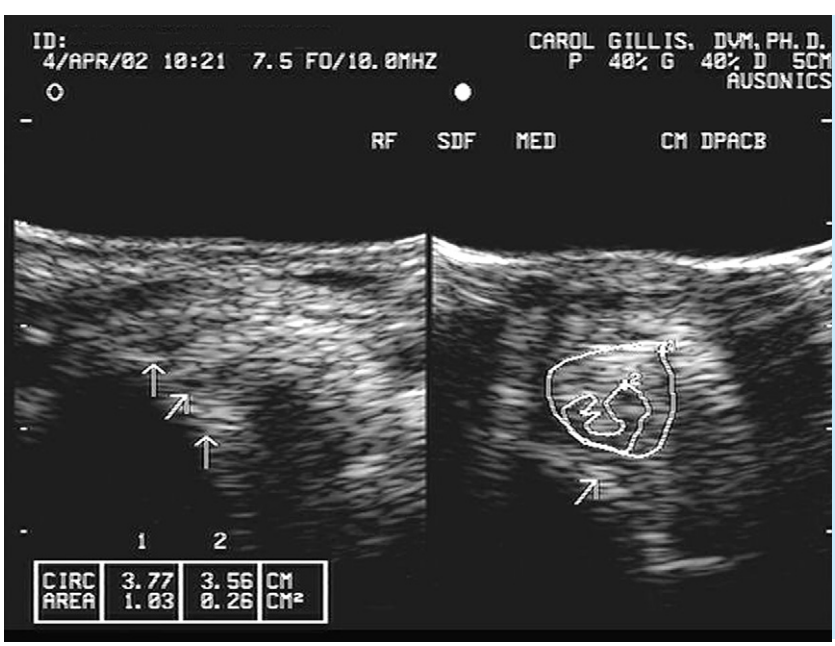


Fig. 20.4
Ultrasonographic image of a SDF medial branch core lesion in the pastern at the level of insertion.

influx of inflammatory mediators, or indirectly through further exercise.

- To provide adequate tendon support, primarily through shoeing.
- To provide adequate rest followed by graduated increases in exercise to allow for optimum tendon healing

Therapy

Initial therapy is directed at controlling excessive inflammation and should include anti-inflammatory therapy such as 1 g of phenylbutazone orally twice daily for 2–3 weeks, based on injury severity.

Cold therapy, such as ice for 20 minutes 2–3-times/day for 3 weeks, is an effective adjunct to reduce inflammation. Treatment with intramuscular polysulfated glycosaminoglycan, 500 mg every 4 days for seven treatments, has been shown to improve tendon healing.[13]

Foot conformation should be evaluated early in the course of injury. Good caudal heel support should be provided using an egg bar shoe that extends to the level of the heel bulbs. Any break in pastern/hoof axis should be corrected at the same time.

Stall (12'by 24') confinement with hand-walking should be initiated following examination. Unless the tendon is so severely damaged that rupture appears likely (rare), hand-walking is an important part of treatment and should not be delayed.

Bandaging is useful to decrease edema in the surrounding tissues. Bandages will not provide significant tendon support. Any concurrent lameness, even slight or chronic, should be treated at the same time.

Table 20.1 Exercise protocol following the first examination (0–60 days). Horse is confined to a stall and equivalent size paddock (12′ × 24′)

Injury	0–30 days	30–60 days
Mild	Hand-walk 15 minutes twice daily	Increase walking time by 5 minutes per week
Moderate	Hand-walk 10 minutes twice daily	Increase walking time by 5 minutes per week
Severe	Hand-walk 5 minutes twice daily	Increase walking time by 5 minutes per week

Table 20.2 Exercise protocol following the second examination (60–120 days). Horse is confined to a stall and equivalent size paddock

Progress	60–90 days	90–120 days
Good	Ride at walk 25 minutes daily, increasing by 5 minutes per week	Ride at walk increasing 5 minutes per week
Fair	As above	As above
Poor	Hand-walk 60 minutes per day	Ride at walk 20–30 minutes daily

Table 20.3 Exercise protocol following the third examination (120–180 days). Horse is confined to a 40′ × 40′ paddock

Progress	120–150 days	150–180 days
Good	Add 5 minutes trot every 2 weeks	Add 5 minutes trot every 2 weeks
Fair	Ride at a walk 60 minutes daily	As above
Poor	Re-evaluate case and discuss further	Treatment options

Table 20.4 Exercise protocol following the fourth examination (180–240 days). Horse can be turned out after riding exercise when it has been cantering 10 minutes for 1 week

Progress	180–210 days	210–240 days
Good	Add canter 5 minutes every 2 weeks, can turn out after exercise	Add canter 5 minutes every 2 weeks, begin ground pole work for jumping
Fair	Add trotting 5 minutes every 2 weeks	Add canter 5 minutes every 2 weeks
Poor	Re-evaluate case and discuss further treatment options	Re-evaluate case and discuss further treatment options

Table 20.5 Exercise protocol following the fifth examination (240–300 days)

Progress	240–270 days	300–330 days
Good	Racing speed work, begin once weekly jumping or other competitive training	Ready for competition
Fair	Add canter 5 minutes every 2 weeks	Full flat work; no racing speed work or jumping
Poor	Re-evaluate case and discuss further treatment options	Re-evaluate case and discuss further treatment options

Following an initial period of stall rest and hand-walking, the SDF tendon should be re-evaluated using physical examination and ultrasonography to assess healing. Increasing exercise should be based upon examination findings rather than time elapsed. When allowed free exercise, the horse should be confined to a space small enough so that it can only walk until the patient is at 20 minutes trot during controlled exercise. Please refer to Tables 20.1–5 for detailed exercise protocols.

Surgical options If an anechoic or mostly anechoic core lesion is seen on ultrasonographic examination, ultrasound-guided tendon splitting to decompress the core lesion should be performed as soon as possible, ideally 2–14 days following injury, to prevent further compression injury of the surrounding normal fibers.

If a subcutaneous hematoma is detected, injection of hyaluronic acid between the tendon and the skin should be performed as soon as possible, ideally 2–14 days following injury to attempt to prevent development of adhesions between the subcutaneous tissue and the SDF tendon.

Superior check ligament desmotomy has been shown to improve SDF appearance in the short term; long-term results have been less encouraging. Superior check desmotomy has been associated with significantly increased strains on the SDF tendon and SL.[14] Horses treated surgically were 1.2 times more likely to develop recurrent or new injuries after returning to training than horses managed non-surgically. Race horses that have undergone a superior check ligament desmotomy are 5.5 times as likely to suffer a subsequent suspensory ligament injury as are horses without desmotomy.[15]

Palmar annular ligament (PAL) desmotomy is very helpful in treatment of SDF injuries that extend to the distal metacarpal/metatarsal region. Resection of the PAL relieves compression of the enlarged SDF and allows for improved tendon gliding. This procedure is most effective when performed soon (within 4 weeks) after SDF tendon injury. If the procedure is not performed, the proximal portion of the SDF on subsequent ultrasound exams will appear to be healing at a normal rate, while the portion of the SDF just proximal to and at the level of the PAL will heal poorly. Resection is still useful as a treatment for chronic distal SDF tendon injury, although improved healing of the tendon is less dramatic. Although several surgical repair methods have been described for SDF tendon luxation, aggressive medical therapy provides a good long-term outcome without the complications that can occur following surgical attachment/stabilization at the original site on the calcaneus.

An experimentally promising treatment that may improve tendon healing in the future is the use of growth factor(s).[16]

Prognosis

The prognosis is excellent for life and good for return to full athletic use, if aggressive treatment followed by controlled rehabilitation is performed. If the tendon appears 95% healed based on size, echogenicity and fiber pattern on the final ultrasound exam, the horse is at no greater risk of reinjury than of any athletic use injury upon return to full work. A superficial digital flexor tendon that has luxated from its calcaneal attachment also has a good prognosis with aggressive medical treatment for inflammation and a full rehabilitation program.

Etiology and pathophysiology

The SDF tendon, in conjunction with the suspensory ligament, acts to keep the fetlock from extending to the ground when the horse is weight bearing. The SDF actively participates in limb flexion during the swing phase of locomotion through contraction of the SDF muscle.

The SDF tendon has little margin of safety as horses in full work such as galloping or jumping generate forces near to its breaking strength.[17,18] Factors that place excess load on the tendon, such as muscle fatigue which places increasing load on the much smaller, tendinous portion of the muscle/tendon unit, poor hoof conformation/shoeing or lameness in another limb, place the tendon at increased risk of failure.

Once a few fibers are damaged, strength is reduced and the tendon is predisposed to further fiber rupture with continued work. Hemorrhage at the site of ruptured fibers and associated inflammatory mediator release cause further fiber damage, either through compression by expansion of the hematoma or from the detrimental effects of inflammatory products.

Athletic performance deteriorates in horses with SDF tendinitis due to initial lameness, followed by prolonged tendon weakness during the recovery phase. If excessive exercise is attempted while the tendon is relatively weak, the risk of tendon reinjury is high, leading to a repetitive syndrome of repeated short periods of acute lameness followed by longer periods of inability to perform regular work. If the tendon is damaged repeatedly, fibroblast damage occurs (tendinosis), resulting in inability to generate normal repair collagen. At this stage the tendon's ability to heal is compromised.

Prevention

SDF tendinitis prevention consists of:

- increasing workload gradually rather than abruptly. A 5% increase in workload per week is generally a safe guideline
- being attentive to hoof shape and shoeing to avoid a long toe, low heel configuration and to prevent a break in pastern/hoof axis
- early recognition and treatment of other lameness to prevent compensatory tendon overload
- recognition that certain conformational faults, particularly 'back at the knee' conformation, load the SDF additionally and place the horse at increased risk of tendon injury when in full work.

Deep digital flexor tendinitis

Recognition

History and presenting complaint

Forelimb deep digital flexor (DDF) damage occurs most frequently in the pastern region of horses used for athletic pursuits which involve twisting and turning, such as endurance riding in rough terrain or roping. In the foot region of fore- and hindlimbs, DDF tendinitis often occurs in middle-aged horses. It is often concurrent with navicular disease, particularly navicular bursitis. Hindlimb metatarsal region DDF tendinitis is most frequently seen in hunters/jumpers, again often middle-aged geldings that have had years of work.

Physical examination

Grade 1–3 out of 5 lameness is observed and is often intermittent or transient. Heat, swelling and pain will be present on palpation of the DDF.

Differential diagnoses depend on location; in the metacarpal/metatarsal region, inferior check ligament desmitis is the major differential. Tarsal sheath synovitis may be associated with hindlimb DDF tendinitis. In the pastern the SDF tendon and the sesamoidean ligaments must be included in the differential diagnoses. Digital sheath synovitis is often associated with pastern region DDF tendinitis. In the foot, navicular bursitis, navicular bone changes and other causes of heel pain should be considered as differential diagnoses.

Special examination

Diagnostic nerve blocks will localize the region of the DDF involved and begin the process of elucidating the source(s) of heel pain, if present. Radiographs of the foot will provide information regarding bone and joint involvement

Diagnostic ultrasonography will define the presence and extent of DDF damage. For the most optimal examination of the DDF within the hoof, as well as the navicular bursa and the impar ligament, the shoe should be removed and the frog should be pared to provide a level surface for good transducer contact. The foot should be soaked overnight to further soften the tissues. The insertion of the DDF on the solar aspect of the distal phalanx, the navicular bursa and the impar ligament can then be evaluated for disease (Fig. 20.5).[19]

Treatment and prognosis

Therapeutic aims

- To control inflammation and prevent further tendon injury either directly, through reducing tendon fiber swelling and influx of inflammatory mediators, or indirectly through further exercise.
- To provide adequate tendon support, primarily through shoeing.
- To provide adequate rest followed by graduated exercise to allow for optimum tendon healing

Therapy

For general tendinitis medical treatment, please refer to the section on SDF tendinitis (pp 415–416).

DDF tendinitis in the region of the navicular bone is frequently associated with navicular bursitis. If this is the case, therapy should include injection of the navicular bursa with hyaluronic acid and steroid. Injection of the coffin joint rarely provides sufficient clinical and ultrasonographic signs of resolution of bursitis, even if the horse responds to coffin joint anesthesia. Reasons could include:

- diffusion of local anesthetic across membranes which are not sufficiently permeable to allow diffusion of larger molecules[20]
- anesthesia of local nerves proximal to the bursa, causing reduction in pain that was not the result of reduction of inflammation within the bursa.

Tarsal sheath synovitis may be treated medically in a similar fashion to the digital sheath (see following section). Tenoscopy of the sheath is an effective treatment for chronic/complicated cases with extensive synovial membrane proliferation and/or adhesions.[21]

Prognosis

Prognosis is good for return to athletic use if the tendon alone is involved. Concomitant tarsal sheath synovitis, digital sheath synovitis, and navicular bursitis need to be aggressively managed or they may prove to be the limiting factor(s) in future athletic performance. If not aggressively treated, DDF tendinitis and synovial sheath synovitis can progress to massive adhesions and a non-functional limb over time (Fig. 20.6).

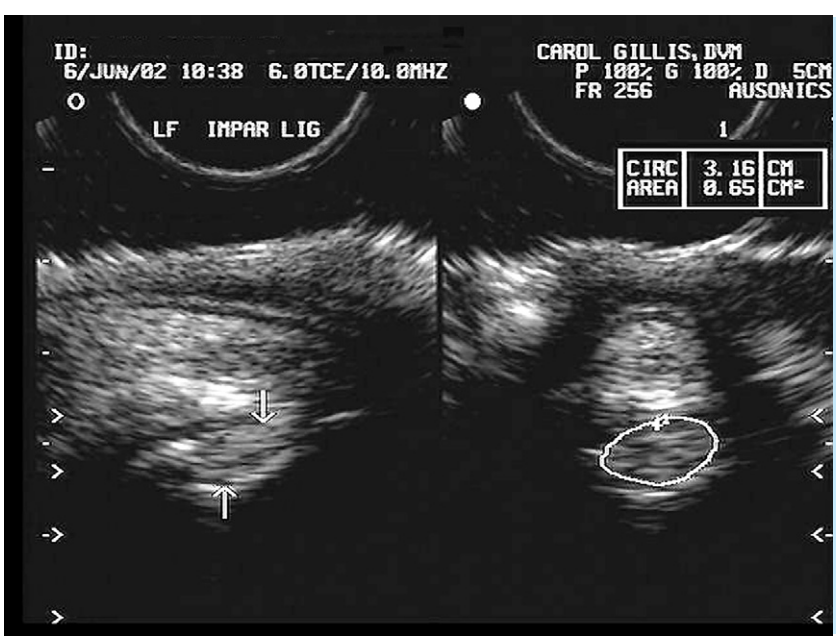


Fig. 20.5
Ultrasonographic image of impar ligament desmitis showing swelling, loss of echogenicity and a fair fiber pattern. The impar ligament origin on the navicular bone is to the left and its insertion on distal phalanx is to the right on the long-axis (left-hand) view.

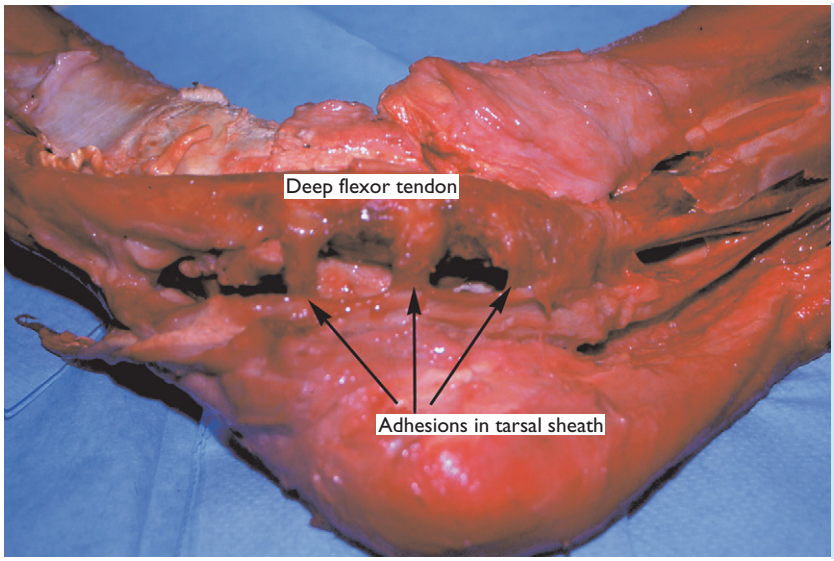


Fig. 20.6
Tarsal sheath severe chronic synovitis with adhesions to a thickened, fibrous DDF tendon.

Etiology and pathophysiology

The DDF tendon acts to keep the third phalanx/toe of the hoof from overextending and actively participates in flexion of the limb during the swing phase of locomotion through contraction of the DDF muscle. Factors that place excess load on the tendon include the following.

- Muscle fatigue, placing increasing load on the much smaller, tendinous portion of the muscle/tendon unit, poor hoof conformation/shoeing or lameness in another limb.
- Once a few fibers are damaged, strength is reduced and the tendon is predisposed to further fiber rupture with continued work.
- Hemorrhage at the site of ruptured fibers and associated inflammatory mediator release cause further fiber damage either through compression by hematoma expansion or the detrimental effects of inflammatory products.

Athletic performance deteriorates in horses with DDF tendinitis due to initial lameness, followed by prolonged tendon weakness during the recovery phase. If excessive exercise is attempted while the tendon is relatively weak, the risk of tendon reinjury is high, leading to a repetitive syndrome of repeated short periods of acute lameness followed by longer periods of inability to perform regular work. If the tendon is damaged repeatedly, fibroblast damage occurs (tendinosis), resulting in inability to generate repair collagen.

Prevention

DDF tendinitis prevention consists of:

- increasing workload gradually rather than abruptly. A 5% increase in workload per week is generally a safe guideline
- being attentive to hoof conformation and shoeing to avoid a long toe, low heel configuration and to prevent a break in pastern/hoof axis
- early recognition and treatment of other lameness to prevent compensatory tendon overload
- recognition that 'heel pain' may be due to excess strain on the DDF and that navicular bursitis my lead to secondary adhesions between the bursa and the DDF, leading to DDF damage.

Accessory ligament of the deep digital flexor tendon desmitis

Recognition

History and presenting complaint

Desmitis of the accessary ligament (AL) of the deep digital flexor tendon (DDFT) is usually observed in horses that are starting into regular work if the condition is developmental or in middle-aged horses (12–16 years) which have been in regular use, particularly as jumpers.

AL desmitis can also occur secondary to moderately severe to severe SDF tendinitis, if the SDF tendon becomes sufficiently enlarged to contact the medial and lateral borders of the AL. Adhesions may subsequently develop which cause AL inflammation and damage.[22]

Physical examination

Grade 2–3 out of 5 lameness is present and is usually persistent. Heat, swelling and pain are felt on palpation, most often at the AL/DDF junction in the palmar/lateral midmetacarpal region. AL desmitis occurs less frequently at the origin of the ligament.

Differential diagnoses include DDF tendinitis and suspensory ligament desmitis. The AL is often damaged at the mid-metacarpal level, where its fibers join those of the DDF tendon.

Special examination

A high two-point nerve block (lateral and medial palmar nerves) should ablate the lameness and will confirm that the lameness is localized to the metacarpal region.

Diagnostic ultrasonography will reveal AL enlargement, loss of echogenicity and deterioration of fiber pattern[23] and reveal if there is any contact with the borders of the SDF tendon. The DDF tendon may be completely encircled and compressed by the SDF and the AL and may be an additional source of the chronic pain often associated with AL desmitis (Fig. 20.7).

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further ligament injury either directly, through fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate ligament support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum ligament healing.

Therapy

For general therapy please refer to the section on SDF medical therapy (pp 415–416).

Surgical desmotomy of the AL is a final option. The client must commit to a full 6–10 month healing process. Within 4 weeks of surgery granulation tissue will fill the gap between the resected AL ends. The AL will initially be 2–4 times normal size, then over months of rehabilitation ligament repair will occur, with a functionally lengthened and healed AL if surgery and rehabilitation have been successful.[24–27]

AL desmotomy in weanlings to correct contracted tendon/club foot syndrome should be followed by a controlled exercise program. It is possible for the horse to develop clinical signs of desmitis when the partially healed ligament is subjected to the forces generated by athletic training years later.

Prognosis

Prognosis is fair for return to athletic use. The AL causes more long-term lameness than other tendon/ligament injuries.[25,28] Often diagnosis is delayed until AL desmitis is chronic and severe, which limits the potential for healing. Horses with AL desmitis respond most favorably to a gradual return to work, often with 4–5 days of work maximum with rest days in between. Breakdown of adhesions between the AL and the SDF tendon may cause transient pain. If the pain, heat and swelling do not respond to 3–4 days of ice, NSAIDs and walking, an ultrasonographic examination is indicated to assess the AL for reinjury.

Etiology and pathophysiology

Factors which cause contracted tendons in foals, such as congenital malformation,[29] diet and exercise, contribute to AL desmitis, as this ligament is part of the affected DDF/AL complex. Chronic overuse of the AL due to hyperextension of the limb during athletic work is a second predisposing factor in the older horse, as are changes in biomechanical properties due to the aging process.[30]

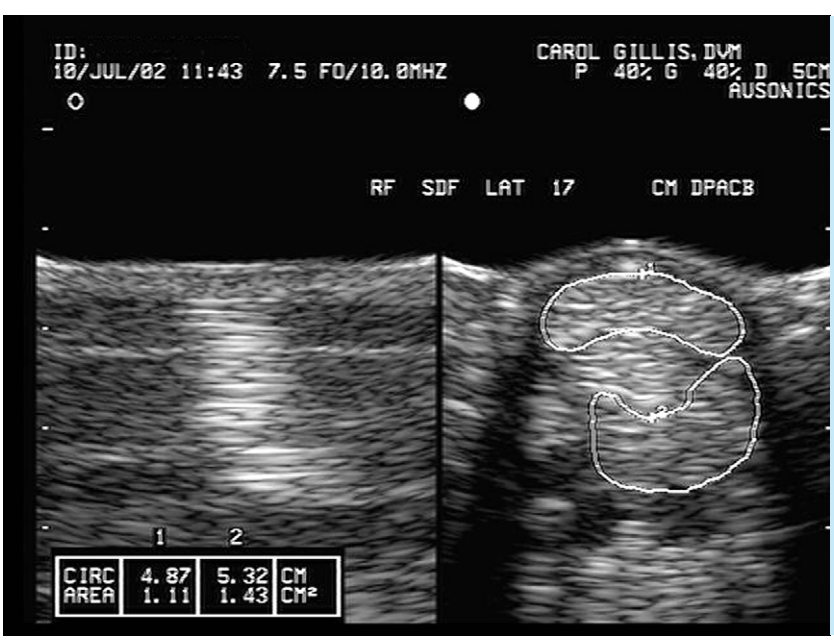


Fig. 20.7
Ultrasonographic image of SDF/AL adhesion compressing the DDF tendon. The cross-sectional area #1 indicates the SDF, cross-sectional area #2 indicates the AL.

Prevention

We are currently unable to detect excess tension on the AL prior to inflammation resulting in pain, heat and swelling.

Prevention of AL desmitis hinges primarily on very careful hoof balance, as many horses with AL desmitis have had long-term high heels on the affected limb and low heels on the opposite limb. Over time this condition tends to become more pronounced.

This condition may have been initiated when the patient was a foal, therefore careful attention to hoof trimming in the foal is a primary preventive step. Attempting to lower the high heel substantially often results in acute AL pain which may be quite severe. It is preferable to raise low heels on the opposite limb until the foot/pastern axis is balanced and then very gradually lower the high heels.

Suspensory ligament desmitis

Recognition

History and presenting complaint

Suspensory ligament (SL) desmitis is seen most frequently in horses that trot for long periods of time, such as Standardbred race horses, endurance horses and dressage horses. Often, pain, heat, swelling and lameness are noted 1–3 days following hard work or competition. Lameness may resolve quickly following the use of NSAIDs, cold therapy and rest, only to return when the horse is worked vigorously again. Hindlimb SL desmitis is often mistaken for disease of the distal tarsal joints. Treatment of the distal intertarsal and tarsometatarsal joints with steroids may reduce inflammation of the SL temporarily and cause reduction of clinical signs until further SL damage occurs. The complaint with these patients is often that 'they only respond short term to hock injections'.

Physical examination

Grade 1–3 out of 5 lameness is observed and is often intermittent or transient. The SL branches are readily palpated for pain, heat and swelling. The SL origin and body, particularly in the hindlimb, are nestled between MCII-III-IV (MTII-III-IV) and are covered superficially by the flexor tendons, so may only reveal clinical signs on careful deep palpation.

It is helpful to differentiate between hock joint pain and SL damage to compare the horse's response to hindlimb flexion and to deep pressure on the SL body with the heel off the ground but without limb flexion (Fig. 20.8). Rarely, the extensor branches of the SL are injured, resulting in pain, heat and swelling of the affected branch in the dorsolateral or dorsomedial pastern. Differential diagnoses include DDF/AL damage, metacarpophalangeal joint or collateral ligament injury and tarsal joint disease.

Fig. 20.8
Pressure being placed on the proximal hind SL on the medial aspect of the proximal third metatarsal bone.

Special examination

Median and ulnar nerve blocks will provide forelimb analgesia with suspensory desmitis.[3,31,32] In the hindlimb, interpretation of nerve blocks is complicated by the potential for anesthesia of the proximal SL and the tarsal sheath when using a high plantar nerve block[33] or, conversely, the possibility of blocking the proximal SL when using a tarsometatarsal joint block.

Radiographic examination of the proximal metatarsus/metacarpus and the tarsus or carpus respectively will help determine if there is concomitant joint disease. Also, changes in proximal metatarsus/metacarpus bone density may indicate abnormalities at the suspensory origin.

Diagnostic ultrasonography will reveal enlargement of the SL, loss of normal echogenicity and deterioration of fiber pattern.[34–36] To fully examine the origin/proximal SL body in the hindlimb, it is necessary to place the ultrasound probe in

a line just below the 'chestnut' and to aim in a dorsolateral direction, otherwise the large proximal portion of MTIV obscures half or more of the SL.

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further ligament injury either directly, through ligament reduction of fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate ligament support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum ligament healing.

Therapy

For general therapy please refer to the SDF tendon section (pp 415–416).

Suspensory ligament injuries respond very favorably to the provision of caudal heel support through the use of an egg bar shoe that extends to the level of the heel bulbs. Horses which stride up to the front feet with the hind feet can wear bell boots to deter shoe pulling. Many horses tolerate egg bars sufficiently well to wear them through the rehabilitation phase and on into return to competition.

Particularly in the first 2 weeks following injury, 'splitting' using an 18 gauge needle and ultrasound guidance is effective for decompression of lesions in the proximal SL body.

Prognosis

Prognosis is good for return to athletic use.

Etiology and pathophysiology

See above.

Prevention

The suspensory ligament functions with the SDF tendon to prevent the fetlock from extending to the ground during stance phase. Tendon and ligament respond to appropriate training by increasing in strength.[37] Ensuring that the equine athlete is trained in a stepwise consistent program, gradually building in difficulty, so that muscle fatigue never becomes sufficient to transfer the bulk of the horse's force on to the much smaller tendons and ligaments, is the best prevention for ligament injury. As in human athletes, a history of rapidly increasing work intensity, particularly upon return to work from another injury or as a young horse enters work or a new training situation, is commonly found as a precursor to ligament or tendon injury.

The second group of athletes which sustain ligament injury are the horses which regularly train using a repetitive protocol; for example, a mature dressage horse which often works 1–2 hours 6 days per week and which repeats the same maneuvers many times each exercise session. This horse, likely working in a balanced fashion on fore- and hindlimbs, subjects his hind suspensory ligaments to wear and tear injury. Prevention entails cross-training such as hacking on a long rein 1–2 times per week and having a complete rest day, with harder work interspersed between training days. This allows for repair of microdamage to the SL incurred on training days.

Long plantar ligament desmitis (curb)

Recognition

History and presenting complaint

Swelling along the plantar/lateral aspect of the calcaneus to the proximal aspect of MTIV is observed. Long plantar ligament (LPL) desmitis most frequently occurs in Standardbred race horses and in jumpers. Differential diagnoses include SDF tendinitis and subcutaneous swelling due to trauma.

Physical examination

Grade 1–2 out of 5 lameness is observed and is often transient. Pain, heat and swelling on palpation of the ligament are found.

Special examination

Diagnostic ultrasound will reveal enlargement, loss of echogenicity and deterioration of fiber pattern.

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further ligament injury either directly, through fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate ligament support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum ligament healing.

Therapy

For general therapy please refer to the SDF tendon section (pp 415–416). The LPL is not a weight-bearing tendon so it can be more readily rested. Generally LPL desmitis healing is sufficiently complete in 4–5 months to allow return to work.

Prognosis

Prognosis is excellent for return to athletic use.

Long digital extensor tendinitis

Recognition

History and presenting complaint

This injury is often seen in horses which jump solid fences such as steeplechase or eventing competitors. The usual presenting complaint is of swelling over the dorsal surface of MTIII and intermittent lameness.

Physical examination

Grade 1–2 out of 5 lameness. Pain, heat and swelling are felt on palpation of the long digital extensor tendon. Damage may extend into the lateral digital extensor tendon as well.

The long digital extensor tendon has a synovial sheath on the dorsum of the tarsus; this may also be involved, filling with hemorrhage, excess synovial fluid, synovial proliferation and adhesions.

Special examination

Diagnostic ultrasound will reveal enlargement of the tendon, loss of echogenicity and deterioration of fiber pattern. Synovitis of the tendon sheath will also be seen, if present, as excess fluid with an increased cell content, synovial proliferation and/or adhesions (Fig. 20.9).

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further tendon injury either directly, through fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate tendon support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum tendon healing.

Therapy

For general therapy please see the section on SDF tendinitis treatment (pp 415–416).

As extensor tendons are located on the dorsal surface of the bony column of the limb, they do not bear the brunt of the horse's weight as flexor tendons do. This allows the extensor tendons to rest and healing occurs more quickly than in flexors, generally being sufficiently complete in 4–6 months to allow return to work.

The extensor tendon sheath, if affected, should be treated at the time of diagnosis with intrathecal injection of anti-inflammatory medication such as hyaluronic acid.

Extensor tendon injuries are often associated with skin wounds or dermatitis secondary to hitting solid fences. These must be treated vigorously to reduce local inflammation and allow tendon healing to progress.

Prognosis

Excellent for return to athletic use.

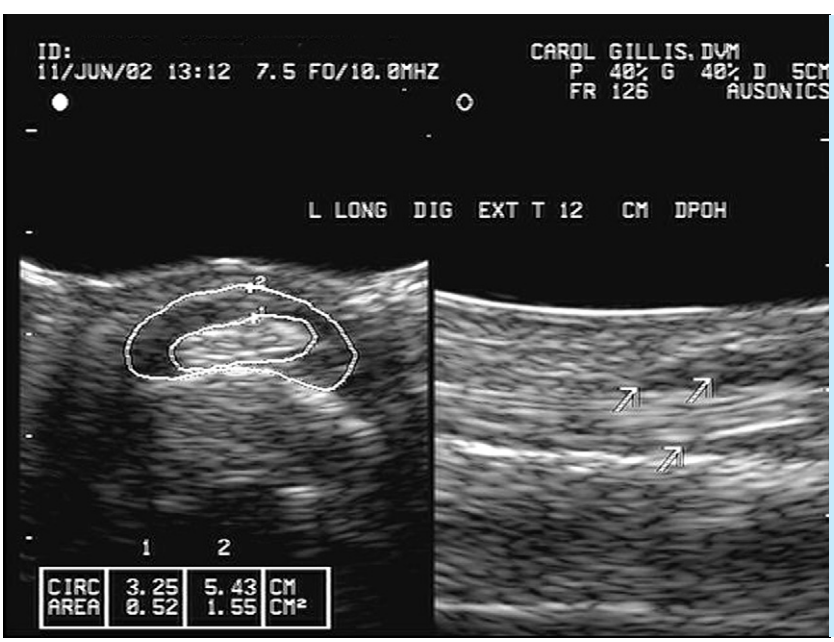


Fig. 20.9
Ultrasonographic image of LDET sheath effusive synovitis. The cross-sectional area #1 indicates the LDET, cross-sectional area #2 indicates the surrounding sheath filled with hypoechoic fluid.

Prevention

As extensor tendon injuries are often associated with a direct blow to the limb from a fence, the most practical prevention is protective boots for the dorsal surface of MTIII.

Common digital extensor tendinitis

Recognition

History and presenting complaint

See long digital extensor tendinitis (above). Long digital extensor tendinitis, as well as tendon laceration, is far more frequently encountered than common digital extensor tendinitis.[38]

Physical examination

Grade 1–2 out of 5 lameness is observed and is often transient and intermittent. Pain, heat and swelling are felt on palpation. The tendon sheath on the dorsal surface of the carpus may also be warm, swollen and sensitive to palpation.

Special examination

Diagnostic ultrasound will reveal enlargement of the tendon, loss of echogenicity and deterioration of fiber pattern. Synovitis of the tendon sheath will also be seen, if present, as excess, often cellular fluid, synovial proliferation and/or adhesions.

Treatment and prognosis

See long digital extensor tendinitis (above).

Straight sesamoidean ligament desmitis

Recognition

History and presenting complaint

Desmitis of the straight sesamoidean ligament (SSL) is usually seen in horses which twist and turn as part of their sport, such as eventers and cutting horses, or which work on uneven ground, such as endurance horses. This injury also occurs fairly frequently in pasture.

Physical examination

Grade 2–3 out of 5 lameness is observed. Pain, heat and swelling are encountered on palpation of the palmar/plantar aspect of the flexed limb. Differential diagnoses include other sesamoidean ligament injury, collateral ligament damage or pastern joint disease.

Special examination

Nerve block at the abaxial sesamoid level will greatly improve or ablate the lameness. Radiographs may reveal bone changes at the site of SSL origin at the base of the sesamoid bones or, more commonly, at the insertion on palmar P2. Diagnostic ultrasound will reveal enlargement, loss of echogenicity and deterioration of fiber pattern. A wedge of muscle tissue located at the SSL insertion on P2 can appear to be a lesion. Placing the limb in strong extension will compress the muscle, while a true lesion will remain unchanged.

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further ligament injury either directly, through fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate ligament support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum ligament healing.

Therapy

For general therapy please refer to the SDF tendon section (pp 415–416).

Caudal heel support through the use of an egg bar shoe to the level of the heel bulbs is very helpful for this injury.

Prognosis

Prognosis is good for return to athletic use.

Etiology and pathophysiology

Torsion of the foot/pastern produces excessive force on the pastern ligaments if:

- the horse is fatigued and muscle contraction is not assisting normally in foot/pastern placement
- the fetlock is sinking excessively during weight-bearing phase due to long toe, low heel foot conformation, muscle fatigue or uneven footing.

Prevention

Balanced shoeing appropriate for the terrain and a well-conditioned horse that does not fatigue excessively during competition are the best prevention.

Oblique sesamoidean ligament desmitis

Recognition

History and presenting complaint

Oblique sesamoidean ligament (OSL) desmitis is usually seen in horses which twist and turn as part of their sport, such as eventers and cutting horses, or which work on uneven ground, such as endurance horses. This injury also occurs fairly frequently in pasture.

Physical examination

Grade 2–3 out of 5 lameness is observed, usually persistent. Pain is elicited on palpation of the affected branch from the base of the sesamoid bone to palmar PI.

Differential diagnoses include other sesamoidean ligament injury, collateral ligament damage or pastern joint disease.

Special examination

Nerve block at the abaxial sesamoid level on the affected side will improve or ablate the lameness. Radiographs may reveal bony changes at the base of the sesamoid or at OSL insertion on palmar (plantar) P1. Diagnostic ultrasound will reveal enlargement, loss of echogenicity and deterioration of fiber pattern.

Treatment and prognosis

See straight sesamoidean ligament (above).

Collateral ligament desmitis of the metacarpophalangeal/ metatarsophalangeal, proximal interphalangeal joints and distal interphalangeal joints

Recognition

History and presenting complaint

Usually seen in horses which twist and turn as part of their sport, such as eventers and cutting horses, or which work on uneven ground, such as endurance horses (Fig. 20.10). This injury also occurs fairly frequently in pasture.

Physical examination

Grade 2–4 out of 5 lameness is observed. Pain, heat and swelling are palpable on the affected ligament. Palpation is easiest when the distal limb is flexed. Signs of joint inflammation (distended joint and pain on flexion) will be present in acute cases. In chronic cases, osteoarthritis may be present, resulting in reduced flexion and a thickened joint capsule.[39]

A low four-point nerve block (medial and lateral palmar/plantar and palmar/plantar metacarpal/metatarsal nerves) greatly improves or ablates the lameness at the level of the fetlock and distal and the abaxial sesamoid block will improve or ablate lameness at the level of the proximal interphalangeal joint. Intra-articular anesthesia generally improves, but does not ablate the lameness.

Fig. 20.10
An endurance horse in competition in the Tevis Cup (100 mile).

Special examination

Stress radiographs may reveal medial/lateral joint laxity if damage results in significant ligament laxity. Bony abnormalities at the origin of the collateral ligaments or insertion may be detected. Diagnostic ultrasound will reveal ligament enlargement, loss of echogenicity and loss of normal fiber pattern. The insertion of the collateral ligaments of the distal interphalangeal joint cannot be evaluated using ultrasound because of the interposition of the hoof capsule.

Treatment and prognosis

Therapeutic aims

To control inflammation and prevent further ligament injury either directly, through fiber swelling and inflammatory mediators, or indirectly through further exercise. To provide adequate ligament support, primarily through shoeing. To provide adequate rest followed by graduated exercise to allow for optimum ligament healing.

Therapy

For general therapy please refer to the SDF tendon section (pp 415–416).

Shoeing with a $\frac{1}{2}''$ extension at the midquarter of the affected side of the hoof will provide support and make the horse more comfortable, as well as reducing stress on the collateral ligament. Shoeing in this manner may be difficult to maintain if the medial collateral ligament is damaged, as the horse may tend to pull the shoe with the opposite foot. Large bell boots may be helpful in preventing this. Shoeing should be maintained for 4–6 months. Extensions may be decreased to $\frac{1}{4}''$ inch as clinical and ultrasonographic signs improve.

Horses with collateral ligament damage may be lame for up to 90 days following injury. Confinement and regular hand-walking exercise are essential.

Often the joint develops synovitis or capsulitis following this type of injury; treatment of the joint with intra-articular hyaluronic acid, as well as intramuscular polysulfated glycosaminoglycan (PSGAG) therapy and oral glucosamine, are helpful to relieve joint inflammation. If there has been hemorrhage into the joint, the horse may be in extreme pain and the joint may need to undergo lavage to rid it of inflammatory products. In cases of complete rupture, surgical repair of the ligament may be necessary.[40,41]

Prognosis

Prognosis is good for return to athletic use.

Prevention

Balanced shoeing which provides adequate foot support is an important preventive measure. A well-conditioned horse will withstand the stresses imposed in competition with less chance of injury than a poorly conditioned horse.

Biceps brachii tendinitis/ bicipital bursitis

Recognition

History and presenting complaint

The injury often occurs due to being kicked by another horse or by hitting a solid object such as a fence. Stress injuries are uncommon.

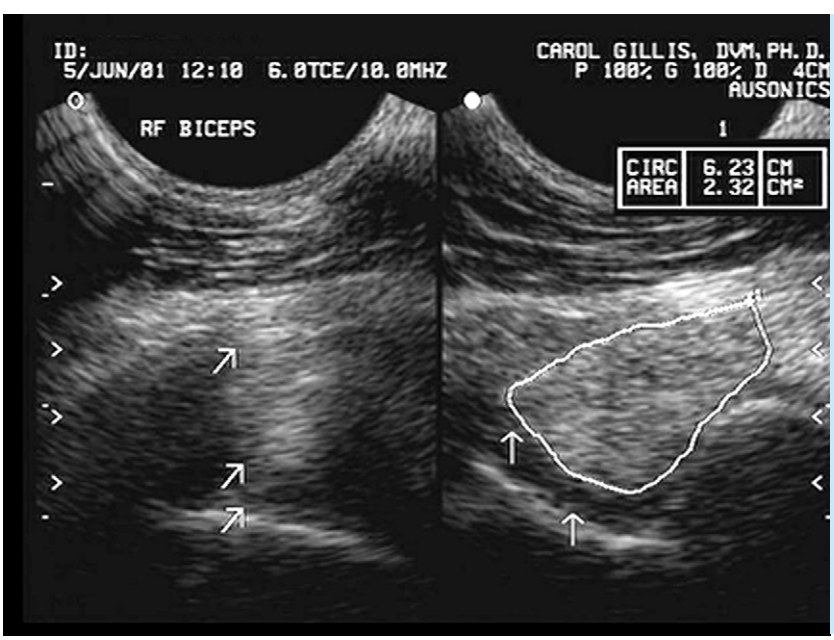


Fig. 20.11
Ultrasonographic image of biceps tendinitis/bicipital bursitis. The short-axis (right-hand) view arrows are indicating synovial proliferation in the bursa.

Physical examination

Pain on palpation of the biceps tendon is usually evident. A tendency to stand with the affected limb slightly caudal to the normal one is frequently seen. Pain on extension of the tendon and compression of the bicipital bursa by pulling the limb caudally may also be seen.

Special examination

A radiographic skyline view will reveal concomitant humeral tubercle injury/pathology. Diagnostic ultrasound will reveal tendon enlargement, loss of echogenicity and fiber pattern.[42] Bicipital bursitis is almost always seen concomitantly. Excess fluid (greater than 3 mm depth) will be seen. The fluid will be anechoic if there is effusive synovitis present or hypoechoic if it is in the early proliferative phase. Adhesions, if present, may be seen between the bursa and the biceps tendon (Fig. 20.11).

Treatment and prognosis

Therapeutic aims

See section on SDF tendon (pp. 414–415).

Therapy

For general therapy, please see the section on SDF treatment (pp 415–416).

Bicipital bursitis, if present, should be treated as soon as it is recognized. Initial treatment should be made with intrathecal hyaluronic acid to prevent adhesion formation and relieve inflammation. The bursa can be readily accessed using a 19 gauge $1\frac{1}{2}''$ needle under ultrasound guidance and confirmation of injection into the bursa can be recorded (Fig. 20.12). Often 2–4 injections are required over a period of 4–6 months to resolve the synovitis. As tendon healing progresses, a steroid may be added to hyaluronic acid to

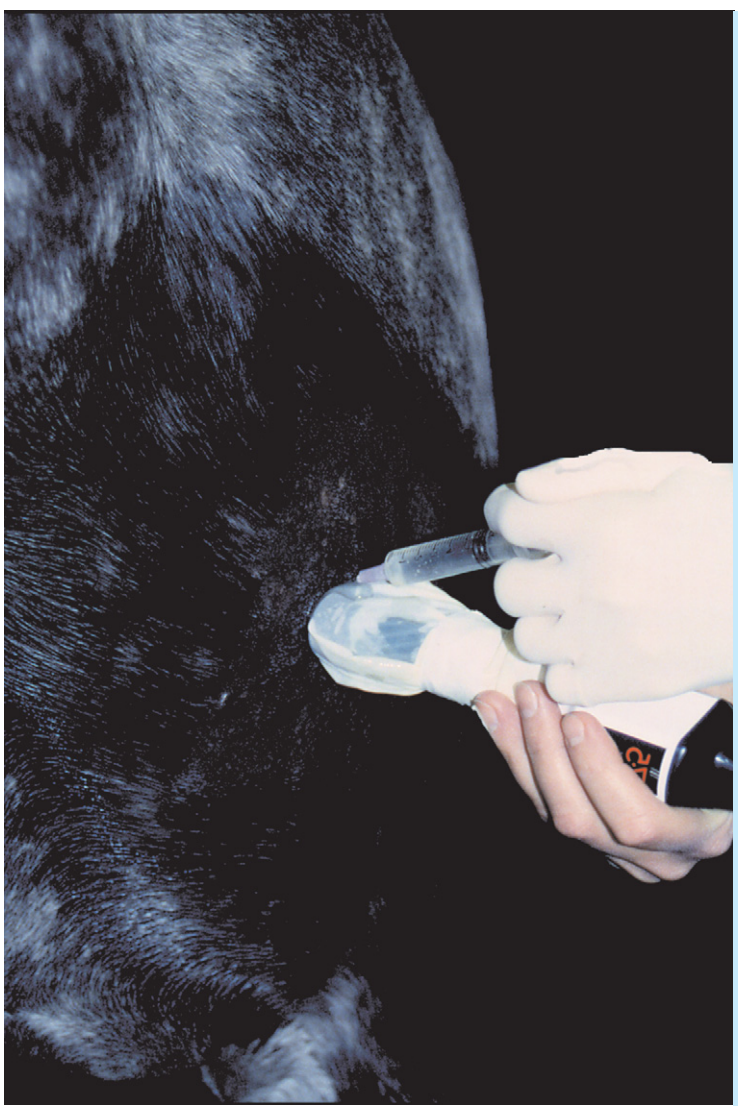


Fig. 20.12
Ultrasound-guided bicipital bursa injection.

increase the anti-inflammatory effect. Physical therapy, such as massage and therapeutic ultrasound to relieve biceps muscle spasm and improve comfort, tends to improve healing.

Prognosis

Chronic biceps tendon/bursa injuries with scar tissue and adhesions respond poorly to treatment, with approximately 25% of such cases returning to athletic use. Early detection of the injury combined with aggressive medical and physical therapy improves the prognosis to 70% return to athletic use.

Etiology and pathophysiology

Direct crushing of the tendon against the humeral tubercles is the most common etiology for biceps brachii damage and concomitant bursitis.

Prevention

This injury is often due to an accident such as a fall or a kick.

Ligament of the dorsal spinous processes

Recognition

History and presenting complaint

Horses with this problem often present with sore or cold backs. They also often resent being saddled or mounted or refuse to jump or to take up a gait, usually the canter. This injury can be seen in any type of equine athlete.[43,44]

Physical examination

Pain on palpation of the affected portion of the dorsal spinous ligament is evident.

Special examination

Radiographs of the dorsal spinous processes may reveal concomitant osteoarthrosis. Diagnostic ultrasonography will reveal enlargement, loss of echogenicity and deterioration of the normal fiber pattern of the affected dorsal spinous ligament.

Treatment and prognosis

Therapy

For general therapy please refer to the section on SDF treatment (pp 415–416).

Horses with dorsal spinous ligament damage may require a prolonged period of exercise such as ponying or walking and trotting on an exerciser before being worked under saddle.

Prognosis

Prognosis is good for return to athletic use.

Ligaments of the tuber sacrale

Recognition

History and presenting complaint

Jumpers are particularly susceptible to this injury. Signs may also develop after a fall, either in work or loose in pasture. Horses are usually presented for evaluation of a 'bump' at the croup (sacroiliac region) or changes in gluteal muscle balance.

Physical examination

Persistent grade 1–3 out of 5 lameness is observed. The tuber sacrale are often uneven when viewed from behind the horse due to concomitant sacroiliac joint subluxation and/or crushing of the tuber sacrum. There is often gluteal wasting of the affected limb.

Special examination

Diagnostic ultrasonography will reveal enlargements, loss of echogenicity and deterioration of fiber pattern of the affected ligament(s).

Treatment and prognosis

See dorsal spinous process ligaments.

Gastrocnemius (achilles) tendinitis

Recognition

History and presenting complaint

Achilles tendon damage is often seen after a fall or after having the hindlimb trapped in a fence or gate.

Physical examination

Persistent grade 1–3 out of 5 lameness is observed. Pain, heat and swelling of the affected portion of the tendon are

palpable. The tarsus will be dropped if sufficient damage of the tendon has occurred.

Special examination

A tibial nerve block will improve the lameness.[45] Diagnostic ultrasound will reveal enlargement, loss of echogenicity and deterioration of fiber pattern. The tendon is seen proximally as two muscular heads, which join at the musculotendinous junction. Just proximal to the tarsus the gastrocnemius tendon twists from its position superficial to the SDF tendon and becomes deep to it.

Treatment and prognosis

Therapy

For general therapy please see the section on SDF tendinitis (pp 415–416). Core lesions, if seen, can be decompressed effectively in the acute stage (less than 2 weeks) using ultrasound guidance.

Prognosis

Prognosis is fair to good for return to athletic use.

Prevention

This is usually an accidental injury.

Digital sheath syndrome

Recognition

The digital sheath is a complex synovial structure[46,47] which surrounds the superficial (SDF) and deep (DDF) flexor tendons from proximal to the fetlock joint distally to midpastern. Normally, the synovium secretes a small amount of fluid which promotes gliding of the flexor tendons around the palmar/plantar aspect of the fetlock joint. With inflammation the sheath can become greatly distended, reaching to midmetacarpus proximally and/or 'herniating' palmar to the SDF tendon on the midline.

History and presenting complaint

Generally, digital sheath (DS) synovitis presents as a cumulative wear and tear type of injury which progresses over time. Horses have often been in hard work for a period of time and progress from a non-painful blemish to a syndrome that causes gradual lameness.

Physical examination

Clinical signs of digital sheath synovitis reflect the degree of inflammation, which is divided into three stages. It is not uncommon for athletic horses to present with mild to moderate effusion of the digital sheaths (stage 1 synovitis) of both

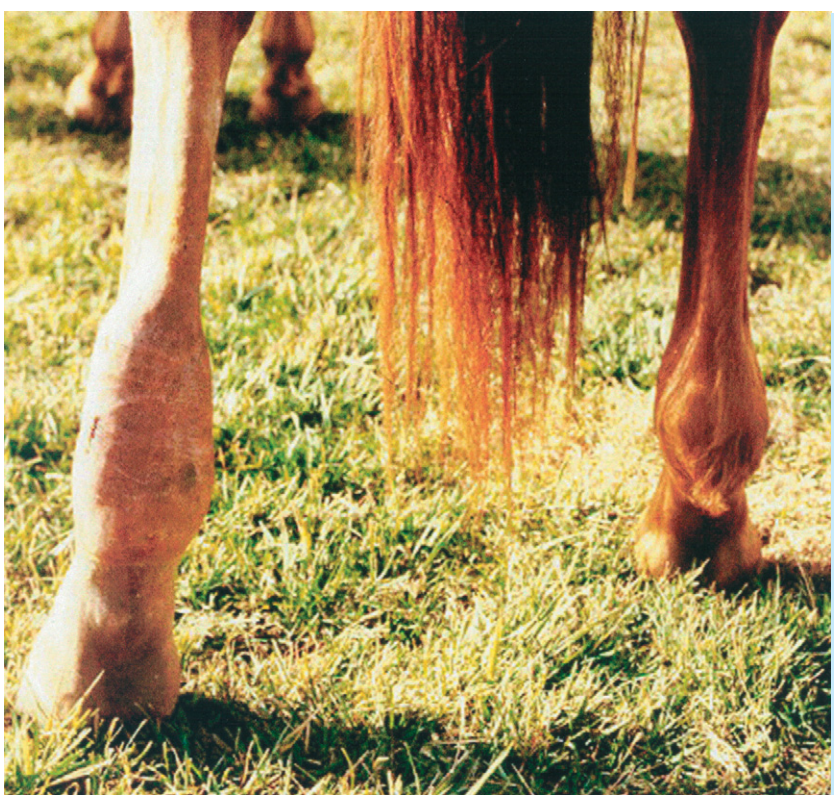


Fig. 20.13
Digital sheath, showing distention of the lateral pouch.

forelimbs, both hindlimbs or all four limbs. Often, sheath distension decreases following exercise. The distension is fluidly fluctuant on palpation. The patient is sound, non-painful to sheath palpation and negative to fetlock flexion. The lay term often used to describe stage 1 DS synovitis is 'wind-puffs'.

If synovitis progresses from the effusive stage to synovial proliferation (stage 2), clinical signs include mild to moderate lameness. This is often first seen as an attempt by the horse to guard the affected sheath by failing to fully extend the fetlock, manifested as a decreased drop in the fetlock during the stance phase of gait in comparison to the opposite fetlock. The digital sheath will feel firm rather than fluid on palpation and one aspect of the sheath, usually the lateral aspect, will be more distended (Fig. 20.13). The horse will be positive to fetlock flexion, as this maneuver compresses the sheath.

If synovitis progresses to stage 3, synovial proliferation and inflammatory product secretion may cause the patient to be severely lame.[48] The horse will be reluctant to place the heels of the foot on the ground and may not tolerate fetlock flexion. The digital sheath will be distended, painful and firm on palpation.

Often, stage 2 and stage 3 digital sheath synovitis are accompanied by damage to either the superficial or deep flexor tendons.[49] This is probably due to the same wear and tear process that caused sheath synovitis. The synovitis advances by prolonged exposure to inflammatory mediators circulating in the sheath, being compressed by synovial proliferation and, finally, due to active pulling on the tendons by adhesions within the sheath. Palmar annular ligament (PAL) desmitis, likely due to chronic stretching of the ligament by the distended digital sheath, may result in a thickened PAL[50] which further compresses the digital sheath, causing a cycle of increasing inflammation, swelling and constriction.

Special examination

Low four-point nerve block will improve/ablate lameness. Ultrasonographic examination of stage 1 synovitis reveals a moderate amount of fluid in the affected sheath(s), with no evidence of synovial proliferation or adhesions between the tendons and sheath walls.

Ultrasonographic examination of stage 2 synovitis will reveal distension of the sheath with fluid and proliferative synovium. Proliferative tissue may also begin to cover the surfaces of the flexor tendons. Ultrasonographic examination of stage 3 synovitis will reveal extensive synovial proliferation, often covering the surfaces of the flexor tendons, and one or more adhesions between the tendons and the sheath wall (Fig. 20.14). At any stage, but particularly in stages 2 and 3, SDF, DDF or PAL pathology may also be observed.

Treatment and prognosis

Therapeutic aims

Inflammation of the digital sheath should be vigorously treated to reduce excessive synovial proliferation and the onset of restrictive scar formation.

Therapy

Treatment of stage 1 synovitis is medical and may consist of 3–4 weeks of rest, anti-inflammatory medication, cold hosing/icing of the affected limb(s), administration of intramuscular PSGAG (more effective for this syndrome than hyaluronic acid) and supplementation with oral glucosamine. Foot balance should be checked and lameness in any other limb should be recognized and treated.

Treatment of stage 2 synovitis includes the above plus injection of the affected sheath with hyaluronic acid[51] (Fig. 20.15), followed by 2–3 weeks of rest (confinement plus

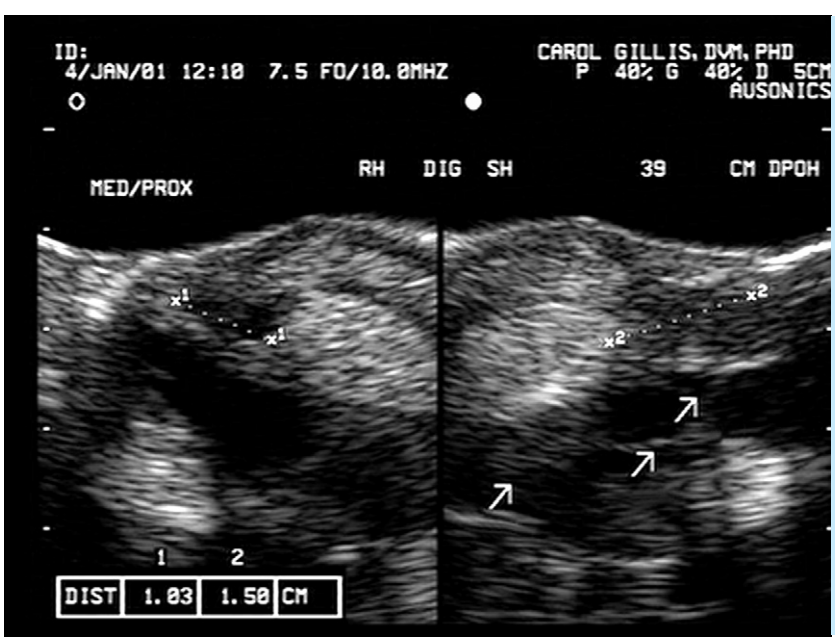


Fig. 20.14
Ultrasound image of DS synovitis with adhesions, as indicated by the arrows in the short-axis (right-hand) view.

Fig. 20.15
Digital sheath injection.

hand-walking). Patients that do not respond promptly and fully to medical treatment require tenoscopy to remove excess proliferative synovial tissue and adhesions. The PAL may be resected[52] tenoscopically at this time to provide relief from compression.

Treatment of stage 3 synovitis requires medical and surgical treatment, as outlined above for stage 2.

Surgical intervention In cases with thickening and constriction of the annular ligament, some portion of the surgery must be designed to relieve the restrictive effects of this structure. Resection of the PAL[53,54] will temporarily interrupt the inflammatory cycle but regrowth of the ligament is inevitable and unless the primary problem of synovitis is corrected, the end result will be a progressively more painful sheath that has distended to meet its new dimensions following PAL resection.

Tenoscopic exploration will detect abnormalities of the tendon sheath, superficial digital flexor tendon, deep digital flexor tendon and intersesamoidean ligament (Fig. 20.16). Proliferative masses can be removed with the assistance of a radiofrequency debrider. Adhesions present between the tendons and the tendon sheath are also debrided.

Paramount to the success of this procedure is the strict adherence to an aggressive postoperative protocol, including medical therapy as outlined above, for a period of weeks followed by a clinical and ultrasonographic re-evaluation.

Prognosis

Prognosis for stage 1 synovitis is good. As long as the horse is in full athletic use, medical treatment may be required to prevent progression to stage 2 synovitis. Prognosis for stage 2 synovitis is good for full athletic work, if appropriate treatment is performed in a timely manner.[52] Prognosis for stage 3 synovitis is fair for full athletic use. Without treatment, these patients may progress to lameness even at a walk.

Etiology and pathophysiology

Either acute direct trauma or overextension of the fetlock can cause hemorrhage into the sheath space that initiates a marked inflammatory reaction. Alternatively, repetitive

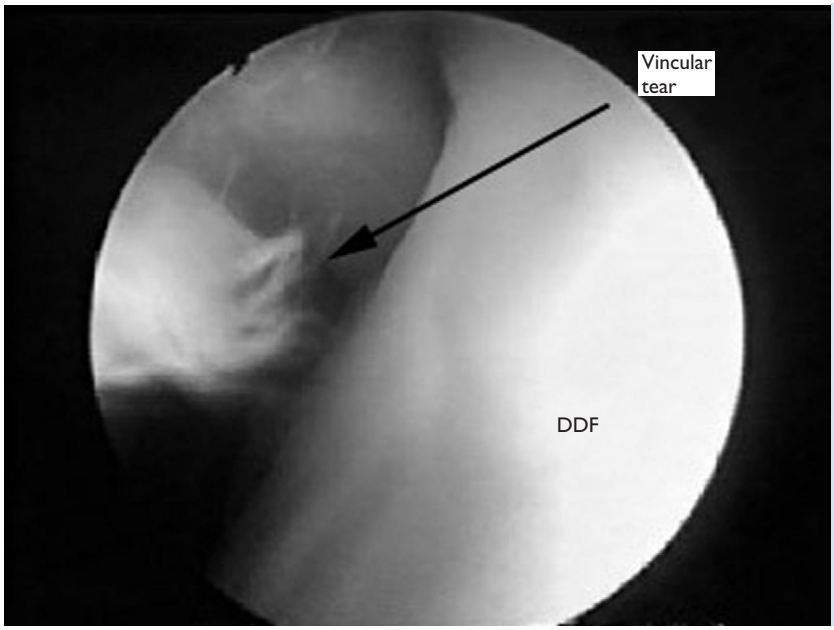


Fig. 20.16
Intratenoscopic photograph showing a tear in the vinculum. (Courtesy of Dr Tom Yarbrough.)

fetlock extension over time results in an ongoing inflammatory process.

References

1. Rapp HJ, Becker M, Heisse K, et al. [Diagnosis and therapy of tendinitis exemplified by the athletic horse]. Sportverletz Sportschaden 1992; 6(2):77–88.
2. Meershoek LS, Lanovaz JL, Schamhardt HC, et al. Calculated forelimb flexor tendon forces in horses with experimentally induced superficial digital flexor tendinitis and the effects of application of heel wedges. Am J Vet Res 2002; 63(3): 432–437.
3. Keg PR, van der Belt AJ, Merkens HW, et al. The effect of regional nerve blocks on the lameness caused by collagenase induced tendinitis in the midmetacarpal region of the horse: a study using gait analysis, and ultrasonography to determine tendon healing. Zentralbl Veterinarmed A 1992; 39(5): 349–364.
4. Gibson KT, Burbidge HM, Anderson BH. Tendinitis of the branches of insertion of the superficial digital flexor tendon in horses. Aust Vet J 1997; 75(4):253–256.
5. Pickersgill CH, Marr CM, Reid SW. Repeatability of diagnostic ultrasonography in the assessment of the equine superficial digital flexor tendon. Equine Vet J 2001; 33(1):33–37.
6. Reef VB. Superficial digital flexor tendon healing: ultrasonographic evaluation of therapies. Vet Clin North Am Equine Pract 2001; 17(1):159–178, vii-viii.
7. van Schie HT, Bakker EM, Jonker AM, et al. Ultrasonographic tissue characterization of equine superficial digital flexor tendons by means of gray level statistics. Am J Vet Res 2000; 61(2):210–219.
8. Micklethwaite L, Wood AK, Sehgal CM, et al. Use of quantitative analysis of sonographic brightness for detection of early healing of tendon injury in horses. Am J Vet Res 2001; 62(8):1320–1327.
9. Gillis C, Sharkey N, Stover SM, et al. Ultrasonography as a method to determine tendon cross-sectional area. Am J Vet Res 1995; 56(10):1270–1274.
10. Gillis C, Meagher DM, Cloninger A, et al. Ultrasonographic cross-sectional area and mean echogenicity of the superficial and deep digital flexor tendons in 50 trained thoroughbred racehorses. Am J Vet Res 1995; 56(10):1265–1269.
11. Cauvin ER, Munroe GA, Boyd JS. Endoscopic examination of the carpal flexor tendon sheath in horses. Equine Vet J 1997; 29(6):459–466.
12. Southwood LL, Stashak TS, Kainer RA. Tenoscopic anatomy of the equine carpal flexor synovial sheath. Vet Surg 1998; 27(2):150–157.
13. Dow SM, Wilson AM, Goodship AE. Treatment of acute superficial digital flexor tendon injury in horses with polysulphated glycosaminoglycan. Vet Rec 1996; 139(17): 413–416.
14. Alexander GR, Gibson KT, Day RE, et al. Effects of superior check desmotomy on flexor tendon and suspensory ligament strain in equine cadaver limbs. Vet Surg 2001; 30(6): 522–527.
15. Gibson KT, Burbidge HM, Pfeiffer DU. Superficial digital flexor tendinitis in thoroughbred race horses: outcome following non-surgical treatment and superior check desmotomy. Aust Vet J 1997; 75(9):631–635.
16. Murphy DJ, Nixon AJ. Biochemical and site-specific effects of insulin-like growth factor I on intrinsic tenocyte activity in equine flexor tendons. Am J Vet Res 1997; 58(1):103–109.
17. Dowling BA, Dart AJ, Hodgson DR, et al. Superficial digital flexor tendinitis in the horse. Equine Vet J 2000; 32(5): 369–378.
18. Meershoek LS, Schamhardt HC, Roepstorff L, et al. Forelimb tendon loading during jump landings and the influence of fence height. Equine Vet J 2001; 33(suppl):6–10.
19. Busoni V, Denoix JM. Ultrasonography of the podotrochlear apparatus in the horse using a transcuneal approach: technique and reference images. Vet Radiol Ultrasound 2001; 42(6):534–540.
20. Hoffer MA, Leach DH, Doige CE. The developmental anatomy of the equine navicular bursa and associated structures. Anat Embryol 1989; 179(4):355–367.

21. Cauvin ER, Munroe GA, Boswell J, et al. Gross and ultrasonographic anatomy of the carpal flexor tendon sheath in horses. Vet Rec 1997; 141(19):489–495.
22. McDiarmid A. Acquired flexural deformity of the metacarpophalangeal joint in five horses associated with tendonous damage in the palmar metacarpus. Vet Rec 1999; 144(17):475–478.
23. Denoix JM, Busoni V. Ultrasonographic anatomy of the accessory ligament of the superficial digital flexor tendon in horses. Equine Vet J 1999; 31(3):186–191.
24. Becker CK, Savelberg HH, Buchner HH, et al. Long-term consequences of experimental desmotomy of the accessory ligament of the deep digital flexor tendon in adult horses. Am J Vet Res 1998; 59(3):347–351.
25. Todhunter PG, Schumacher J, Finn-Bodner ST. Desmotomy for treatment of chronic desmitis of the accessory ligament of the deep digital flexor tendon in a horse. Can Vet J 1997; 38(10): 637–639.
26. White NA 2nd. Ultrasound-guided transection of the accessory ligament of the deep digital flexor muscle (distal check ligament desmotomy) in horses. Vet Surg 1995; 24(5): 373–378.
27. Buchner HH, Savelberg HH, Becker CK. Load redistribution after desmotomy of the accessory ligament of the deep digital flexor tendon in adult horses. Vet Q 1996; 18(suppl 2):S70–74.
28. van den Belt AJ, Becker CK, Dik KJ. Desmitis of the accessory ligament of the deep digital flexor tendon in the horse: clinical and ultrasonographic features. A report of 24 cases. Zentralbl Veterinarmed A 1993; 40(7):492–500.
29. Embertson RM. Congenital abnormalities of tendons and ligaments. Vet Clin North Am Equine Pract 1994; 10(2): 351–364.
30. Becker CK, Savelberg HH, Barneveld A. In vitro mechanical properties of the accessory ligament of the deep digital flexor tendon in horses in relation to age. Equine Vet J 1994; 26(6): 454–459.
31. Keg PR, Schamhardt HC, van Weeren PR, et al. The effect of the high palmar nerve block and the ulnar nerve block on lameness provoked by a collagenase-induced tendinitis of the lateral branch of the suspensory ligament. Vet Q 1996; 18(suppl 2):S103–105.
32. Muylle S, Desmet P, Simoens P, et al. Histological study of the innervation of the suspensory ligament of the forelimb of the horse. Vet Rec 1998; 142(22):606–610.
33. Dyson SJ, Romero JM. An investigation of injection techniques for local analgesia of the equine distal tarsus and proximal metatarsus. Equine Vet J 1993; 25(1):30–35.
34. Dyson SJ, Arthur RM, Palmer SE, et al. Suspensory ligament desmitis. Vet Clin North Am Equine Pract 1995; 11(2): 177–215.
35. Dyson S. Proximal suspensory desmitis in the hindlimb: 42 cases. Br Vet J 1994; 150(3):279–291.
36. Dyson S. Proximal suspensory desmitis: clinical, ultrasonographic and radiographic features. Equine Vet J 1991; 23(1):25–31.
37. Bukowiecki CF, Bramlage LR, Gabel AA. In vitro strength of the suspensory apparatus in training and resting horses. Vet Surg 1987; 16(2):126–130.
38. Belknap JK, Baxter GM, Nickels FA. Extensor tendon lacerations in horses: 50 cases (1982–1988). J Am Vet Med Assoc 1993; 203(3):428–431.
39. Simmons EJ, Bertone AL, Weisbrode SE. Instability-induced osteoarthritis in the metacarpophalangeal joint of horses. Am J Vet Res 1999; 60(1):7–13.
40. Collard XR, Danse EM, Rombouts JJ. [The syndrome of external ligament sprain in the horse.] Acta Orthop Belg 2000; 66(3):229–241.
41. van der Harst MR, Rijkenhuizen AB. The use of a polypropylene mesh for treatment of ruptured collateral ligaments of the equine metatarsophalangeal joint: a report of two cases. Vet Q 2000; 22(1):57–60.
42. Crabill MR, Chaffin MK, Schmitz DG. Ultrasonographic morphology of the bicipital tendon and bursa in clinically normal quarter horses. Am J Vet Res 1995; 56(1):5–10.
43. Jeffcott LB. Disorders of the thoracolumbar spine of the horse – a survey of 443 cases. Equine Vet J 1980; 12(4): 197–210.
44. Gillis C. Spinal ligament pathology. Vet Clin North Am Equine Pract 1999; 15(1):97–101.
45. Dyson SJ, Kidd L. Five cases of gastrocnemius tendinitis in the horse. Equine Vet J 1992; 24(5):351–356.
46. Hago BE, Plummer JM, Vaughan LC. Equine synovial tendon sheaths and bursae: an histological and scanning electron microscopical study. Equine Vet J 1990; 22(4):264–272.
47. Hago BE, Vaughan LC, Plummer JM. Equine synovial tendon sheaths and bursae: a transmission electron microscope study. Equine Vet J 1991; 23(6):475–478.
48. Dyson SJ, Dik KJ. Miscellaneous conditions of tendons, tendon sheaths, and ligaments. Vet Clin North Am Equine Pract 1995; 11(2):315–337.
49. Barr AR, Dyson SJ, Barr FJ, et al. Tendinitis of the deep digital flexor tendon in the distal metacarpal/metatarsal region associated with tenosynovitis of the digital sheath in the horse. Equine Vet J 1995; 27(5):348–355.
50. van den Berg MJ, Rijkenhuizen AB, Nemeth F, et al. The fetlock tunnel syndrome: a macroscopic and microscopic study. Vet Q 1995; 17(4):138–142.
51. Gaughan EM, Nixon AJ, Krook LP, et al. Effects of sodium hyaluronate on tendon healing and adhesion formation in horses. Am J Vet Res 1991; 52(5):764–773.
52. Fortier LA, Nixon AJ, Duchorme NG, et al. Tenoscopic examination and proximal annular ligament desmotomy for treatment of equine 'complex' digital sheath tenosynovitis. Vet Surg 1999; 28(6):429–435.
53. Dik KJ, Dyson SJ, Vail TB. Aseptic tenosynovitis of the digital flexor tendon sheath, fetlock and pastern annular ligament constriction. Vet Clin North Am Equine Pract 1995; 11(2): 151–162.
54. Rothlisberger U, Kaegi B, Geyer H, et al. [The fetlock tunnel syndrome in horses: literature review and retrospective study.] Schweiz Arch Tierheilkd 2001; 143(6):285–293.

CHAPTER 21

Back and pelvis

Leo B. Jeffcott and Kevin K. Haussler

Introduction and historical perspectives

Historical reports of back disorders in horses provide few firm facts from the many lengthy accounts in old farriery and veterinary textbooks. In 1876 Lupton remarked that back injuries 'are among the most common and least understood of equine afflictions'.[1] In those days diagnosis was based simply on clinical observation (Fig. 21.1) and the opinions expressed were many and varied. These early writers were often excellent horsemen and were particularly knowledgeable on aspects of conformation. In relation to the incidence of spinal damage, Youatt believed that the short-backed horse showed less tendency to back problems and could be expected to carry more weight and possess greater endurance, but it did not have much potential for speed.[2] The long-backed horse was built for speed but was much more prone to weakness when ridden. Conformationally correct horses should have a gentle ventral curve immediately behind the withers, followed by a straight line to the lumbar region. An increase in this vertebral curvature (i.e. lordosis, saddle-backed, sway-backed) would increase the tendency to weakness and strain. Dorsal curvature (roach-back), however, was considered to be a more severe defect, which seriously impaired usefulness and performance.

Back problems in horses cause a considerable degree of wastage and lost performance in almost all types of athletic horses. However, reports of their incidence are limited to a survey from general practice in the United Kingdom in the 1960s that showed an incidence of only 0.9% in 6588 horses.[3] This is probably an underestimate and no breakdown of these cases into the specific diagnosis was made, but a later review of 443 horses with back problems did categorize cases further into osseous, soft tissue and miscellaneous disorders.[4] Definitive diagnosis is often difficult due to vague clinical signs and the lack of good pathological reports.[5,6] This has inevitably resulted in widespread controversy engendering many unsubstantiated opinions, which only increase the state of confusion. Much of this controversy has resulted from the general dearth of knowledge of the functional aspects of the equine thoracolumbar spine and scientific studies on the pathogenesis of back problems in horses. It is also clear that many horses perform poorly without an underlying back problem and many other horses perform surprisingly well in spite of one. In recent years there has been an encouraging progression of studies and biomechanical research to improve this situation.[7–12] There is also much more willingness for those involved with traditional methods of clinical medicine to work closely alongside those involved with spinal manipulative therapy and

Fig. 21.1
A test for rick of the back (from reference[1]).

complementary medicine.[13] The purpose of this chapter is to try and combine all these aspects for the benefit and treatment of suspected cases of back pain.

Anatomic and functional considerations

Thoracolumbar vertebral column

Individual vertebrae are connected by an intricate system of ligaments and musculotendinous structures that provide stability while at the same time supporting movement of the vertebral column. The three principal mechanical functions of the vertebral column are:

1. protection of the spinal cord and associated nerve roots (i.e. vertebral arch)
2. providing support for weight bearing and soft tissue attachment (i.e. vertebral body and vertebral processes)
3. maintaining movement for flexibility and locomotion (i.e. articulations, ligaments, and muscles).

The equine thoracolumbar vertebral region consists of an average of 24 individual vertebrae, based on the typical vertebral formula (C7, T18, L6, S5, Cd15–21).[14] Variations in the number of vertebrae within the thoracolumbar vertebral region are common and are often compensated by a reduction or increase in the number of vertebrae in an adjacent vertebral region.

Vertebral motion segment

The structural and functional unit of the vertebral column is the vertebral motion segment. A vertebral motion segment consists of two adjoining vertebrae and interposed soft tissue structures (Fig. 21.2). The typical vertebra is characterized by a vertebral body, vertebral arch and vertebral processes that vary in each vertebral region according to structural and functional demands. The vertebral body is a ventral cylindrical structure covered dorsally by the vertebral arch, which includes bilateral pedicles and laminae. Vertebral processes include one spinous process, two transverse processes and two pairs of cranial and caudal articular processes on each vertebra. Mamillary processes are additional vertebral processes found only in the thoracolumbar region that provide added paraspinal muscle attachment sites. Dorsally, the articular processes create bilateral synovial articulations (i.e. zygapophyseal joints) that provide segmental stability and mobility to the vertebral motion segment. Ventrally, the vertebral bodies and intervertebral disks form fibrocartilaginous joints that also provide segmental vertebral stability and mobility. Additional connecting soft tissues include both short and long spinal ligaments and muscles. The vertebrae, vertebral articulations and ligaments are innervated segmentally by sensory branches of the dorsal rami and recurrent meningeal nerves. These nerves mediate nociception and proprioception within the vertebral column.

The vertebral motion segments of the upper cervical region (i.e. occiput-C1–C2) are a highly mobile, specialized joint complex. The cervical vertebrae have rudimentary spinous processes and characteristic transverse foramina for the passage of vertebral vessels. The thoracic vertebrae are characterized by tall spinous processes (highest at T4–6), costal articulations and an anticlinal vertebra at T16. The lumbar vertebrae have long, horizontally flattened transverse processes and intertransverse joints in the caudal region (L4–S1) that are unique to horses. The sacrum is usually made up of five fused segments and has bilateral sacroiliac joints for articulation with the pelvis. The caudal vertebrae are characterized by progressively rudimentary vertebral arches and vertebral processes.

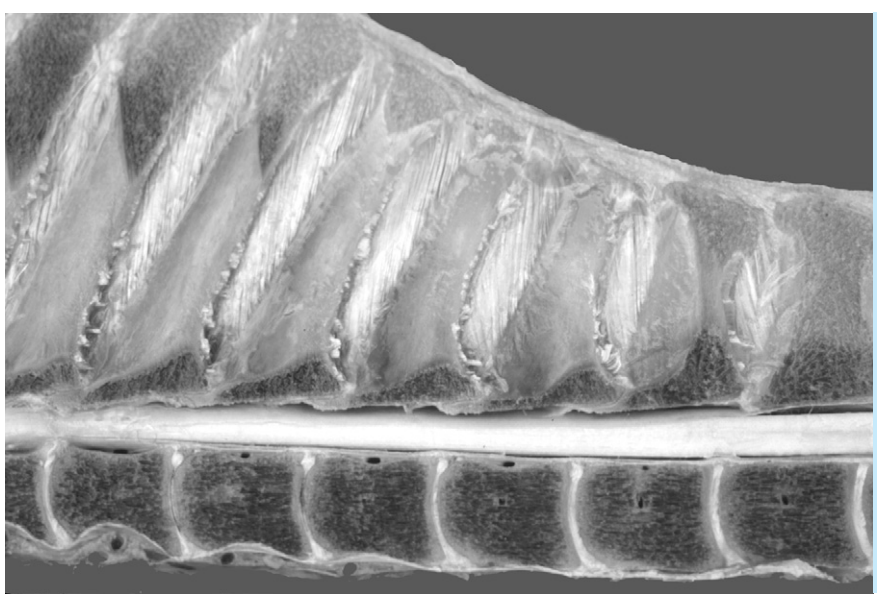


Fig. 21.2
Sagittal section of the thoracic vertebral region (T8–T14) demonstrating osseous vertebral structures and supporting spinal ligaments.

Vertebral body and intervertebral disk

The vertebral bodies form the foundation on which the remaining vertebral structures are placed. The cranial vertebral body is convex in shape and the caudal vertebral body is concave (Fig. 21.2). Therefore, most equine intervertebral joints resemble a ball-and-socket configuration, which provides stability without restricting mobility. Vertebral bodies provide support for weight bearing, connective tissue attachment and muscular attachment sites for the diaphragm and psoas muscles in the lumbar vertebral region. The intervertebral disks connect adjacent vertebral bodies and together are classified as fibrocartilaginous articulations. An intervertebral disk consists of an outer annulus fibrosus and central nucleus pulposus. The nucleus pulposus is rudimentary in the thoracolumbar vertebral regions compared to the cervical and caudal vertebral regions (Fig. 21.2). The dorsal and ventral longitudinal ligaments, and the costovertebral ligaments, provide additional reinforcement to the periphery of the intervertebral disk. The intervertebral disk is active in weight bearing, axial shock absorption and maintaining vertebral flexibility. The outer one-third of the intervertebral disk is innervated by both proprioceptive and nociceptive fibers.

Spinous processes

The spinous processes project dorsally from the vertebral arch and vary in size, shape and orientation in different vertebrae and vertebral regions (Fig. 21.3). The spinous processes function as a series of levers for muscle and ligamentous attachment that provide support and movement to the vertebral column. Spinal extension and rotation are produced by contraction of muscles attached to the spinous processes. The supraspinous ligament stabilizes the apex of the spinous processes and aids in resisting excessive spinal flexion. The spinous processes in the cranial thoracic vertebral region are angled caudally and elongated in the region of T2 to T12 to form the withers. The cranial thoracic vertebral region must resist forces produced by the head, neck and forelimbs, whereas the caudal thoracic and lumbosacral vertebral region has to resist significant forces associated with the rear limbs and locomotion. The divergent spinous processes of the lumbosacral junction produce a wide interspinous space, compared with the adjacent interspinous spaces.[15–17] The lumbosacral spinous process divergence supports an increased range of motion at the lumbosacral junction without the risk of spinous process impingement.

Articular processes

Two pairs of cranial and caudal articular processes arise dorsolaterally from the vertebral arch. An articular surface on the articular processes contributes to the formation of bilateral synovial articulations (i.e. zygapophyseal joints). The articular surfaces in the thoracic vertebral region lie horizontally (i.e. dorsal plane) with the cranial articular surfaces facing dorsally and the caudal articular surfaces facing ventrally. Vertebral motion in the thoracic vertebral region is limited mostly to rotation and lateral flexion. The lumbar vertebral region has articular surfaces that predominantly lie vertically (i.e. sagittal plane). Vertebral motion in the lumbosacral vertebral region is limited mostly to dorsoventral flexion. The articular processes function in support and movement of the vertebral arch. The amplitude and direction of segmental vertebral motion are related to the size, shape and orientation of the articular surfaces and functional status of the articulations.[15,16,18] Regional and overall spinal motion is due to the cumulative effects of small amounts of segmental vertebral motion. The zygapophyseal joint capsule has a dense outer fibrous layer, vascular central layer and an inner layer consisting of the synovial membrane. The zygapophyseal joint capsule is richly innervated with sensory nerve fibers from the medial branch of the dorsal rami of several adjacent nerve roots. Proprioception and nociception are two important neurologic functions of the zygapophyseal joints.[19,20] Multilevel spinal innervation of the zygapophyseal

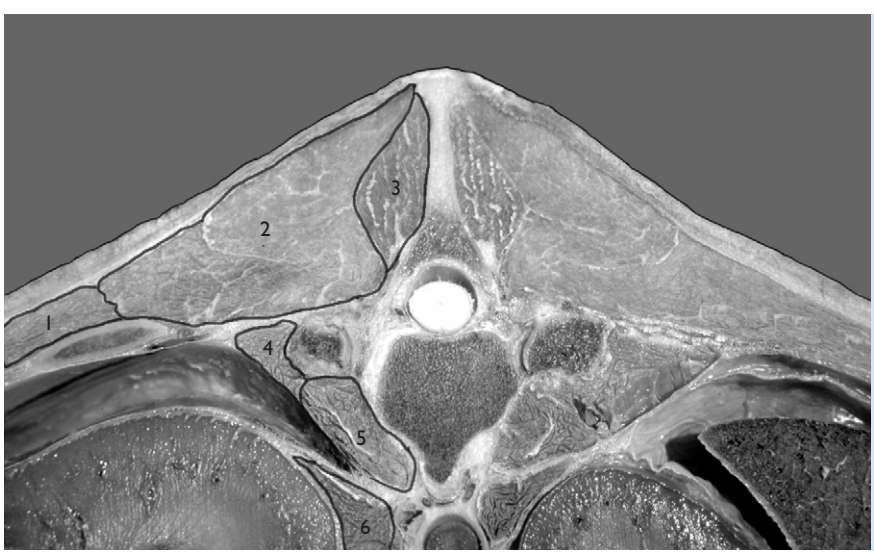


Fig. 21.3
Transverse section at the T18 vertebral region. Outline of the muscles represented are: (1) iliocostalis, (2) longissimus, (3) multifidi, (4) psoas major, (5) psoas minor and (6) crus of the diaphragm.

articulation produces non-localized pain patterns, which contribute to the difficulty of identifying and localizing back problems.[21]

Transverse processes

The transverse processes provide support and movement to the vertebral column via muscular and ligamentous attachments. Transverse processes are used as lever arms by the deep spinal muscles to maintain posture and to induce rotation and lateral flexion.[21] In the thoracic region, the transverse processes contain articular surfaces that contribute to the costotransverse articulations. The lumbar vertebral region has elongated, horizontally flattened transverse processes that provide attachment sites for the large dorsal paraspinal muscles and ventral psoas muscles. Species of the genus *Equus* have intertransverse synovial articulations between the transverse processes of the last two or three lumbar vertebrae and at the lumbosacral junction.[15,16] Biomechanically, the intertransverse joints aid in the transfer of propulsive forces from the hindlimbs to the vertebral column and provide resistance to lateral bending and axial rotation of the spine.

Sacroiliac joint

The pelvis articulates with the vertebral column at bilateral sacroiliac articulations, located at the junction between the ventral wing of the ilium and the dorsal wing of the sacrum (Fig. 21.4). Dynamically, the sacroiliac joints aid in locomotion via transfer of hindlimb propulsive forces to the vertebral column.[22] The articular surfaces of the sacroiliac joint are nearly flat and closely apposed to support gliding movements. The sacroiliac joint is usually L-shaped with the convex border directed caudoventrally. The sacroiliac joint capsule is thin and closely follows the margins of the sacroiliac articular cartilage. The sacroiliac joint is supported by three bilateral sets of strong sacroiliac ligaments that act to support weight of the caudal vertebral column. The dorsal sacroiliac ligaments, consisting of a dorsal and lateral portion, connect the tuber sacrale to the sacrum. The interosseous sacroiliac ligaments are the most robust of the sacroiliac ligaments, spanning the space between the ventral wing of the ilium and the dorsal wing of the sacrum. The ventral sacroiliac ligaments connect the ventral wings of the sacrum to the ilium. The sciatic nerve, cranial gluteal nerve and cranial gluteal artery and vein travel through the greater sciatic foramen, immediately ventromedial to the sacroiliac articulation.

Spinal ligaments

A series of long and short spinal ligaments contribute to vertebral column stability. Three separate longitudinal spinal ligaments span the length of the vertebral column and provide regional vertebral stability. The nuchal ligament in the cervical vertebral region continues as the supraspinous ligament in the thoracolumbar vertebral region and joins the tips of the spinous processes. The dorsal longitudinal ligament connects the dorsal vertebral bodies within the vertebral canal and acts to reinforce the intervertebral disk (Fig. 21.2). The ventral longitudinal ligament attaches to the ventral vertebral bodies and blends with fibers of the intervertebral disk. The short spinal ligaments interconnect individual vertebral structures and function to protect the spinal cord and to provide segmental vertebral stability. Interspinous ligaments connect adjacent spinous processes. The ligamenta flava span the space between adjacent vertebral laminae. Specialized costovertebral and costotransverse ligaments provide additional stability to the thoracic vertebral region and ribs. The intertransverse ligaments connect adjacent transverse processes in the lumbar vertebral region and limit lateral flexion. The intervertebral disk can be considered a specialized connective tissue structure that connects adjacent vertebral bodies.

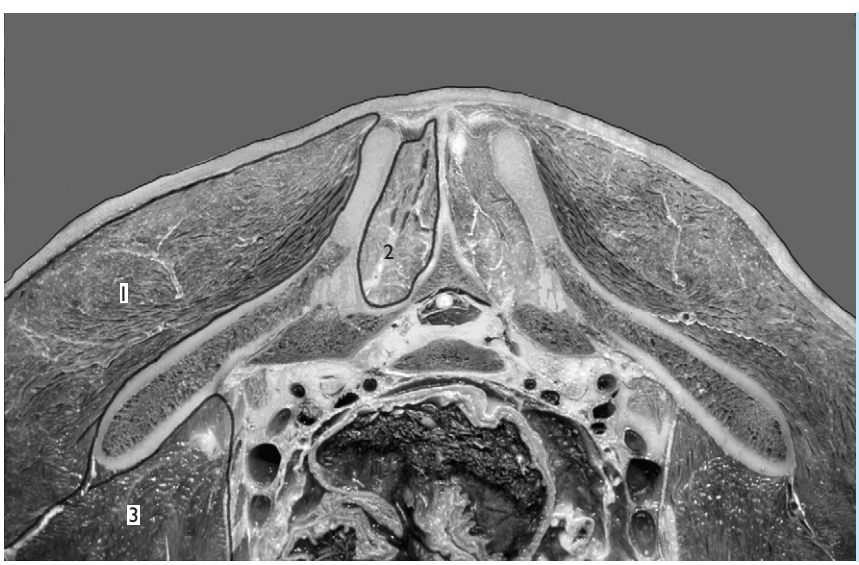


Fig. 21.4
Transverse section at the lumbosacral and sacroiliac articulations. Outline of the muscles represented are: (1) gluteus medius, (2) sacrocaudalis dorsalis, (3) iliopsoas (psoas major and iliacus). The tuber sacrale and the interosseous and ventral sacroiliac ligaments are also shown.

Intrinsic spinal muscles

Muscles that attach only to the axial skeleton are considered intrinsic spinal muscles. The spinal musculature can be categorized into epaxial or hypaxial muscle groups based on their location compared with the transverse processes of the vertebral column. The epaxial muscles lie dorsal to transverse processes, are segmentally innervated by dorsal branches of spinal nerves and produce spinal extension and lateral flexion. Hypaxial muscles lie ventral to transverse processes, are segmentally innervated by ventral branches of spinal nerves and produce spinal flexion and lateral flexion. The thoracolumbar fascia is an aponeurosis that serves as an attachment site for many spinal and proximal limb muscles. The thoracolumbar fascia is strong and attaches to the thoracolumbar spinous processes and the cranial edge of the ilial wing. The largest group of epaxial muscles is organized into three parallel columns. These include (from lateral to medial) the iliocostalis, longissimus and spinalis muscle groups (Fig. 21.3). The iliocostalis muscles are a thin muscle group that attaches to the angle of the ribs and the tips of the lumbar transverse processes. The longissimus muscles are by far the largest and longest group of back muscles. These muscles primarily attach to the dorsal spinous and transverse processes of the thoracolumbar vertebral region and the wing of the ilium and help to support the weight of saddle and rider. The spinalis muscles cover the lateral aspects of spinous processes of the withers and may be compromised by a narrow saddle. The transversospinalis muscle group is the deepest and most medial muscle group (Fig. 21.3) and is largely composed of multifidi muscles in the thoracolumbar vertebral region. The multifidi muscle group is a series of short musculotendinous units that originate from transverse, articular and mamillary processes and insert on adjacent spinous processes. These short muscles span 2–4 vertebrae and are segmentally innervated by dorsal spinal branches.

The epaxial muscles produce spinal extension when activated bilaterally, and lateral flexion and rotation when activated unilaterally. Superficial muscle groups usually span one or more vertebral regions, whereas deep spinal muscles usually only span a few vertebrae.[22] The spinal musculature is important for movement, posture and flexibility. The superficial spinal muscles are usually more dynamic and play a role during regional vertebral motion, energy storage and force redistribution during locomotion.[22] Deep, short spinal muscles have more of a static function and are active in segmental stabilization, proprioception and posture.

Extrinsic spinal muscles

Muscles that have attachments on the proximal limbs and the axial skeleton can be considered extrinsic spinal muscles (or extrinsic limb muscles). The general function of the extrinsic spinal muscles is to induce proximal limb motions required in locomotion or to assist vertebral mobility, depending on whether the vertebral column or limbs are held stationary relative to each other. The shoulder girdle muscles can be categorized into dorsal or ventral muscle groups.[23] The dorsal muscles of the shoulder girdle act to suspend the forelimbs from the neck and trunk. The dorsal shoulder muscles include the brachiocephalicus, omotransversarius, trapezius, rhomboideus, cutaneous trunci and latissimus dorsi. The ventral muscles of the shoulder girdle function in suspending the neck and trunk from the forelimbs. The ventral shoulder muscles include the subclavius, superficial pectoral, deep pectoral and serratus ventralis.

The pelvic girdle muscles are best characterized as cranial-caudal and lateral-medial muscle groups.[23] The cranial muscles of the pelvic girdle function in hindlimb protraction and hip flexion. Muscles in this group include the sartorius, iliopsoas, tensor fasciae latae and rectus femoris. The caudal muscles of the pelvic girdle produce hindlimb retraction and hip extension. Muscles in this group include the biceps femoris, semitendinosus and semimembranosus. The lateral muscles of the pelvic girdle mostly cause hindlimb abduction and include the superficial, middle and deep gluteal muscles. The medial muscles of the pelvic girdle produce hindlimb adduction and include the gracilis, pectineus and adductor muscles.

The hypaxial or sublumbar muscles include the psoas minor, psoas major and iliacus. The psoas minor and psoas major originate on the ventral vertebral column (T16 to L6) and insert on the pelvic inlet and lesser trochanter of the femur, respectively. Together, the psoas major and iliacus form the iliopsoas, the largest flexor of the coxofemoral joint (Fig. 21.4). If the rear limb is stabilized, then the iliopsoas muscle induces flexion of the lumbar spine and pelvic flexion about the sacroiliac articulations.

Diagnostic challenges

Back pain perception

Quantifying the degree of pain in horses and establishing the precise site of pain has always been difficult[24] and horses with back pain are no exception. The situation is further complicated as the major clinical sign recognized in many horses with a back problem is impaired performance and not thoracolumbar pain. On the other hand, many horses apparently perform satisfactorily in spite of some low-grade back pain. To add to this confusion, some horses appear to be naturally sensitive or 'thin-skinned' and resent being groomed or palpated along the back. In these patients, both owners and clinicians can falsely interpret an evasive response to innocuous stimuli as a sign of back pain. Another difficulty in the assessment of back pain involves the condition known as 'cold back' in which there is apparent hypersensitivity over the back with a transient stiffness and ventroflexion (i.e. extension) of the spine as the rider gets into the saddle. There are usually no other demonstrable clinical signs, although in severe cases the horse may buck and rear when first ridden. In some instances the back is roached (i.e. flexed) and the

back muscles are kept rigid. The initial stiffness from being saddled or mounted usually wears off within a few minutes and thereafter no effect on performance is noted. Whether this condition is actually painful, associated with some previous back pain or is merely a matter of temperament is unclear.

Many of the difficulties in clinical diagnosis of back problems would be solved if some meaningful criteria for the assessment of pain and an objective system of quantifying it could be established. In human medicine, back pain is considered to be as much a problem of pain as a problem of the back. The origin of primary back pain is irritation of the dorsal nerve roots and the branches of the spinal nerves. The back, like most tissues of the body, is equipped with a specific system of nerve endings that are particularly sensitive to tissue dysfunction (Fig. 21.5). Nociceptive receptors are represented in the back by plexiform and freely ending arrangements of unmyelinated nerve fibers. Nociceptive fibers are distributed throughout the skin and subcutaneous tissues, adipose tissues, fasciae and ligaments, periosteum, dura mater, adventitia of blood vessels and fibrous capsules of interneural articulations and sacroiliac joints. In normal circumstances this receptor system is relatively inactive but it is activated when chemical, mechanical or other damaging factors are applied to the tissues containing the unmyelinated nerve endings. Primary back pain therefore results from trauma or irritation of these nociceptive receptor nerve endings. Various other pain syndromes are recognized in man and include secondary, referred and psychosomatic backache, but their importance in the horse is unproven as yet.

Another important factor to be considered is the marked variation in response to pain. Even in humans a meaningful measurement of 'pain threshold' is unrealistic as patients can vary in the intensity of their experience of pain from day to day and even at different times during the day. In horses, temperament is felt to be an important contributory factor. It is suggested that the lowered performance is sometimes due to the horse attempting to 'save its back' even though the clinical signs of pain have abated some time previously. Some credence has been given to this idea by the induction of back pain in trotting horses.[25] Pain was induced by multiple injections of concentrated lactic acid into the left longissimus dorsi muscle. The effect was local pain, stiffness and a noticeable reduction in performance capacity as analyzed by high-speed cinematography on a treadmill. The principal sign of induced back pain in these horses was not lameness, but stiffness and reduced competitive performance.

Lack of specific clinical signs

The most common reason for presentation of a back problem is for poor performance rather than overt back pain. It is not surprising, therefore, that the clinical signs involved will be many and varied and often not specifically related to a pathoanatomic site in the thoracolumbar spine.[26] For these reasons each potential back case should be viewed as a diagnostic challenge and should receive as holistic approach to both diagnosis and treatment as possible.[6] A definitive diagnosis is more often made by the elimination of other differential diagnoses rather than by identification of specific clinical signs related to spinal pathology.[27]

Difficulties of palpating the anatomical structures involved

Many of the lesions associated with back problems involve osseous structures of the thoracolumbar spine that are difficult, if not impossible, to palpate effectively (e.g. vertebral bodies, articular and transverse processes). In the thoracolumbar spine it is only possible to palpate the small apexes of the dorsal spinous processes, although this will vary to some extent with body conditioning and the presence or amount of longissimus muscle atrophy. Locating the site of pain in the back muscles is also difficult as typical palpation procedures may precipitate spasm or contraction of the entire longissimus muscle. The longissimus muscle runs the entire length of the back from its origin at the caudal cervical spine to the insertion on the wing of ilium and sacral spinous processes. The sacroiliac and lumbosacral joints are also

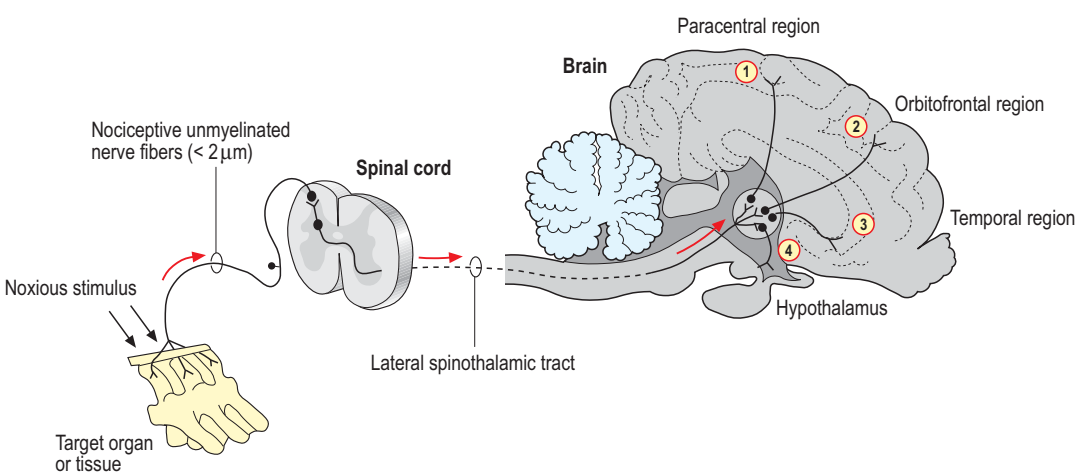


Fig. 21.5 Pain pathways associated with the thoracolumbar spine.

virtually impossible to palpate; the nearest one can get is by rectal palpation. The supraspinous ligament and a portion of the dorsal sacroiliac ligaments are readily palpable, but unfortunately other vertebral or pelvic ligaments (e.g. interspinous, ventral sacroiliac, etc.) are not accessible.

Dearth of appropriate pathological studies

There have been no systematic pathological studies on a large series of back cases in horses. There have been a number of studies on congential deformities[28,29] and reports on diskospondylitis.[30,31] Some investigations on acute and chronic sacroiliac disease have been reported.[32,33] Much has been written about the clinical and surgical treatment of over-riding or impinged dorsal spinous processes (i.e. kissing spines),[34] but very little research has been done on its etiopathogenesis. The widespread use of ultrasonography to diagnose soft tissue injuries of the epaxial structures has dramatically increased the ability to diagnose desmitis, but no pathological studies have been completed to confirm these clinical findings.[35,36]

Box 21.1 Distribution of the general categories of chronic back problems (1992–97).

Total number of horses	268
Primary back problem	268
Secondary back problem	105
Tertiary back problem	32
Total diagnoses	395

Frequency of multiple lesions at multiple sites

Many back problems in horses are associated with chronic or long-standing injuries. It is also common for there to be more than one spinal lesion that contributes to the clinical signs and poor performance. A breakdown of diagnoses of one of the authors' cases (LBJ) from 1992 to 1997 shows a total of 395 diagnoses made from 268 cases presented for examination of the back to a referral clinic (Box 21.1). It is particularly common for cases of over-riding or impinged dorsal spinous processes to be associated with injury of the supraspinous ligament, sacroiliac disease or low-grade hock

Table 21.1 Differential diagnoses to consider for a horse with potential back problems

Type of back problem	General category	Specific lesion or problem
Primary back problem	Soft tissue injury	Longissimus muscle strain
		Supraspinous ligament sprain or desmitits
		Dorsal sacroiliac ligament sprain or desmitits
		Exertional rhabdomyolysis (tying up)
		Non-specific soft tissue injury
	Osseous injury	Conformational or developmental abnormality
		Over-riding or impinged dorsal spinous processes
		Osteoarthritis (e.g. articular processes)
		Vertebral fracture
		Spondylosis
		Diskospondylitis
		Spinal neoplasia (primary and secondary)
	Neurologic disorders	Equine protozoal myeloencephalitis (EPM)
		Equine degenerative myeloencephalopathy (EDM)
		Equine herpesvirus myeloencephalitis (EVH–1)
		Equine motor neuron disease (EMND)
	Tack associated	Poor saddle fit or excessive pressure
	Idiopathic	No clinical abnormalities detected
Secondary back problem		Hindlimb lameness (e.g. spavin)
		Forelimb lameness
		Neck problem (e.g. stenotic myelopathy)
		Acute sacroiliac injury
		Chronic sacroiliac disease
		Pelvic fracture
Presumed back problem		Bad temperament
		Lack of ability (rider or horse)
		Lack of fitness
		Improper tack fit or use
		Dental problems

lameness. Therefore confirmation of such secondary lesions can have important implications for the management and prognosis of horses with primary back problems.

Types of back problems

A serious stumbling block to progress in the diagnosis and treatment of equine back problems is the wide range of opinions that exist. This is true not only within the veterinary profession, but between veterinarians and physical therapists, horse owners and trainers. The lack of authenticated reports and specific studies in this field makes it impossible to set standards for definitive diagnosis and therefore clear guidelines for treatment. The primary clinical sign of back problems in horses is a loss or reduction in performance, whatever the underlying pathogenesis; other clinical signs may be more difficult to precisely define.

Opinions vary as to whether horses genuinely suffer from back problems at all or whether the signs exhibited are referable to damage elsewhere in the skeleton. In our experience genuine back problems do occur, but in a variety of forms (Table 21.1). First, there are those with identifiable lesions in the thoracolumbar spine or epaxial structures (i.e. primary back problems). A second important category are those due to secondary back problems that occur as a result of the pressure or strain exerted from lesions in the appendicular or axial skeleton (i.e. particularly fore- or hindlimb lameness). Finally, there is a category of apparent or alleged back problems which, despite popular opinion, have limited anatomic or pathophysiologic evidence to support their occurrence (Table 21.2). This group of 'back problems' forms the basis of much controversy between veterinarians and other professionals (e.g. chiropractors) or non-professionals (e.g. lay practitioners). These difficulties are exacerbated by the fact that many horses suffer low-grade and chronic lesions. Malalignment or displacement of the caudal thoracic or lumbar dorsal spinal processes is reputed to be a common cause of back trouble in horses.[37] One or more spinous summits are said to become laterally displaced (i.e. 'out of place') and these can apparently be replaced by sharp pressure at the appropriate site (i.e. 'put back into place'). From an anatomic point of view this claim is not acceptable; these structures are not moveable like this either in life or at post-mortem. In spite of the tendency for intervertebral disks to degenerate with age in the thoracolumbar spine, they do not appear to cause any clinical signs similar to those seen so commonly in humans and in dogs. Nerve 'pinching' and peripheral nerve lesions are often claimed to be important causes of back problems, but as yet there has been no scientific evidence to substantiate this belief in horses.

Table 21.2 Conditions alleged to cause back problems in horses for which there is currently no definitive scientific evidence

General category	Specific lesion or problem
Vertebral subluxation	Subluxation of thoracolumbar vertebral bodies or articular processes Misalignment of thoracolumbar dorsal spinous processes
Intervertebral disk injury	Intervertebral disk prolapse or herniation
Peripheral neuropathy	Compromise of thoracolumbar spinal nerves at the intervertebral foramen

Frequency of spontaneous recovery

Many of the problems causing poor performance in horses are long-standing (i.e. many weeks or months in duration) and there is a tendency for these cases to recover spontaneously. In a survey of cases followed over 2 years, a 65% recovery rate was reported irrespective of the diagnosis and the treatment or management regime.[5] The prevalence of spontaneous recovery therefore can hamper elucidation of diagnosis and make evaluation of treatment regimes difficult.

Relationship of back pain to lameness

Lameness is not a typical feature of horses suffering primary back problems. However, secondary back pain is often associated with lameness as the underlying condition causing poor performance. Most primary back cases exhibit only low-grade hindlimb lameness, which is often bilateral and most commonly associated with hock injury. A study in which back pain was induced using lactic acid injections into the longissimus muscles did not produce any signs of hindlimb lameness.[25]

Causes of sacroiliac joint pain or injury have been postulated to be the result of sacroiliac or lumbosacral osteoarthritis, sacroiliac desmitis or sprain, sacroiliac subluxation or luxation, pelvic stress fractures, complete ilial wing fractures or sacral fractures.[38] Additional differential diagnoses include thrombosis of caudal aorta or iliac arteries, exertional rhabdomyolysis, trochanteric bursitis and impinged dorsal spinous processes in the lumbar vertebral region.[39] Horses with presumed thoracolumbar vertebral problems may also have concurrent chronic sacroiliac joint injuries. In a report on 443 horses with back problems, chronic sacroiliac joint problems were identified in 15%.[4] Clinical signs of lower hindlimb lameness may overlap and mimic signs of presumed sacroiliac joint pathology. It is important that a thorough and complete lower limb lameness evaluation is completed prior to or in conjunction with a proximal hindlimb or sacroiliac joint work-up.

Diagnostic protocol to assess back problems

A standardized protocol should be used to systematically examine horses with potential back problems (Box 21.2).

Box 21.2 Diagnostic protocol for the evaluation of horses with potential back problems

Case history
- Signalment and use of the horse
- Onset and duration of clinical signs
- Response to treatment, particularly NSAIDs and manipulation
- Temperament and ability to perform
- Assessment of management and training routine
- Evaluation of predisposing factors
- Experience of the rider

Clinical examination
- Visual inspection of conformation, posture and musculoskeletal symmetry
- Gait evaluation: in hand, lunged, ridden or driven
- Evaluation of concurrent lameness
- Neurologic evaluation
- Postexercise palpation and manipulation
- Soft tissue and osseous palpation
- Regional and segmental joint manipulation
- Rectal palpation
- Examination of tack, particularly saddle fit

Diagnostic imaging
- Radiographic examination – osseous pathology
  Standing: lateral view of the thoracolumbar (T2–L4) and sacrocaudal (S2–Cd4) regions
  General anesthesia: ventrodorsal view of the lumbosacral (L4–S5) region
- Ultrasonography – articular or spinous processes, supraspinous or sacroiliac ligament desmitis
- Nuclear scintigraphy – active inflammation or bone turnover
- Thermography – back or gluteal muscle injury, altered vasomotor tone
- Linear tomography – sacroiliac joint pathology

Laboratory examination
- Hematology
- Biochemistry: muscle-derived enzymes (AST and CK), before and after exercise test
- Serology: vitamin E and selenium levels, viral isolation
- Cerebrospinal fluid analysis
- Muscle biopsy

Additional diagnostic aids
- Diagnostic injections of interspinous spaces, articular processes or sacroiliac joint
- Electrical muscle stimulation
- Therapeutic trial of NSAIDs – effect on performance
- 'Slap test' for evidence of cervical vertebral stenosis causing hindlimb ataxia

History

The value of obtaining a thorough clinical history cannot be overestimated, as the clinical signs and behavioral changes of thoracolumbar disorders are many and varied.[27] Details dating back to the time when the owner first acquired the horse are extremely helpful in deciding whether or not one is dealing with a genuine back problem. In this regard, information on management, tack and performance should always be sought.

Acute versus chronic onset

The history in acute back injuries is usually straightforward as some traumatic incident will have been noticed. For example, young horses with multiple fractures of the dorsal spinous processes from T2 to T10 often have a history of rearing up and falling over backwards onto the withers. Most acute cases involve soft tissue injuries and strain of the longissimus muscles is particularly common.

Chronic problems are commonly encountered when no obvious initiating incident is recognized. One consistent feature of a long-standing back problem is an alteration in the horse's behavior or temperament. This may be insidious in onset and it may take some time before the owner fully appreciates that the change has taken place (e.g. a normally good-natured horse becomes sour and rather fractious to handle or there may be a loss of enthusiasm to work). There also seems to be a correlation between nervous or temperamental horses and the presence of back problems.

Use of the horse

There also seems to be an association with the type of back injury and the type of work the horse is involved in. Jeffcott reported that the differences in incidence of specific back problems varied quite noticeably according to whether the horse jumped at speed, jumped competitively or was not used for jumping at all.[5] Acute sacroiliac strain or subluxation was more prevalent in horses jumping at speed, whereas impinged or over-riding dorsal spinous processes were most common in showjumpers. The incidence of soft tissue damage was much the same in both of these groups and age was not nearly such an important factor in equine back disorders as it is in humans. Spondylosis appeared more frequently in mares, whereas over-riding dorsal spinous processes was most often seen in short-backed Thoroughbred geldings.

Sacroiliac pain is common in dressage horses and causes impaired performance, usually without lameness. Standardbred harness racing also shows a high incidence of sacroiliac and hindquarters problems but over-riding or impinged spinous processes are rare. Back injuries in reining, barrel racing and rodeo horses are not common but are usually associated with muscle injuries. In endurance horses back problems resulting from long periods of extreme exercise and saddle-induced injuries are common.

Concurrent lameness and loss of performance

Positive clinical signs at exercise may include uni- or bilateral hindlimb lameness, a loss of enthusiasm for work or an inability to stride out at fast paces. Owners will often mention a stiffness in the hindlimb action and a loss of suppleness of the back when ridden, although the action when loose in the paddock appears satisfactory. Jumping with a fixed hollow back is frequently encountered or there may well be a reluctance to jump, particularly combination-type fences. The horse may also lose its fluidity and timing during jumping and

become tense, tending to rush over the fences. Signs of head shaking and an increased tendency for tail swishing are other occasional features found in horses with back problems.

Medication and treatment

Since many back problems are chronic in nature, the horse may well have received multiple treatments before your examination. It is therefore important to know what type of medications or therapy have been tried and whether or not they provided any improvement. A clinical trial of phenylbutazone (2 g, p.o., b.i.d. for 4–5 days) is often used to assess the inflammatory component of a back problem. The use of non-steroidal anti-inflammatory drugs (NSAIDs) will often produce an improvement in osseous or articular pathologies although this may be partial and short-lived. A similar clinical trial of methocarbamol (15–44 mg/kg, p.o., s.i.d.) will help some horses with muscle-related back soreness or hypertonicity. Inquiries into the response to rest or changes in activities, such as cross-training, are often helpful in assessing the mechanism of action of the back problem. Some horses, like humans, appear to get burnt out when asked to do repetitive or monotonous disciplines without any changes in routine. Many forms of physiotherapy or spinal manipulative treatment may give temporary improvement, but a lasting success is unlikely without establishing a definitive diagnosis of the back problem.

Management and training ability

It is common for owners to blame poor competitive ability on a problem in the thoracolumbar spine when it is simply due to poor schooling or equitation. It is now well recognized that the most consistent feature in a back problem is a loss of performance, particularly in the ability to jump effectively. Acute soreness in the back muscles is often associated with falling or some other traumatic incident, but a history of obvious pain in the thoracolumbar spine is not always reported, particularly in long-standing cases. Horses with severe back pain may have difficulty in standing to urinate or defecate or there may be a reluctance to lie down or to roll. There may also be resentment to placement of a blanket or to grooming over the loins and hindquarters. In some cases the farrier may note resentment to having a hindlimb picked up or difficulty in standing while being shod.

A history of resentment to any weight on the horse's back is sometimes reported with a tendency to collapse behind when ridden. Saddling up may become a problem, particularly when the girth is tightened. The horse may buck when first mounted, although this is usually due to temperament rather than back pain. The owner may also note reluctance to move backwards or reining back when being ridden. Dramatic signs of bucking and rearing are not usually associated with acute back injuries as it is too painful for the horse to fully flex or extend the spine.

Query into the size and the time spent in stalls, paddocks, or turnout in pasture is indicated for any horse with back problems. In humans, a primary contributing factor for recurrent back problems is bed rest and inactivity.[40] Horses that are stalled for the majority of the day or large portions of the year do not have the opportunity to maintain back flexibility, which may contribute to back stiffness and dysfunction. In addition, horses that are turned out in paddocks with knee-deep mud, large rocks, poor footing or steep hills may aggravate pre-existing back problems.

Rider ability

Equestrian competition involves two athletes – the horse and the rider. There is no question that poor riding can either predispose to a back problem or exacerbate an existing one. Inexperienced or poor riders may blame the poor performance of their horse on a back problem when in fact the blame lies with them. It is also crucial that the saddle used not only fits but is also appropriate for the type of work or competition being undertaken.

Predisposing factors

The conformation and intended use of the horse can have an important bearing on the injury involved. For example, specific spinal malformations (e.g. lordosis and scoliosis) tend to predispose to injury through the inherent weakness of the thoracolumbar spine.[5] These conditions place extra strain on the epaxial muscles of the back that can lead to recurrent soft tissue injuries. The majority of horses do not have severe gross deformities, but conformational defects are common. Horses which are short-backed with restricted flexibility of the spine tend to exhibit more vertebral lesions than the longer backed horses, which have relatively more suppleness and seem to be more prone to muscular or ligamentous strain. Large-framed horses with comparatively weak hindquarters appear to be more susceptible to sacroiliac problems.

Age and gender of the horse are not nearly as important as predisposing factors as they are in humans. The highest incidence of back problems in horses is during middle age, 5–10 years of age,[4] although older horses, like elderly humans, are susceptible to loss of vertebral column flexibility, joint degeneration and loss of muscle strength. Aged horses also have increased healing times and increased chances of having chronic conditions or abnormal musculoskeletal compensations from prior injuries.

Management problems

There are a wide range of management issues that may lead either to a back problem or a suspected one from poor performance. Many of these issues may be due to inexperience or ignorance by the owner and result in inappropriate management, producing signs suggestive of back pain.

Temperament

Horses with an excitable temperament seem to be more prone to back-related problems. This may simply be due to low pain threshold or hypersensitivity, but hyperexcitability often results in excessive tension or spasm of the back muscles. This in

turn reduces spinal flexibility and causes impaired impulsion from the hindquarters, which is seen clinically as poor hindlimb action and performance. In some instances these horses become uncontrollable and will buck and kick violently rather than settle down to exercise properly. A careful examination is required in these horses to be confident there is no underlying spinal pathology or pathoanatomic explanation for the perceived avoidance behavior suggestive of back pain. In addition to employing diagnostic imaging, a short course of analgesics (e.g. NSAIDs) is useful as some improvement would be expected if any musculoskeletal inflammation or injury exists.

Cold back

The signs of a cold back are usually exhibited when the saddle is put on, the girth tightened or as the rider mounts. The horse will then dip or roach its back and keep it very stiff as it moves off. In most cases these signs disappear quickly and within a few minutes the horse's performance is satisfactory. There is no doubt that horses with a cold back worry owners a great deal. In our experience, many of these cases are not associated with underlying pathological findings and are therefore thought to be temperamental or behavioral in origin. There are many different ways to manage these horses, including using saddle pads, warming the horse up before saddling (e.g. lungeing) or medicating mares with estrogen.

Mares in season

Owners sometimes report that mares in estrus have associated back pain and poor performance. It is often difficult to substantiate these claims, although some mares do improve during the winter or if medicated with estrus-suppressive drugs (e.g. altrenogest). Rectal palpation and evaluation of abnormal ovarian structures are indicated in any mare with recurrent or refractory back problems.

Schooling and work regime

Failure to keep a horse properly fit for its purpose may lead to fatigue or muscle strain. Horses can be bored with a dull work schedule and become soured or reluctant to work. This can easily be misinterpreted as poor performance related to a back problem.

Dental problems and bitting

General management of the teeth is part of good equine husbandry. Any problem in the mouth, from sharp teeth to an inappropriate bit, can lead to evasion when working. Affected horses often have a raised head carriage, tension or stiffness of the back muscles and poor hindlimb impulsion.

Inspection

Visual inspection is often the most important initial aspect of examining horses with back problems. The general temperament and behavior are evaluated for signs of pain or discomfort. Horses with back problems often have a sudden change in behavior and become easily irritated by previously innocuous stimuli. Pinning the ears, swishing the tail, refusal to move or exaggerated movements away from everyday objects (e.g. curry comb or saddle pad) are signs of changes in behavior.

Evaluation continues with observation of the patient from a distance while turned loose in the stall or paddock while assessing the use and co-ordination of the limbs and trunk. The exam is focused on evaluating the dynamic characteristics of the musculoskeletal system. Owners may report that the head or neck is carried in an abnormal position, the trunk is held rigid or the horse refuses to move or bucks when asked to go forward. The horse should be able to readily raise and lower its head and neck and bend the trunk to either side. Neck injuries can present as the inability to lower the head

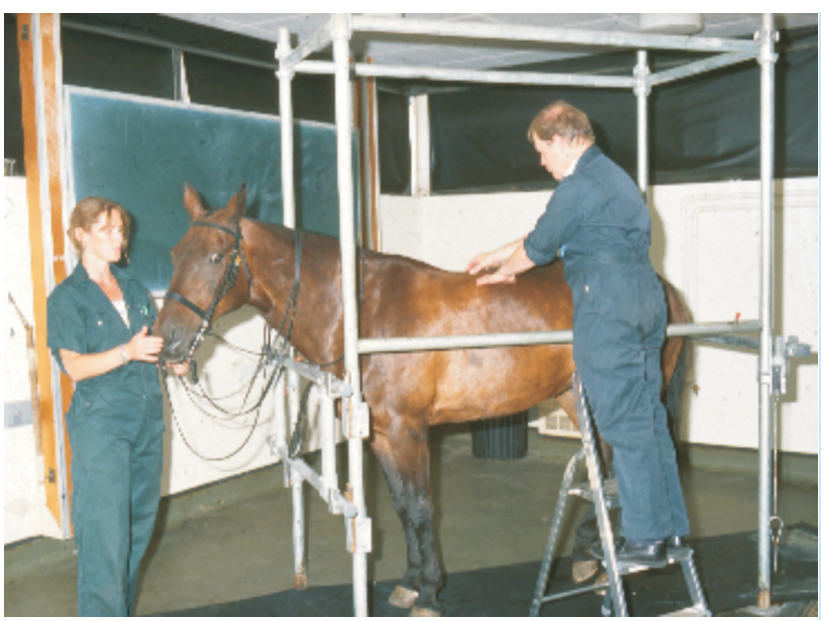


Fig. 21.6
Examination of the horse's back while restrained in stocks. The clinician uses a set of steps to facilitate palpation and manipulation of the thoracolumbar spine.

and neck to graze or, just as common, the consistent inability to raise the head and neck above a certain level. Both instances often have a history of substantial head or neck trauma associated with getting the head or neck trapped in a fence or pulling back or flipping over in the cross-ties. It is important to note the general body conditioning of the horse and to differentiate poor condition (i.e. cachexia) from specific wastage of the longissimus, gluteal and thigh musculature. The presence of any lumps, scars, saddle marks on the back or any undue curvature of the spine must also be noted as they may have some bearing on the underlying condition.

A more detailed examination of the back is best carried out with the horse restrained in stocks (Fig. 21.6). However, it is important that the horse is not stressed or tense, as this will make assessment of back pain even more difficult. If the horse resents the stocks it is better to carry out the examination in the stable. For in-hand evaluation, the horse should be standing quietly and comfortably with all four limbs on a firm, level surface. The horse is then evaluated for the static characteristics of the musculoskeletal system, which include conformation, posture and muscular and osseous symmetry.

Conformation

Conformation is defined as the static or structural relationship of body segments, whereas postural analysis involves the dynamic or functional assessment within and between body regions. Vertebral column conformation is evaluated with special attention to neck development, height and shape of the withers, length of the trunk relative to the height and osseous pelvic symmetry. Conformationally, it is thought that short-backed horses have a higher incidence of osseous disorders whereas long-backed horses are more prone to soft tissue injuries.[6]

Posture

The posture is evaluated for head and neck carriage, development and symmetry of the trunk, tail carriage and a preferred or shifting stance. Alterations in trunk posture include lordosis (sway-back), kyphosis (roach-back) and scoliosis. Abnormal spinal curvatures are often readily visualized and are common primary presenting complaints. Altered spinal posture has both structural and functional etiologies that can often be differentiated based on history, onset and duration of the condition. Congenital vertebral malformations often produce structural changes in the trunk conformation, whereas developmental injuries produce functional changes in the trunk posture. In adult horses, acute changes in spinal curvatures are often functional adaptations to back pain or muscle imbalances. Correction of the underlying problem often returns the trunk to its original posture. Excessive lordosis is often an age-related change in trunk posture and may be improved with induced trunk elevation (i.e. flexion) and abdominal muscle-strengthening exercises. Horses with sacropelvic injuries will often carry their tail off to one side, lack tail tone or movement or have an abnormal tail set.

Muscular symmetry

The pectoral region, dorsal scapular and wither region, epaxial and gluteal muscles are carefully evaluated for abnormal muscle development and left-to-right asymmetries. This is a crucial part of the examination and needs to be carried out in as objective a fashion as possible. Muscular asymmetries are often due to disuse or neurogenic atrophy.[27] Alterations in the pectoral or pelvic girdle muscles need to be localized to the affected muscles, to aid in the differentiation of a primary lower limb, upper limb or vertebral column dysfunction. Localized or segmental muscle atrophy of the epaxial muscles may be due to vertebral segment dysfunction or a consequence of poor saddle fit. Generalized back muscle atrophy needs to be differentiated from lack of muscle development (i.e. poor conditioning) and disuse atrophy associated with chronic hindlimb lameness. Neurologic diseases that produce local or regional muscle atrophy (e.g. equine protozoal myeloencephalitis) need to be ruled out in horses that present with back problems and gluteal muscle asymmetry. It is unwise to assume that instances of asymmetric hindquarters or a 'hunter's bump' are caused by sacroiliac damage.

Osseous symmetry

The dorsal midline of the back is viewed from above (i.e. by standing on a mounting block behind the horse) with the

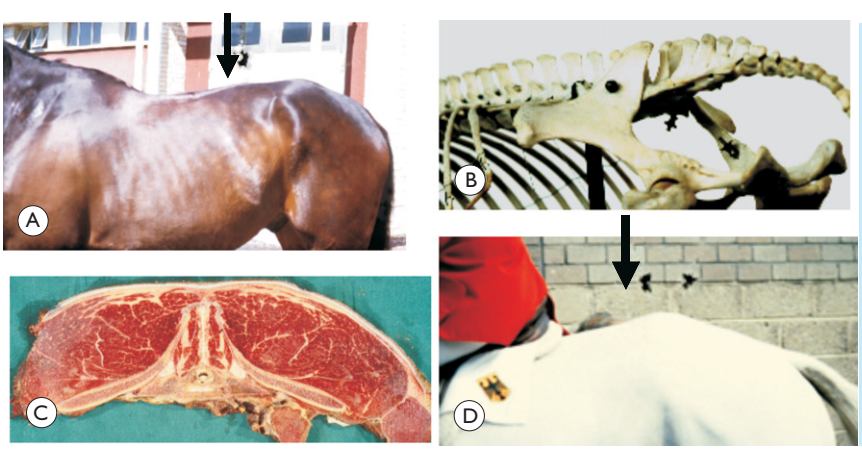


Fig. 21.7
Photograph of a hunters' bump and associated muscle wastage in the lumbar and gluteal regions. (A) Five-year-old Thoroughbred gelding with prominent lumbar spinous processes. (B) Horse's skeleton showing the pelvic and lumbosacral region with the lumbar and sacral spinous processes. (C) Transverse section of the quarters showing the wings of ilium and normal musculature of the region. (D) Fourteen-year-old showjumper with prominent tuber sacrale and poor muscling of quarters.

horse standing squarely on all four limbs to see if the back is straight and evenly developed bilaterally. Any lateral curvature of the spine is suggestive of a degree of muscle spasm on one side (i.e. spastic scoliosis). The presence of a so-called 'hunter's bump' may be seen in some horses although it is not necessarily associated with overt clinical signs of a back problem. This feature is associated with a prominence of the tuber sacrale due to atrophy of the longissimus and gluteal muscles (Fig. 21.7). Changes in the height of the tuber sacrale should be assessed relative to the apex of the second sacral spinous process (S2). Visual acuity is high and even slight (<5 mm) deviations can be perceived. Confirmation of pelvic bone asymmetry can also be performed by palpating the main skeletal features (i.e. tuber sacrale, tuber coxae and tuber ischii) while standing directly behind the horse or by getting two assistants to identify the osseous landmarks for left and right comparisons.

The following guidelines are helpful.

- Unilateral gluteal muscle atrophy on one hindquarter without pelvic bone malalignment: suspect hindlimb lameness (hock or stifle) or acetabular damage.
- Elevation of one tuber sacrale with or without gluteal muscle atrophy: suspect thickening and damage to dorsal sacroiliac ligament or stress fracture of wing of ilium on opposite side (i.e. lowered quarter).
- Lowering of tuber sacrale with muscle atrophy and lowering of the ipsilateral tuber coxae: suspect ipsilateral chronic sacroiliac disease or ipsilateral complete ilial wing fracture.
- Lowering of tuber coxae without lowering of tuber sacrale or tuber ischii: suspect fracture of the tuber coxae.
- Lowering of tuber ischii without deviation of tuber sacrale or tuber coxae: suspect fracture of tuber ischii.

Evaluation of tack fit and use

Saddle fit

A frequent cause of back discomfort can be either an inappropriate saddle used or the saddle not fitting properly. Most poorly fitting saddles produce pressure or pinching over the caudal withers region, hence the appearance of white hairs in the midline. Horses change shape, particularly the contour of the back, when they are out of work (i.e. deconditioned) or if they have an increase in bodyweight. Many saddle-fitting techniques provide a static assessment of the fit of the saddle to the shape and contour of the withers and back. Unfortunately, saddles do not come in a wide variety of sizes for individual fit and comfort, like clothes or shoes for humans. Most horses have to conform to only a few different tree widths and saddle types. Ideally, the saddle should fit comfortably and provide as large an area of contact as possible to help to distribute the rider's weight across the withers and back musculature. Computerized pressure pads help to provide both a static and dynamic assessment of saddle fit, pad thickness and placement, rider influences and changes in pressure associated with different gaits.

Assessment of saddle fit begins with checking the tree for straightness, symmetry and intact bars. The panels are evaluated for left-to-right symmetry and any lumps or depressions that might contribute to uneven pressure. The gullet should be 2–3 fingers wide to provide clearance for the dorsal spinous processes and to provide uniform weight distribution on the panels. The best saddles have wide panels that provide maximal weight distribution of the rider over the thoracolumbar epaxial musculature. Deep palpation of the entire fleece surface of the Western saddle should be done to identify any sharp points from nails or loose conchos.

The owner is asked to place only the saddle, without any pads, on the horse's back in the usual position. The analogy of properly fitting shoes (i.e. saddle) and the appropriate socks (i.e. saddle pad) to your feet works well for assessing saddle fit in horses. The chances are that if the shoe does not fit your foot then adding socks will not, in most instances, make the shoe fit any better. Optimally, there should be 2–3 fingers width of dorsal clearance between the pommel at the front of the saddle and the spinous processes of the withers. If there is less clearance, then the additional weight of the rider in the saddle will most likely reduce the space and cause direct contact and dorsal wear of the pommel on the withers. Greater than three fingers width of clearance is indicative of too narrow a tree that will cause increased lateral pressure on the withers. The rider may also feel unstable in the saddle due to an elevated center of gravity relative to the horse.

Most saddles are positioned with the front panels over the caudal border of the scapula. During locomotion, the scapula normally rotates caudally as the forelimb is fully protracted. If the panels are not flared outward slightly to accommodate the scapula, then the scapula cannot rotate caudally during limb protraction. This results in a shortened stride of the forelimbs. This is a common fault of many Western saddles with rigid, non-flared front panels. The contact between the front panel and the caudal scapula should be constant and uniform. An analogy of the desired pressure is the contact felt with your hand as it slides between the seat of the chair and the bottom of your thigh when you are sitting down. Saddles that are too wide will have increased pressure and contact at the dorsal withers, but the bottom of the panel will gape and protrude away from the lateral scapula. Saddles with too narrow a tree will have severe focal pressure on the dorsal scapular cartilage and you will not be able to fit your hand between the saddle and the scapula, even without the weight of the rider in the saddle. A simple correction on most horses is to slide the saddle back 0.5 to 1″ off the dorsal scapula. The seat should remain level to maintain rider comfort and to prevent unnecessary cranial or caudal displacements of the rider.

Saddle pads

The use of extraneous saddle pads or wedges is often a sign of potential saddle fit problems. When it comes to saddle pads, less is often better. The saddle pad should be tented up into the gullet of the saddle so that it provides clearance over the withers and dorsal spinous processes. Unfortunately, gel pads

and other specialty pads often do not extend to the ventral edge of the front panel and cause a step defect and concentration of forces at the edge of the pad, which usually occurs directly over the caudal border of the scapula. Properly fitting saddles and pads can be evaluated by the dirt or sweat marks present on the saddle pad. Proper fit is identified by the presence of a symmetric or butterfly-shaped dirt pattern, indicative of uniform panel contact over the dorsum of the withers and back. Asymmetric, clean or dry spots on the saddle pad suggest bridging or uneven saddle contact. Blankets, if not fit properly, can also cause severe wear injuries over the withers.

Restraint devices

Evaluation of proper tack fit and use requires that the horse and rider are evaluated while participating in their specific equestrian activities. Harness racing utilizes a plethora of restraint devices, such as stickers, overchecks and hobbles, that need to be assessed as potential contributors to back problems. Additional tack that needs to be evaluated is the appropriate use and fit of the noseband or cavesson, standing or running martingales, draw reins and the chambon during lungeing exercises. Most of these devices are used to correct altered body positioning or use associated with pain or avoidance, inexperience, inability or the induction of artificial gaits. If horses are sound and have good flexibility and strength, then most of these devices are unnecessary.

Gait evaluation

A careful examination at exercise is an important part of the clinical assessment of a horse with a potential back problem. Gait analysis for back problems focuses on evaluating regional vertebral mobility and pelvic motion symmetry, in addition to the typical lameness assessment. Gait analysis may help to rule out lower limb disorders and rule in vertebral dysfunction although limb lameness has been reported in about 85% of horses with back problems.[41] Motion asymmetries, restricted vertebral or pelvic mobility, not tracking straight or lack of propulsion are a few characteristics that are evaluated. Tape on the vertebral column midline may help to visualize subtle lateral bending motion asymmetries or scoliosis. Tape on the tuber coxae may help to visualize subtle pelvic motion asymmetries.

Exercise in hand

The horse is first walked and then trotted on a loose rein in hand in a straight line to detect any obvious abnormalities in gait. Many horses with chronic back trouble show a restricted hindlimb action with poor hock flexion and a tendency to drag the toes of one or both hindlimbs. If there is moderate to severe pain, a wide straddling hindlimb gait is usually seen, but in horses with a low-grade problem the action behind will be very close (i.e. plaiting). Next, the horse is turned as short as possible in both directions to induce lateral bending of the trunk. If back pain is present and there is loss of suppleness, turning is often difficult, resulting in rather jerky movements and spasm of the back muscles. On backing there is sometimes an initial reluctance to move, then the head is raised, the back arched more than usual and some spasm of the back muscles occurs. Another sign of discomfort is the dragging of the forelimb toes on moving backwards. Horses with chronic sacroiliac joint injury will often resent being backed up or down a slope. Severe lameness in one or both hindlimbs is not usually a feature of a thoracolumbar disorder and diagnostic nerve blocks should be used to differentiate this from a genuine back problem. Mild shifting lameness or simply an unevenness of action of one hindlimb is much more commonly seen in horses with back problems. Flexion tests (i.e. spavin test) rarely have any effect on the gait in horses with primary back problems, but are very useful in identifying secondary hock or stifle problems.

Lungeing exercise

A session of 10–15 minutes exercise on the lunge line in a sand ring helps to critically assess a horse's gait. This also provides an opportunity to see any improvement or deterioration in the action as the horse warms up. Horses with stiff backs often show exaggerated contractions or spasms of the longissimus muscles with each stride although this is also seen in horses that are unfit. Horses with restricted hindlimb gait often show poor tracking of the hindfeet (i.e. placement of the hindfeet behind the imprint of the ipsilateral forefoot) and a tendency to drag or plait with the hindtoes. The head carriage may be elevated and the horse looks uncomfortable in work. A poor action is usually best seen at the trot. Some horses with back pain will lunge only at a collected canter. Some difficulty is often seen when changing gait (i.e. transitions) along with an inability to lead on the correct leg (i.e. disunited). The action behind appears to lack impulsion and swishing of the tail is often a feature. However, tail swishing is not always indicative of back pain. Placing a surcingle around the thorax and tightening it has also been used to demonstrate acute or active back pain.

Ridden or driven exercise

Evaluation of the response to placing a saddle and being ridden is important for a complete assessment of horses with back problems. Inspection of the tack for proper use and fit is always suggested on initial examination. Saddles and restraint devices should be evaluated for proper fit, padding and positioning on the horse. It is useful to see the horse saddled up and to note if there is any pain or resentment to tightening the girth or when mounting. A horse may have a 'cold back' when mounted, but this does not necessarily imply an underlying spinal problem. The horse should next be ridden in its intended use or discipline by its regular rider, if possible, during a routine training exercise to assess back and limb use at the walk, trot and canter. Showjumpers should also be jumped over the type of fences that usually cause the most challenge (i.e. combination-type fences). For harness racing horses it is of great benefit to have the horse

driven so as to assess the performance and trotting or pacing gait at fast exercise.

Postexercise examination

After allowing the horse to cool down, it should be exercised in hand again to see if there is any change in the action. This is particularly useful in horses with a low-grade exertional myopathy (i.e. mild rhabdomyolysis or tying up) as they show increased stiffness of the hock and hindquarters.

Orthopedic evaluation

The objective of carrying out an orthopedic evaluation of suspected back cases is to be able to rule out or identify concurrent cervical problems and distal limb lameness, and so assist in confirming a primary thoracolumbar or lumbosacral condition.

Cervical conditions

Neck pain or stiffness will often be associated with poor performance, thoracolumbar stiffness and restricted hindlimb impulsion. Systematic palpation of the cervical region may pinpoint a painful region. Flexion and lateral bending of the neck, either manually or by offering food or a treat to induce cervical bending, will confirm neck stiffness. Further diagnostic tests, including scintigraphy, radiography and thermography, are indicated to confirm diagnosis of a neck problem.

Forelimb lameness

Gait evaluation in a straight line and on the lunge line should highlight the presence of forelimb lameness. Hoof testers, flexion tests and diagnostic nerve or joint blocks assist in identifying and localizing the site of forelimb lameness.

Hindlimb lameness

Gait evaluation may be more difficult particularly if lameness is mild and bilateral (e.g. hock or stifle). Horses with chronic sacroiliac joint injuries often have compensatory stiffness and pain in the proximal hindlimb.[39] Induced hock flexion (i.e. spavin test) is often negative in horses with back problems.[33] In many cases the use of nuclear scintigraphy will help in identifying areas of increased bone activity that may be the seat of lameness. Hoof testers, flexion tests and diagnostic nerve or joint blocks should confirm that you are not dealing with a primary back problem.

Neurologic evaluation

The majority of horses with back problems do not have concurrent neurologic disorders. If a neurologic disease is suspected, then a thorough neurologic evaluation should be pursued before any further back evaluation or imaging modalities are completed. A neurologic examination is indicated in the evaluation of horses with back problems to rule out traumatic, infectious and toxic etiologies. Postural reactions also help to assess the proprioceptive status (i.e. ataxia), weakness or spasticity, which often occur in spinal cord compromise.[42] Suspect horses are moved in tight circles to evaluate fore and hindfoot placement and backed up to assess willingness, strength and co-ordination of the hindlimbs. Walking up and down curbs or over ground poles also helps to assess foot placement. Horses with back pain may drag the hindlimbs.[27] Once a neurologic disease has been diagnosed or treated, any residual back problems should be assessed in light of the past or current neurologic signs.

Medical evaluation

Rectal palpation

Rectal palpation is an important diagnostic test in horses with back problems. Soft tissue injuries, osseous pathology and articular instability of the sacropelvic region may not be evident externally, but only palpable internally. It is also possible to rule out urogenital or gastrointestinal causes of back pain (e.g. colic, infection, masses). The psoas major and psoas minor muscles are palpable at the ventral aspect of the lumbar vertebrae. The iliacus and psoas major together form the iliopsoas muscle, which lies along the lateral wall of the pelvic inlet. These hypaxial muscles are evaluated for pain, swelling (i.e. hemorrhage) or asymmetry, and muscle hypertonicity. In horses with vague, upper hindlimb lameness, the terminal aorta and iliac arteries also need to be examined for the presence of strong and regular pulses or possible thrombi.

Osseous palpation during rectal examination is useful for evaluating pelvic or sacral fractures, pelvic canal symmetry and lumbosacral or sacroiliac degenerative joint disease. Acute pelvic fractures produce substantial pain and possible crepitus with rocking of the pelvis side-to side. Bony callous or bony asymmetries palpable on the shafts of the ilium or ventral sacrum are indicative of prior fractures. The ventral aspects of the caudal lumbar vertebrae are evaluated for irregular bony proliferation, indicative of spondylosis. The sacroiliac joints lie deep to the bifurcation of the iliac arteries, at the dorsolateral pelvic canal. Some horses with acute sacroiliac joint injuries will strongly resent deep palpation either unilaterally or bilaterally over the sacroiliac joint region. Rectal palpation while walking or during externally induced pelvic motions (e.g. dorsoventrally or laterally) helps to directly assess lumbosacral and sacroiliac joint motion internally. Rectal palpation for chronic sacroiliac joint subluxation is usually unrewarding and not diagnostic unless bony proliferation, excess sacroiliac joint motion or joint crepitus during externally applied movements is identified.[39]

Laboratory analysis

A thorough laboratory diagnostic work-up, when clinically indicated, is important for the appropriate differential diagnosis and rehabilitation of horses with back problems. Two

common serum enzymes indicative of skeletal muscle injury or inflammation include creatine kinase (CK) and aspartate aminotransferase (AST). Lactate dehydrogenase (LDH) is not as specific for skeletal muscle injury but the elevation of specific isoenzymes does have diagnostic value.[43] In most instances, these enzymes are not elevated in horses with primary back problems. In suspect horses, a submaximal exercise tolerance test can be performed in a treadmill or after trotting for 10 minutes.[27] Baseline serum samples are taken prior to exercise and compared to 4-hour (peak CK) and 24-hour (peak AST) postexercise values. Urinalysis is indicated if exercise-associated muscle damage (i.e. exertional rhabdomyolysis) is suspected in horses with back muscle pain or hypertonicity. The presence of myoglobinuria is indicative of recent or active ongoing muscle injury.[43]

Hematology is indicated in suspected vertebral osteomyelitis and diskospondylitis to evaluate the presence of anemia, hyperproteinemia, hyperfibrinogenemia, leukocytosis or neutrophilia.[42] Cerebrospinal fluid (CSF) analysis and culture is useful if meningitis is also present. Electrolyte imbalances can be found in exhausted endurance horses, especially when coupled with dehydration or poor thermoregulation. To rule out hyperkalemic periodic paralysis (HYPP), serum potassium levels or the submission of whole blood for genetic testing may be indicated in Quarter Horses with muscle fasciculations and weakness.[43] Serum vitamin E (α-tocopherol) and selenium levels are important in the pathogenesis of nutritional myodegeneration (white muscle disease), sporadic exertional rhabdomyolysis and equine degenerative myeloencephalopathy (EDM). In suspect horses, whole-blood analysis of selenium-dependent glutathione peroxidase (GSH-Px) may also be indicated to assess the selenium status.[43]

Viral isolation and PCR techniques on nasopharyngeal swabs or peripheral blood samples are indicated in suspected outbreaks of equine herpesvirus myeloencephalitis (EVH-1).[42] Paired serum titers can reveal elevated or increasing titers in suspect horses. Serology (e.g. titer or Western blot) may also be indicated in horses with a history or clinical presentation suggestive of Lyme disease or equine protozoal myeloencephalitis (EPM). However, due to difficulties in serology interpretation, synovial tissue biopsies and CSF immunoblot analysis are preferred tests. CSF analysis may reveal elevated protein levels, xanthochromia or pleocytosis in cases of EVH-1, polyneuritis equi, EPM and equine motor neuron disease (EMND). CSF creatine kinase may also be elevated in horses infected with EPM or EMND.[42]

Muscle biopsies may be indicated to rule out EMND, polysaccharide storage myopathy (PSSM) and recurrent exertional rhabdomyolysis (RER).[44] Muscle biopsies provide assessment of muscle fibers, neuromuscular junctions, nerve branches, connective tissue and blood vessels.[43] Both light and electron microscopy, combined with histochemistry, are required for the diagnosis and prognostication of muscle disorders. Dietary analysis is indicated in horses with RER and PSSM. High grain diets may need to be replaced with fat supplementation, rice bran and access to high-quality hay.

Physical examination

The focus of the physical examination of the vertebral column is to identify if a back problem exists and to localize the injury to either soft tissue, osseous or neurologic structures. Traditional orthopedic and neurologic evaluations are important adjunctive assessments used to rule out other, more common causes of lameness and neurologic disorders. The spinal examination also helps to determine if the back problem is acute or chronic and if the vertebral dysfunction is segmental and localized or regional and diffuse.

Subjective assessment and grading of back problems

Vertebral dysfunction is most often characterized by localized pain, muscle hypertonicity, reduced joint motion and subsequent functional disability. The challenge, as with any musculoskeletal injury, is to identify the specific musculoskeletal structures affected and quantify the associated disability or altered function. The most common categorization of musculoskeletal injury consists of mild, moderate or severe degrees. Further quantification may involve the use of a 0–10 scale in an attempt to objectively monitor changes in pain, muscle hypertonicity, reduced joint motion or functional disability (Table 21.3). Subjective parameters can then be assigned a numerical value that can be assessed before and after treatment. The progression or regression of the individual parameters can then be recorded over time since most clinical back problems tend to be chronic or recurrent in nature.

Regional joint motion

Joint range of motion can be assessed either regionally via induced vertebral movements or segmentally via motion palpation of individual vertebral motion segments. Vertebral range of motion is evaluated to detect whether a particular movement is normal, restricted or hypermobile. Regional causes of vertebral movement restrictions may include intra-articular pathology (i.e. osteoarthritis), periarticular soft tissue adhesions, musculotendinous contractures or protective muscle spasms.

Active range of motion The diagnostic evaluation of regional active range of motion (AROM) involves using a carrot or other treat to induce flexion, extension and lateral bending of the neck and trunk. The willingness, coordination and amount of vertebral motion are compared bilaterally. Resistance, struggling to grasp the treat and left-to-right range of motion asymmetries are documented. Similar procedures can be used therapeutically as stretching exercises to increase neck or trunk range of motion.

Active lateral bending range of motion The horse is positioned parallel against the stall wall to stabilize the trunk and pelvis and to provide a surface for the horse to lean against if needed during the active stretches. The positioning also helps to prevent the horse from chasing the treat holder around the stall during the evaluation. The treat is directed towards the elbow and held against the lateral girth region. This

Table 21.3 Subjective assessment and grading of spinal dysfunction

Grade	Scale	Pain	Muscle hypertonicity	Joint stiffness	Overall functional ability
Absent	0	No clinical evidence of pain	No clinical evidence of muscle hypertonicity	No clinical evidence of joint stiffness	Full functional capability
	1	Mild pain	Mild muscle hypertonicity	Mild joint stiffness	Mild restriction in ability
		Precipitate with firm pressure only	Precipitate with firm pressure only	No resistance to any induced movement	Able to work at the walk and trot
		Localized pain	Segmental muscle hypertonicity	Segmental joint stiffness	Able to perform while ridden
Mild	2	Deep structures affected	Unilateral muscle hypertonicity	Unilateral joint stiffness	Work limited during canter, gallop or jumping
		Soft tissue *OR* osseous structures	One muscle group affected	Good overall flexibility	Unable to do advanced maneuvers
		Chronic pain condition	No fasciculations induced with firm palpation	Reduced dorsoventral *OR* lateral bending	Noticeable dysfunction during certain activities
	3	Occasional, mild reaction to grooming	Hypertonicity varies with applied pressure	Stiffness due to muscular restrictions	Mild inco-ordination present
	4	Moderate pain	Moderate muscle hypertonicity	Moderate joint stiffness	Moderate restriction in ability
		Precipitate with moderate pressure	Precipitate with moderate pressure	Tolerates some induced movements	Able to work adequately at the walk
		Regional pain	Regional muscle hypertonicity	Regional joint stiffness	Difficult to perform with rider
Moderate	5	Superficial *OR* deep structures affected	Unilateral *OR* bilateral muscle hypertonicity	Unilateral *OR* bilateral joint stiffness	Work limited to walk or trot only
		Several soft tissue *AND* osseous structures	Two different muscle groups affected	Limited flexibility in one *OR* more directions	Unable to do lateral work or inclines
		Chronic *OR* acute pain condition	Fasciculations induced with firm palpation	Reduced dorsoventral *AND* unilateral bending	Performs activity with much effort
	6	Consistent, moderate reaction to grooming	Hypertonicity worse with applied pressure	Stiffness due to connective tissue restrictions	Moderate inco-ordination present
	7	Severe pain	Severe muscle hypertonicity	Severe joint stiffness	Severe restriction in ability
		Precipitate easily with mild pressure or touch	Precipitate easily with mild pressure or touch	Resents any induced movements	Able to stand comfortably
		Generalized pain	Generalized muscle hypertonicity	Generalized joint stiffness	Unable to perform with rider
Severe	8	Superficial *AND* deep structures affected	Bilateral muscle hypertonicity	Bilateral joint stiffness	Work limited to walk only
		Multiple soft tissue *AND* osseous structures	Multiple muscle groups affected	Poor flexibility in multiple directions	Unable to back up
		Acute pain condition	Spontaneous fasciculations present	Reduced dorsoventral *AND* bilateral bending	Resents all activities
	9	Consistent, strong avoidance response	Constant, severe muscle spasms	Stiffness due to intra-articular restrictions	Severe inco-ordination present
Incapacitated	10	Severe, generalized, unrelenting pain	Severe, generalized, constant muscle spasms	Severe, generalized joint stiffness	Unable to perform at any level
		All soft tissue and osseous structures affected	All muscle groups affected bilaterally	No flexibility induced in any direction	Unable to stand comfortably

motion assesses mid to lower neck flexibility in lateral bending and rotation. Normally, horses should be able to readily touch their nose to the girth and hold the stretch for 5 seconds. The treat is then advanced along the ribs towards the point of the hip (i.e. tuber coxae). This motion assesses trunk flexibility in lateral bending. Normally, horses should be able to readily touch their nose to the point of the hip and hold the stretch for 5 seconds. Horses with back pain or stiffness will not be able to reach their nose to their tuber coxae and notable left-to-right asymmetries in range of motion will

be seen if a back problem only affects structures on one side of the body. The distance of the nose from the tuber coxae can be measured (e.g. 10″ or able to reach the 15th rib) and changes assessed over time.

Active flexion range of motion A treat is directed cranially between the forelimbs and towards the front feet. This motion assesses flexion flexibility of the mid to lower neck and withers. The clinician needs to place a hand on the ipsilateral carpus to prevent knee flexion during the range of motion assessment. Normally, horses should be able to readily touch their nose between the front feet and hold the stretch for 5 seconds. Those with pain or stiffness in the withers or back will not be able to reach their nose to their front feet and will flex one or both of their knees to compensate while reaching for the treat.

Passive range of motion Passive range of motion (PROM) is assessed by measuring the amount and characteristics of joint motion beyond the active joint ranges of motion. These procedures require muscle relaxation so that passive joint motion can be induced and evaluated. However, there may be a high risk of injury if the excessive forces are applied to the body regions, without protective muscle tone. This is especially true when evaluating joint range of motion while under sedation or anesthesia. Most passive joint range of motions are assessed segmentally in non-sedated horses with more refined and detailed motion palpation techniques (see later section).

Active assisted range of motion Active assisted range of motion (AAROM) or spinal reflexes are often assessed with firm pressure applied to specific body regions that secondarily induce characteristic vertebral column movements. Diagnostically, the induced movements are graded as reduced, normal and exaggerated. Therapeutically, the induced movements are often held for a set period of time to induce stretch of hypertonic muscles and creep relaxation of shortened connective tissue (i.e. fascia or ligaments) or to strengthen weak or unco-ordinated agonist muscles via concentric contractions.

Wither elevation Firm pressure applied along the ventral midline at the level of the sternum and cranial linea alba will induce elevation of the withers via isometric contraction of the thoracic portion of the serratus ventralis muscle. Pressure is applied with the fingertips or fingernails of one or both hands. Normally, horses will readily elevate the withers and midthoracic vertebrae (T7–T17) approximately 3–4 cm and hold the position for 5–10 seconds. Horses with cranial thoracic pain or stiffness will not be able to elevate the withers and will resent the applied pressure. Caution needs to be applied to horses with girth sensitivity or pain, since they often resent the applied pressure and may kick out with a hindlimb. This exercise is often indicated therapeutically to induce relaxation of a hypertonic spinalis muscle associated with poor saddle fit (i.e. too narrow a tree).

Trunk elevation Firm pressure applied bilaterally along the muscular groove between the biceps femoris and semitendinosus muscles induces elevation of the back via isometric contraction of the rectus abdominis muscle. The muscular groove is located approximately 10 cm (4″) lateral to the base of the tail. Pressure is applied bilaterally with equal pressure from the fingernail of the index fingers or needle caps, if needed. A variation of the technique involves the application of firm manual compression at the sacrocaudal junction but the response is often less consistent or dramatic. Normally, horses should readily elevate the thoracolumbar vertebrae (T12–L5) approximately 10–12 cm. The induced movement should be controlled and co-ordinated and able to be held for 20–30 seconds. Horses with back pain or stiffness will not be able to elevate the trunk and will resent the applied pressure. Other horses may immediately flex their pelvis and slightly hop upwards on the hindlimbs or step away from the applied pressure. This exercise is similar to muscular efforts required during collection while performing certain dressage movements. It is often indicated therapeutically to induce relaxation of the thoracic or lumbar longissimus muscle hypertonicity associated with back pain, poor collection and coupling of the lumbosacral region and lack of impulsion from the hindlimbs.

Spinal reflexes Firm pressure applied unilaterally along the length of the longissimus muscles will induce localized contraction of the stimulated back or croup musculature. Light pressure with a needle cap or ballpoint pen is applied either along the long axis of the spine or transversely across the longissimus or middle gluteal muscles. There seems to be some confusion as to the clinical significance of the observed response to the applied stimuli. Some clinicians place significance on exaggerated or rapid movement away from the applied pressure, which is believed to be indicative of muscle pain. However, horses often have differing amounts of skin sensitivity or inconsistent responses to various stimuli, which may not be reliable indicators of back pain.[27] Some clinicians believe that resistance or lack of movement away from the applied pressure is clinically significant and indicative of severe muscle guarding or pain and the horse is unable or unwilling to move its back despite the applied pressure. In the author's opinion, the procedure often appears to be an unnecessary and noxious stimulus for most horses with back pain. Other, less noxious means of assessment are more informative in most horses with back pain. The procedure should be reserved for very stoic horses, where a question exists about the ability to actively lateral bend or flex and extend the trunk.

Blunt pressure applied unilaterally to the epaxial musculature will induce three characteristic and repeatable spinal reflexes. The first portion of the reflex occurs as a stimulus is applied to the saddle region (T10–L3). Normally, the horse will respond with an induced contralateral lateral bending and extension of the trunk away from the applied stimulus. Horses with back pain may have an exaggerated response and will rapidly and dramatically move away from the applied stimuli. Other horses, presumably due to excessive muscle guarding or nervousness, will not move away from the applied stimulus and will resist moving their trunk in the characteristic pattern of contralateral lateral bending and extension. The second portion of the reflex occurs as a stimulus is continued along the cranial croup region (L4–S3). Normally, the horse will respond with an induced extension

of the lumbosacral joint. Horses with back pain may have an exaggerated response and will rapidly and dramatically move away from the applied stimulus. Horses with hypertonic or injured iliopsoas muscles would theoretically resent any induced extension of the lumbosacral junction due to secondary stretching of the iliopsoas muscles. The third portion of the reflex occurs as a stimulus is continued along the caudal croup region (S4–tuber ischii) along the muscular groove between the biceps femoris and semitendinosus muscles. Normally, horses will respond with an induced flexion of the lumbosacral joint and ipsilateral lateral bending of the trunk towards the applied stimuli. Horses with back pain may have an exaggerated response to the applied stimuli and will rapidly and dramatically immediately flex the pelvis and step away from the applied pressure. Bilateral application of pressure in the same location will induce flexion of the lumbosacral joint without lateral bending, as described above.

Soft tissue palpation

Any palpation of the musculoskeletal system requires a quiet and co-operative patient. Horses that are moving around and not willing to stand quietly are difficult to assess fully for back problems. The horse's response to being approached and its anticipation of palpation are often used as an indication of potential back pain or hypersensitivity. Many owners will report a change in behavior (i.e. pinned ears, swishing tail) as a horse with back pain anticipates being touched or having the saddle placed on its back. Other complaints include a newly developed sensitivity to being groomed in one particular location on the trunk. The hallmarks of vertebral segment dysfunction include localized pain and abnormal paraspinal muscle tonicity.[45]

Palpation is often a reliable technique used to localize and identify soft tissue and osseous structures for changes in texture, tissue mobility or resistance to pressure.[6,46] The soft tissue layers are evaluated from superficial to deep without simply increasing digital pressure but also shifting attention with discrete palpatory movements. Shapes of structures, transitions between structures and attachment sites may also be palpated.[40] Soft tissue texture and mobility can be compared between the skin, subcutaneous tissues, thoracolumbar fascia and muscle.

Skin and subcutis Acute back pain and inflammation will produce local areas of palpable heat, whereas chronic back problems can be identified by focal regions of colder temperatures, relative to the surrounding or contralateral tissues. Thermography provides an objective measure of temperature variations within the superficial tissues of horses with back problems. The hair, epidermis, dermis and subcutaneous tissues should be evaluated systematically with detailed palpation and observation for potential contributing factors to back pain or discomfort. The hair coat is evaluated for changes in hair texture or alopecia, which are often indicative of abnormal saddle or blanket wear. Asymmetric dirt or sweat patterns after removal of the saddle pad are also important indicators of poor saddle fit. A common presenting complaint for horses with back problems is localized sensitivity to routine grooming or brushing.

The skin around the withers should be evaluated for evidence of acute injuries associated with poor saddle fit or improper blanket wear, which are characterized by localized hair loss, open skin lesions (saddle galls) and signs of inflammation. Chronic saddle fit or blanket wear lesions are identified by the presence of white hairs and scar tissue over the dorsal or lateral aspects of the withers. In some horses, localized sites of edema or hives may occur after riding with a poor-fitting saddle or pad.[27] The epidermis should be evaluated for scabs, scrapes, lacerations, fly bites (ventral dermatitis), sarcoids and dermatophilus (rain scald), which may be primary causes of back pain or are irritated with saddle or girth placement. The dermis is palpated over the trunk region for eosinophilic granulomas or melanomas. Eosinophilic granulomas may regress spontaneously or enlarge and become ulcerated with continued friction in the saddle region. The subcutaneous tissues are palpated for edema or cellulitis, masses, fat deposits and the mobility of the skin over the underlying loose connective tissue. Chronic scar tissue, adhesions and fibrosis may produce back pain if the affected tissues are restricted or pulled on during locomotion or trunk movements. Blood vessels, nerves and lymph nodes are important structures that reside within the subcutaneous tissues.

Connective tissue palpation Connective tissue structures, such as the fascia and ligaments, are systematically evaluated for clinical signs of acute or chronic injury.

Fascia The dense connective tissue that forms the superficial and deep fascia is systematically evaluated for masses, rents, scar tissue and tonicity. The overlying skin and subcutaneous tissues are mobilized by a firm, broad contact. The superficial fascia is assessed for smoothness and uniform tonicity or compliance. The superficial fascia typically forms a superficial covering of muscle bellies, whereas the deep fascia forms folds of connective tissue between muscle bellies and anchors to deeper osseous structures. Severe or deep trauma to the myofascial tissues (e.g. kicks, deep lacerations or abscesses) can produce residual fibrosis that limits adjacent muscular activity and fascial extensibility. The thoracolumbar fascia is the most prominent fascia of the trunk and is particularly evident at the thoracolumbar junction as it blends medially with the supraspinous ligament. In the lumbar region, the thoracolumbar fascia attaches to the cranial aspects of the tuber sacrale and iliac wing, deep to the overlying middle gluteal muscle.

Spinal ligaments The spinal ligaments are systematically palpated for masses, fiber disruption, fibrosis and signs of desmitis (i.e. swelling or pain). The nuchal ligament forms a broad attachment to the dorsal apexes of the spinous processes of the withers and continues caudally as the supraspinous ligament. The supraspinous bursa lies between the nuchal ligament and the T3–T5 dorsal spinous processes. The supraspinous bursa is not normally palpable, unless distended or possibly infected (i.e. fistulous withers). Firm digital pressure is applied dorsally and laterally to the nuchal and supraspinous ligaments and ligamentous attachments at the dorsal spinous processes. The entire length of the

supraspinous ligament is palpated by lateral compression between the index finger and thumb. The induction of spinal flexion will cause the supraspinous ligament to be more prominent and readily palpable.

Pelvic ligaments Unfortunately, most of the pelvic ligaments are inaccessible due to their location deep to the gluteal musculature or within the acetabular region of the hip. The dorsal portion of the dorsal sacroiliac ligament and the caudal portion of the sacrosciatic ligaments are the only palpable ligaments of the pelvic region. The dorsal sacroiliac ligaments are palpable in the croup region as two large round ligaments that originate on the caudal aspect of the tuber sacrale and converge caudally on the sacral spinous processes. Firm digital pressure is applied dorsally and laterally to the dorsal sacroiliac ligaments, bilaterally and individually, to lateralize any localized pain or swelling, indicative of desmitis. The caudal attachment of the sacrosciatic ligament at the tuber ischii is palpable and should be evaluated for pain and symmetry in tonicity. Horses that consistently carry their tail off to one side or have a history of sacral fractures may have palpable differences in sacrosciatic ligament tonicity. The trochanteric bursa is located between the tendon of the accessory gluteal muscle and the greater trochanter of the femur. Like other bursae, it is not palpable unless inflamed or distended. Trochanteric bursitis often presents as upper hindlimb lameness and not as a back problem.

Muscle palpation The trunk and pelvic musculature is evaluated systematically from superficial to deep with detailed palpation of abnormal muscle tonicity, pain or fasciculations. Muscle palpation is done with light but firm pressure applied by a broad contact with the entire hand, not only the fingertips, which may unduly localize the applied pressure and precipitate a pain response (i.e. false positive). Regional muscle tone and development of the neck, trunk and proximal limb musculature is assessed and compared left to right. Muscles are then individually identified and evaluated for masses, fibrosis, swellings or depressions. Individual muscles and their attachments are assessed unilaterally and then compared bilaterally for tonicity and the response to manual palpation (i.e. sensitivity). Local or regional alterations in temperature or texture are carefully palpated for signs of active inflammation.

Muscle development Muscle evaluation begins with observation and palpation of the neck, shoulder, pectoral, wither, trunk, gluteal and thigh muscle development and symmetry. Muscle atrophy can be due to partial or complete denervation, disuse, malnutrition or immune-mediated disorders.[43] Obese horses are often difficult to palpate due to poor muscle development and indistinct myofascial borders. Epaxial muscle development is assessed by laying a hand transversely across the longissimus and middle gluteal muscles. Horses with exceptional back muscle development should have a palpable convexity or outward curvature of the muscles along the entire distance from the withers to the croup. Deconditioning or poor flexibility may contribute to epaxial muscles that are palpably flat between the dorsal spinous processes and the ribs laterally. Horses with chronic back problems or poor saddle fit will have a palpable concavity or inward curvature of the epaxial muscles at the withers or along the trunk. Asymmetries in muscle development may be palpable cranial to caudal, medial to lateral or left to right. The thoracic portion of the spinalis muscle is the most commonly affected muscle in the wither region. The longissimus muscle is the most commonly affected trunk muscle. The middle gluteal and the vertebral portions of the biceps femoris, semitendinosus and semimembranosus muscle are common areas to visualize or palpate muscle asymmetries in the pelvic region.

Muscle tonicity The general muscle tone varies between horses and breeds. Nervous or excited horses will have overall increased muscle tone, whereas stoic, depressed or systemically ill horses will have reduced or sometimes flaccid muscle tone. Arabians tend to carry more muscle tone whereas most Warmbloods or draft breeds will allow deep palpation of their generally relaxed muscles. Muscle tonicity is an indirect measure of muscle activity or contraction. Electromyography (EMG) provides a direct assessment of muscle activity but it is not readily available in most clinical situations and it is often difficult to perform and interpret.[43]

Muscle tonicity is categorized as hypotonicity, normal tonicity and hypertonicity. Normal epaxial muscles are not contracted in a quietly standing horse, but are relaxed and malleable. Muscle hypotonicity or flaccidity is indicative of neuropathies, such as disuse or denervation atrophy. Muscle hypertonicity is the most commonly palpable abnormality in horses with acute or chronic back problems and can have either neural or myopathic origins.[43] Generalized muscle hypertonicity may affect a small portion of a muscle (i.e. trigger point), an entire muscle belly or a regional group of muscles. Muscle spasms are an acute, severe form of muscle hypertonicity, with substantial pain and loss of muscle function. Detailed palpation and a thorough knowledge of muscular anatomy will help to identify which muscle or muscles are primarily affected, and which adjacent muscles are likely to have secondary guarding due to common biomechanical or neurologic factors. In general, localized muscle hypertonicity is considered an acute or primary back problem whereas regional longissimus muscle hypertonicity is often associated with a chronic hindlimb lameness or systemic disease.

Trigger points are characterized as localized bands or foci of muscle contracture and pain within a muscle belly.[47,48] Muscle contractures are not associated with normal neural firing and subsequent depolarization of the muscle membrane.[43] Trigger points occur in consistent and predicable locations, presumably due to alterations in local muscle function caused by changes in posture or biomechanics. In horses with back or pelvic problems, focal hypertonic muscle bands with a lower pain pressure threshold (i.e. increased sensitivity) can often be found in the middle gluteal muscle. The clinical significance of trigger points in the middle gluteal muscle is difficult to determine since they do not always correlate with the presence or severity of lameness or back problems.

Muscle spasms or splinting are characterized as involuntary, pronounced and unremitting muscle contractions in response to severe and unrelenting pain (e.g. colic) or meta-

bolic disturbances (e.g. electrolyte imbalances or exertional rhabdomyolysis). Horses with acute or severe back pain may present with muscle splinting but other underlying medical conditions that may be more life threatening or critical need to be ruled out immediately. Muscle splinting severely restricts the ability to evaluate trunk mobility and the palpation of underlying soft tissue structures. Therefore, medical treatment of the primary problem or the administration of muscle relaxants is often required before a complete evaluation of the vertebral column can be accomplished.

Muscle pain The assessment of muscle pain is often subjective and is dependent on the evaluator's tactile skills and interpretation of clinical significance. The clinical assessment of acute versus chronic pain is relatively straightforward but determination of the exact etiology and appropriate treatment regime are diagnostically challenging. Acute muscle pain is characterized by heat, firm swelling or edema, substantial hypertonicity and pain and dysfunction of the affected muscle region. Acute muscle pain may be due to direct trauma (e.g. kick or other blunt trauma) or metabolic disorders (i.e. exertional rhabdomyolysis). The thoracic portion of the spinalis muscle is a common site of muscle pain, associated with a poor-fitting saddle (i.e. too narrow a tree). Chronic muscle pain has a more neurogenic basis and is due less to direct inflammatory mediators.

Horses with acute sacroiliac joint injuries may have localized sensitivity to palpation of the gluteal musculature and surrounding soft tissues in the dorsal croup region.[33] Protective muscle spasms may be palpated in the adjacent middle gluteal musculature and the vertebral portions of the biceps femoris, semitendinosus and semimembranosus muscles. A localized region of edema may occasionally be palpated over the lumbosacral junction[38] but this is not a specific finding related to sacroiliac joint injury.

Algometry In humans, the diagnosis of chronic fatigue syndrome or fibromyalgia is often based on the presence of decreased pain thresholds at a set number of standardized musculoskeletal locations. The clinical syndrome of myofascial pain in horses is common and quite similar to humans. Unfortunately, we often have a poor understanding of the etiopathogenesis and the objective assessment of muscle pain. Algometry (dolorimetry) of soft tissue structures provides an objective measure of muscle or ligamentous pain pressure thresholds (i.e. the minimum force that causes discomfort or pain).[49] It utilizes a force gauge and plunger to measure left-to-right asymmetries or identify subnormal values.[48] In horses, normal algometry values for soft tissue landmarks are typically 20–30 pounds/cm.[2] Horses with myofascial pain often have algometry values of less than 10 pounds/cm.[2]

Guarding of the back is an exaggerated response to typically innocuous stimuli or sudden movements. This abnormal response is commonly seen in nervous horses or those with back pain. Pronounced muscle guarding with movement away from any anticipated contact or placement of the saddle is considered abnormal. Horses should not react adversely to any grooming or superficial or deep muscle palpation[27] although a few sensitive horses may have a mild, temporary avoidance to deep muscle palpation. Any exaggerated attempts to avoid palpation or the presence of prolonged muscle contractions or fasciculations should be considered abnormal. Horses with back pain and muscle soreness may have localized areas of muscle fasciculations depending on the amount and type of pressure applied.

Muscle fasciculation Muscle fasciculations are usually indicative of profound muscle weakness, electrolyte imbalances or primary muscle pathology although, muscles may fasciculate at characteristic locations distant to an area of palpation.[27] In humans, this is indicative of referred pain, which is difficult to truly assess in horses due to the lack of verbal feedback. In horses with back or gluteal muscle pain, it is common to find areas of muscle fasciculations in the mid-lumbar longissimus muscles when firm, localized pressure is applied to hypertonic or painful areas (i.e. trigger points) within the middle gluteal muscles. This is an intriguing response since the motor innervation of the reactive lumbar longissimus muscles is provided segmentally by dorsal branches of the spinal nerves of L2–L4 and the middle gluteal muscle is innervated by ventral branches of the spinal nerves that contribute to the cranial gluteal nerve (L6–S2).

Osseous palpation

Osseous palpation involves evaluating osseous structures for pain, morphology, asymmetries and alignment. Individual thoracic, lumbar and sacral spinous processes are palpated for a painful response with firm digital pressure applied to the osseous structures of the dorsal midline.[50] Typical signs of discomfort include tossing the head upwards, extension of the back or withers away from the applied pressure or localized secondary muscle spasms. Algometry (pain pressure thresholds) of osseous landmarks provides an objective measure of bony pain and allows monitoring of the effectiveness of treatment protocols. Normal algometry values for osseous landmarks are higher than soft tissue values and typically exceed 30–40 pounds/cm^2. Horses with bone pain often have osseous algometry values less than 10 pounds/cm^2.

Dorsal spinous processes The morphology of individual dorsal spinous processes is compared to adjacent spinous processes. It is common to palpate seemingly higher, wider or laterally displaced dorsal spinous processes. However, unless there is also localized pain or muscle hypertonicity adjacent to the affected dorsal process, then the spinous process deviation is probably not clinically significant. Individual spinous process deviation is common but it is not often associated with spinous process fracture or vertebral malposition (i.e. bone out of place), as is commonly thought. Overlapping or malaligned dorsal spinous processes are often caused by spinous process impingement, developmental asymmetries in the neural arch or isolated dorsal spinous process deviation of unknown etiology.[51,52] Palpably taller or wider dorsal spinous processes occur presumably due to avulsion fractures or osseous proliferation within or at supraspinous ligament insertion sites (i.e. enthesiopathies). Radiographs, ultrasonography and scintigraphy are useful modalities to

document the cause of palpable differences in dorsal spinous processes.

Tuber sacrale The tuber sacrale of the pelvis are palpated for height asymmetries and pain response to manual compression. Unilateral or bilateral prominence of the tuber sacrale may be noted, but is not usually clinically significant unless associated with clinical signs of localized pain or inflammation or positive findings on diagnostic imaging (e.g. scintigraphy). In acute sacroiliac injuries, asymmetry in gluteal muscle development is uncommon, unless pronounced osseous pelvic asymmetry is also present. Firm digital pressure applied to the dorsal aspect of the tuber sacrale has been reported to produce a variable and inconsistent pain response.[53] In the author's opinion, dramatic and consistent pain responses have been produced in affected horses with specific provocation tests that are useful to establish a presumptive diagnosis of sacroiliac joint injury or pelvic stress fractures. The procedure involves simultaneous manual compression of the dorsal aspects of both tuber sacrale, which induces a bending moment on the iliac wing and presumably compresses the sacroiliac articulations (Fig. 21.8). Normally, horses will not have any response or only a mild response to the applied pressure. Mild contraction of the lumbar longissimus muscles and slight extension of the lumbosacral joint is normal for most horses. Acutely affected horses may have a dramatic reaction to this manipulation and will demonstrate severe longissimus muscle contractions and sudden collapse of the hindlimbs which is indicative of pelvic injury or sacroiliac joint pain.[27] Practitioners should gradually apply increasing pressure since affected horses may actually collapse in the hindlimbs and fall to the ground if excess force is applied to the painful tuber sacrale. This test is not specific for sacroiliac joint pathology, as horses with incomplete or stress fractures of the ilial wing may respond even more dramatically to the applied pressure.

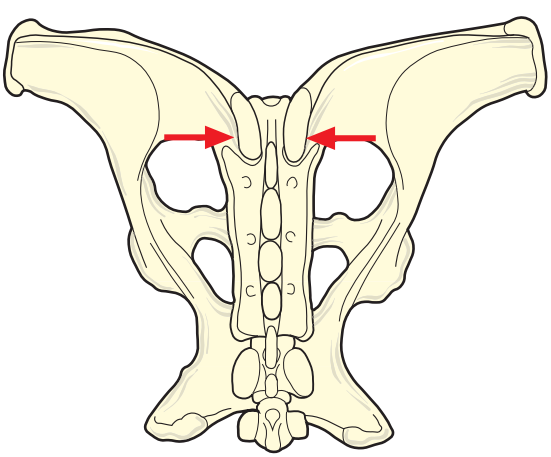


Fig. 21.8
Forces applied during a sacroiliac joint provocation test (dorsal view). Firm pressure is applied bilaterally with both hands, compressing the dorsal aspects of the tuber sacrale.

The apex of the second sacral spinous process is a reliable landmark used to evaluate relative tuber sacrale displacement. Normally, the dorsal apices of the tuber sacrale and the second sacral spinous process lie in close apposition and follow the contour of the croup. Using palpation, ultrasound or radiographs, a physical discrepancy in height can often be identified between the dorsal profile of the sacral spinous processes (which should remain constant, unless fractured) and the potentially ventrally or dorsally displaced unilateral or bilateral tuber sacrale. In this manner, either unilateral (i.e. tuber sacrale height asymmetry) or bilateral tuber sacrale displacement (i.e. hunters' or jumpers' bumps) can be diagnosed, depending on whether one or both tuber sacrale are elevated relative to the apices of the sacral spinous processes. Tuber sacrale height asymmetry is evident in sacroiliac joint subluxation (the higher side is affected) and complete ilial wing fractures (the lower side is affected). Bilateral tuber sacrale displacement has an unknown clinical significance and may be present in many high-level competition horses.[38] Theoretically, the hunters' or jumpers' bumps may provide a longer lever arm for the strong longissimus and thoracolumbar fascia to produce extension at the lumbosacral joint, resulting in increased impulsion and range of hindlimb motion with subsequent improved performance.

Pelvis Lateral compression of the tuber coxae and tuber ischii is indicated in horses with acute pelvic lameness to help rule out complete pelvic fractures. Palpation or auscultation of the dorsal pelvic region during repetitive side-to-side movements also assist in the diagnosis of pelvic crepitus. Normally, the tuber sacrale move in unison during locomotion. A palpable or visible independent movement of the tuber sacrale at a walk or during treadmill locomotion is indicative of sacroiliac joint luxation or a complete pelvic fracture. Horses with acute sacroiliac joint injuries may also resent flexion of the contralateral hindlimb. Rectal palpation is also indicated to assess osseous morphology (e.g. displaced fracture fragments or callus) and soft tissue pain or swelling (i.e. hemorrhage) in horses with suspected pelvic fractures.

Segmental joint motion

A vertebral motion segment is the functional unit of the spine and includes two adjacent vertebrae and the associated soft tissues that bind them together. To utilize palpation in the evaluation of the musculoskeletal system fully, an understanding of how joint motion is assessed is required.[40] Joint motion can be categorized into three zones of movement: physiologic, paraphysiologic and pathologic. The physiologic zone of movement includes both active and passive ranges of motion and is the site where joint mobilization is applied. Moving an articulation from a neutral position first involves evaluating a range of motion that has minimal, uniform resistance. As the articulation is moved toward the end of that range of motion there is a gradual increase in the resistance to movement (i.e. joint end-feel). End range of motion starts when any change in resistance to passive joint manipulation is palpable. Joint end-feel is evaluated by bringing the

articulation to tension and applying rhythmic oscillations to the joint to qualify the resistance to movement. The normal joint end-feel is initially soft and resilient and gradually becomes more restrictive as maximal joint range of motion is reached. A pathologic or restrictive end range of motion is palpable earlier in passive joint movement and has an abrupt, restrictive end-feel when compared with normal joint end-feel. The paraphysiologic zone of movement occurs outside the joint's normal elastic barrier and is the site of joint cavitation and manipulation. The anatomic barrier of the joint marks the junction of the paraphysiologic and pathologic zones of movement. The pathologic zone of movement lies outside the limits of normal anatomic joint integrity and is characterized by joint injury (e.g. sprain, subluxation or luxation).

Combining the evaluation of segmental joint range of motion and the presence or absence of pain at the extremes of motion, diagnostic interpretations can be implied.[54] Normal joint motion is painless, suggesting that articular structures are intact and functional. Normal joint mobility that has a painful end range suggests that a minor sprain of the associated articular tissues is present. Painless joint hypomobility suggests that a contracture or adhesion is present. Painful hypomobility suggests an acute strain with secondary muscle guarding. Painless hypermobility may indicate a complete rupture and a painful hypermobility suggests a partial tear of the evaluated structure.

Motion palpation Motion palpation is used to evaluate each individual vertebral and pelvic articulation for loss of normal joint motion and overall resistance to induced motion. The goal of palpating joint movement is to evaluate the initiation of motion resistance, the quality of joint motion and end-feel, and the overall joint range of motion (ROM). Similar palpatory findings can be noted in other soft tissues such as skin, connective tissue, muscles or ligaments.[46] Each vertebral segment is evaluated for altered motion palpation findings in flexion and extension, right and left lateral flexion and right and left rotation. Segmental causes of vertebral movement restrictions include soft tissue (e.g. capsular fibrosis, muscle spasms or contractures) and osseous (e.g. malformations, osteoarthritis, ankylosis) pathologies. Vertebral segments with altered motion palpation findings (i.e. joint stiffness) can occur with or without localized muscle hypertonicity and pain. Comparisons of motion palpation findings before and after manipulation or stretching exercises are made to evaluate the vertebral motion segment response to treatment.

Wither motion palpation Lateral forces are applied to individual dorsal spinous processes of the withers (T3–T12) to assess lateral bending and rotation of individual thoracic vertebral motion segments. The practitioner stands facing the withers. To stabilize the cranial and caudal vertebral segments, the bases of both hands are applied to the ipsilateral surface of the spinous processes adjacent to the vertebra being evaluated. The index fingers contact the contralateral surface of the dorsal spinous process to be assessed. A compressive force is applied between the index fingers and base of the hands to induce slight rotation of an individual thoracic spinous process. Normally, 3–4 mm of spinous process movement is palpable, without any evidence of pain or muscles spasms in response to the applied force. In horses with wither discomfort due to poor saddle fit, an obvious pain response (e.g. a rapid elevation of the head, depression of the withers) and local muscle hypertonicity will be precipitated with the applied pressure. In chronic forelimb lameness (e.g. laminitis), individual spinous process motion will not be detectable and the entire withers will move as a unit due to presumed chronic fibrosis and muscle guarding.

Trunk lateral bending motion palpation Lateral forces are applied to individual dorsal spinous processes of the trunk (T13–L6) to assess lateral bending and rotation of individual thoracolumbar vertebral motion segments. The practitioner stands facing the trunk. The base of the tail is grasped in the caudal hand, which provides side-to-side motion during the procedure. The base of the cranial hand is positioned against or between the spinous processes of interest. A lateral bending moment (i.e. wiggle) is induced as the cranial hand rhythmically pushes laterally and the caudal hand pulls laterally. The cranial hand is repositioned at the sequential dorsal spinous processes from cranial to caudal in order to assess lateral bending and rotation at individual thoracolumbar vertebral segments. Normally, a slight springy end-feel of joint motion is palpable at each motion segment, without any evidence of pain or muscle spasms in response to the applied force. In horses with back problems, restricted vertebral motion or stiffness is palpable and there is evidence of local pain and muscle spasms in response to the applied pressure. In general, acute or primary back problems produce segmental stiffness, pain and muscle hypertonicity. Chronic or secondary back problems produce regional stiffness, pain and muscle hypertonicity or atrophy.

Rib motion palpation Lateral compressive forces are applied to the individual ribs and costochondral junctions to assess pain and mobility. The base of the hand is positioned over individual ribs as a medial motion is induced, similar to expiration. The hand is repositioned at the sequential ribs and costochondral junctions from cranial to caudal. The amount of rib motion, resentment and secondary muscle spasms are noted during the induced movements. Normally, a slight springy feel is palpable at each rib, without any evidence of pain or muscle spasms. In horses that are girthy or have back problems, restricted rib motion or stiffness is palpable and there is evidence of local pain, resentment and muscle spasms in response to the applied pressure.

Trunk flexion-extension motion palpation While standing on an elevated surface, ventrally directed forces are applied rhythmically over individual dorsal spinous processes to assess flexion and extension of individual thoracolumbar (T13–L6) vertebral motion segments. The palm of one hand is placed over the dorsal aspect of the spinous process of interest. The other hand grasps the wrist and both hands apply a ventral force equally. An extension moment and rebound flexion (i.e. bounce) is induced as the hands rhythmically push ventrally. The hands are repositioned at sequential dorsal spinous processes from cranial to caudal. Normally, a slight springy end-feel of joint motion is palpable at each motion segment, without any evidence of pain or

muscle spasms. In horses with back problems, restricted motion or stiffness is palpable and there is evidence of local pain and muscle spasms in response to the applied pressure.

Lumbosacral flexion-extension motion palpation Ventrally directed forces are also applied rhythmically over the tuber coxae to induce extension of the sacroiliac and lumbosacral articulations. The practitioner stands facing the pelvis. The fingers are placed over the dorsal aspect of the tuber coxae to induce the ventral motion. A normal response to the induced movement is fluid vertical motion of the lumbosacral region with 1–2 cm of dorsoventral displacement over the lumbar dorsal spinous processes. Horses with pelvic or lumbar dysfunction will have a noticeable pain response, resent the induced movement or will have protective gluteal or sublumbar muscle spasms that limit the induced movement. The vertically directed force primarily induces movement at the lumbosacral junction, but sacroiliac joint motion and potential injury must also be differentiated with this procedure.

Sacroiliac ligament stress tests The sacroiliac ligaments are not readily palpable in horses. However, specific forces applied to the pelvic prominences (i.e. tuber sacrale, tuber coxae or tuber ischii) or the sacral apex can provide an indirect method to assess the structural and functional status of the supporting ligaments.

Dorsoventral sacroiliac ligament stress tests Sacroiliac ligament injury can be identified by rhythmically applying a ventrally directed force over the lumbosacral dorsal spinous processes in an effort to stress the supporting sacroiliac ligaments. This procedure requires the practitioner to get up on an elevated surface (i.e. mounting block) so that the two separately applied forces can be directed vertically over the L6 and S2 dorsal spinous processes, respectively. Horses with sacroiliac ligament injuries would be expected to resent the induced movement over the L6 dorsal spinous process since it specifically stresses the interosseous sacroiliac ligament (i.e. ligamentous sling of the sacropelvic junction). Horses with lumbosacral vertebral joint dysfunction (i.e. localized pain, reduced joint motion and muscle hypertonicity without structural pathology) may also resent this procedure. Rhythmically applied ventrally directed forces over the dorsal spinous processes at the sacrocaudal junction would be expected to specifically stress the dorsal portion of the dorsal sacroiliac ligament. A positive response to this test combined with positive ultrasound findings of desmitis of the dorsal sacroiliac ligament would be highly suggestive of clinically significant dorsal sacroiliac ligament injury.

Lateral sacroiliac ligament stress test Sacral apex deviation can be assessed by applying simultaneous, but opposite directed, lateral forces to the tuber sacrale and the sacrocaudal junction (Fig. 21.9). Sacroiliac joint or ligament injuries can also be localized by evaluating pain and ligamentous laxity in the sacroiliac joint. These procedures are similar to valgus-varus stress tests used to evaluate the collateral ligaments of the distal limb articulations. Care should be taken not to apply excessive force due to the long lever arm action of the sacral apex on the sacroiliac ligaments, which can unduly stress unstable or partially torn ligaments or aggravate an acutely inflamed sacroiliac joint. The proposed mechanism of action of these tests is to use the base of the tail and sacrum as a handle to apply a lateral (horizontal plane) stress to the sacroiliac joint as the wing of the ilium is stabilized.

The technique involves two parts. First, the base of the hand closest to the horse's head is placed over the lateral aspect of the tuber sacrale. The hand closest to the tail grasps the base of the tail head (Cd2–3). The sacroiliac joints are then evaluated as firm pressure is simultaneously applied by both hands, pushing with the hand at the tuber sacrale away from the examiner and pulling with the hand at the tail head toward the examiner (Fig. 21.9A). Theoretically, this maneu-

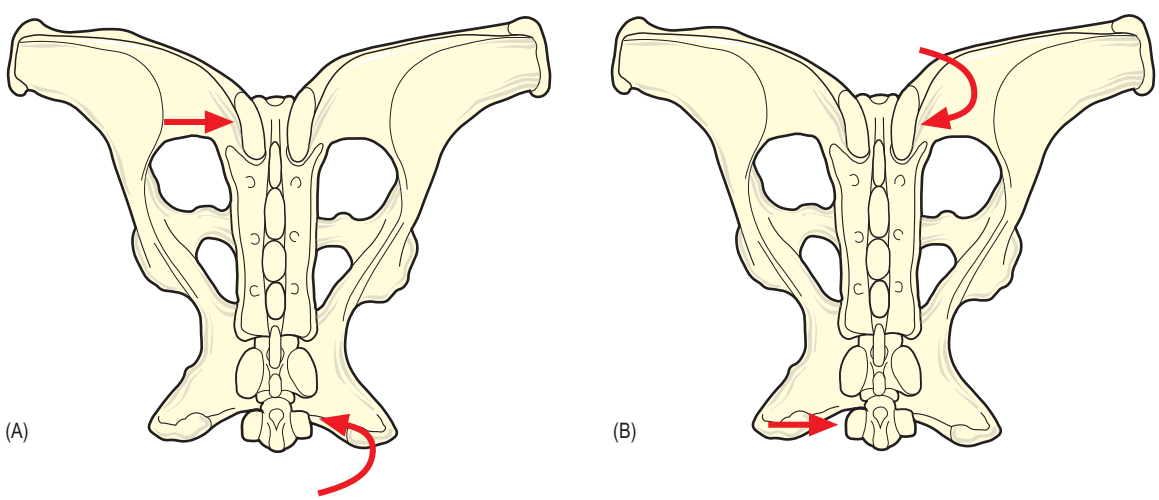


Fig. 21.9
Forces applied during a sacroiliac ligament stress test (dorsal view). (A) Firm pressure is applied by both hands, pushing with the hand at the ipsilateral tuber sacrale away from the examiner while simultaneously pulling with the hand at the tail head toward the examiner. (B) Firm pressure is applied by both hands; pulling with the hand at the contralateral tuber sacrale toward the examiner while simultaneously pushing with the hand at the tail head away from the examiner.

ver produces compression of contralateral and distraction of ipsilateral sacroiliac articular surfaces.

The second portion of the technique involves repeating the procedure and reversing the direction of the applied forces (Fig. 21.9B). The fingers of the hand closest to the horse's head are placed over the contralateral tuber sacrale and the base of the hand closest to the tail is placed against the ipsilateral base of the tail head (Cd2–3). The sacroiliac joints are again evaluated as firm pressure is applied by both hands, pulling with the hand at the tuber sacrale toward the examiner and pushing with the hand at the tail head away from the examiner. Theoretically, the contralateral sacroiliac articular surfaces are distracted and the ipsilateral sacroiliac articular surfaces are compressed. A pain response to the induced movements may be identified either unilaterally or bilaterally, depending on the extent of inflammation or injury present. In general, sacroiliac joint compression would be expected to aggravate osteoarthritic changes, whereas joint distraction would be expected to stress any injured or inflamed sacroiliac ligaments.

Proximal limb evaluation

In horses with back or pelvic problems, the proximal limbs are often affected either primarily or secondarily. Primary thoracic or pelvic girdle muscle or joint dysfunction is often evident as lameness in the affected limb. However, back or pelvic problems can also induce secondary proximal limb dysfunction that needs to be differentiated. Muscular or osseous asymmetry of the shoulder or pelvic regions are often indications of limb dysfunction or lameness. The pectoral region is viewed cranially to assess muscular symmetry. The dorsal scapula and wither region are viewed caudally from an elevated surface to assess bilateral symmetry and muscle development related to proper saddle fit. The croup or gluteal region is also viewed caudally to assess symmetry and muscle development. Horses with pelvic lameness or EPM often have noticeable gluteal muscle atrophy or asymmetry. The tuber sacrale are assessed for osseous asymmetry associated with pelvic fractures, sacroiliac joint subluxation or developmental factors. Changes in the height of the tuber sacrale should be assessed relative to the apex of the second sacral spinous process (S2).

Abnormal tonicity of the thoracic or pelvic girdle muscles is identified by hypotonicity or flaccidity, and hypertonicity associated with local trigger points or regional muscle spasms. The proximal limbs are also evaluated for normal ranges of motion or flexibility. In the forelimb, the scapulothoracic and shoulder joints are evaluated. In the hindlimb, the sacroiliac and coxofemoral joints are assessed. The fore and hindlimbs are individually examined in protraction, retraction, abduction, adduction and flexion for resistance to the applied movements, joint stiffness or muscle hypertonicity. Horses with back or pelvic problems will resent certain movements, have reduced limb motion and will not actively extend and stretch the limbs. Normally, horses will actively stretch their fore and hindlimbs when positioned in protraction and retraction. Extension of the hindlimb caudally will apply a stretch to the hindlimb protractor muscles, which include the iliopsoas, rectus femoris and tensor fascia latae. Injury to these muscles will produce resentment to passive stretching of the hindlimb. Iliopsoas muscle injury or hypertonicity can also be confirmed with rectal palpation.

Diagnostic injections

The use of injections of local anesthetics into painful or inflamed musculoskeletal structures is the basis of lameness evaluation. Fortunately, the same principle can be applied to painful soft tissue, articular or osseous structures of the back and pelvis.

Muscle

Injection into areas of perceived muscle pain or reactive acupuncture points helps to assess the contribution of muscle pain to the observed back problem, cause of poor performance, vague gait abnormalities or resentment to placement of the saddle.[27] Before and after comparisons of the muscle response to applied pressure (i.e. algometry) or changes in gait help to confirm the clinical significance of the muscle pain to the primary presenting complaint. In humans, trigger point therapy relies on the use of intramuscular injections of local anesthetic to reduce focal areas of muscle pain and hypertonicity. Similar techniques have been applied in horses with mixed results, which are mostly related to the inability to adequately define and measure muscle pain and dysfunction.

Interspinous spaces

Injections of local anesthetics into narrowed interspinous spaces or areas of interspinous pseudoarthrosis can be used diagnostically and therapeutically to assess the influence of over-riding or impinged spinous processes on back pain. The clinical significance of impinged spinous processes is often difficult to assert based solely on radiographic findings, since impinged spinous processes are often diagnosed in horses without obvious back pain. Firm digital palpation of affected dorsal spinous processes often produces a localized painful response (e.g. cutaneous trunci reflex or active extension of the back). Confirmation of the clinical significance of potential impinged spinous processes can be achieved with injections of local anesthetics. At sites of severe impingement or proliferation, it is often impossible to pass a needle directly on midline into the interspinous space. In this instance, a paramedian approach to the interspinous space provides lateral access to the area of pathology, which reduces the need to advance a needle through a collapsed interspinous space, although bilateral injections of the affected interspinous spaces are required. Nuclear scintigraphy is also an important adjunct in the definitive diagnosis and localization of impinged spinous processes as a contributing cause to back pain. Therapeutically, interspinous injections with anti-inflammatories (i.e. corticosteroids) provide variable

effectiveness and durations of pain relief and normal spinal function.

Articular processes

Articular process osteoarthritis is a common pathology and an important contributor to back pain. Like articular limb lameness, intra- or periarticular injections of the articular processes can assist in the localization and treatment of the presumed back pain. Periarticular injections of articular processes in the thoracolumbar spine can be used both diagnostically and therapeutically. Ultrasound guidance is recommended due to the deep location and close proximity to the spinal neurovascular structures that exit the intervertebral foramen.[35] Intra-articular injections of the articular processes are difficult due to the small articulation and sparse joint capsule; therefore periarticular injections are often performed. A 15 cm spinal needle can be used with ultrasound guidance to assess the articular process joint capsule in most horses.

Sacroiliac joint

The ante-mortem diagnosis of sacroiliac osteoarthritis is often frustrating and based on exclusion of other possible causes of hindlimb lameness.[33,55] In humans, periarticular injections of the sacroiliac joint are easy to perform, safe and seemingly effective in controlling pain associated with sacroiliac joint osteoarthritis.[56–58] The deep overlying croup musculature and seemingly inaccessible anatomic location of the sacroiliac joint has limited the clinical application of intra-articular or periarticular sacroiliac joint injections in horses.[33,55,59] Injection of the general sacroiliac region for diagnostic and therapeutic purposes has been performed, but inappropriate needle placement or the use of too short needles explain why most techniques have had suboptimal diagnostic or therapeutic effects.[38,60,61]

A medial approach to the sacroiliac joint provides the most direct, safe and consistent periarticular injection technique (Fig. 21.10).[62] Periarticular injections are made as close as possible to the caudomedial sacroiliac joint margin due to the high prevalence of degenerative changes affecting the caudomedial sacroiliac joint margin.[52,63] Important neurovascular structures to be avoided include the sciatic nerve and the cranial gluteal nerve, artery and vein that pass through the greater sciatic foramen, directly caudal to the sacroiliac joint.[64] Osseous topographic landmarks used to identify the needle entry site and the direction of needle advancement include the contralateral tuber sacrale and the ipsilateral tuber coxae and greater trochanter of the femur. The midpoint of the distance from the cranial aspect of the tuber coxae and the cranial aspect of the greater trochanter is used as a target for needle advancement. The needle entry site is 2 cm cranial to the contralateral tuber sacrale. The needle entry site and the midpoint of the tuber coxae and greater trochanter are connected with white tape to indicate the direction of needle advancement. A 25 cm, 15 gauge spinal needle is bent slightly in the direction of the bevel of the needle to match the medial curvature of the iliac wing. The needle is inserted with the bevel facing toward the targeted sacroiliac joint and advanced along the medial aspect of the iliac wing until it firmly engages the dorsal surface of the sacral wing, near the medial border of the sacroiliac joint. Poor performance or vague proximal hindlimb lameness associated with sacroiliac osteoarthritis can be diagnosed and treated with this reliable and easy-to-use injection technique.[62]

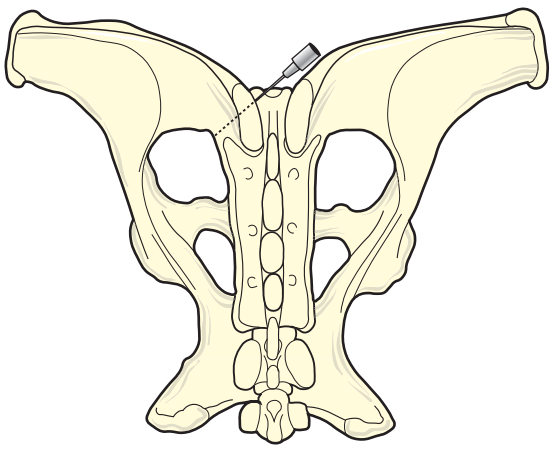


Fig. 21.10
Diagram of a medial approach to the sacroiliac joint for diagnostic or therapeutic purposes (dorsal view). The needle is directed from the cranial aspect of the contralateral tuber sacrale toward the caudomedial aspect of the affected sacroiliac joint.

Diagnostic imaging

Radiographic examination

For diagnosing lower limb lameness, radiographs are usually the first imaging modality used. However, due to difficulties associated with radiographing the equine back, other diagnostic imaging modalities may be used initially to localize the presumed inciting cause of back pain or dysfunction.

Standing position It is possible to take good-quality lateral views of the thoracic (T1–T18) and cranial lumbar spine (L1–L4) in the standing position.[65] Using portable equipment, the dorsal apexes of the spinous processes for T2–L3 can usually be visualized. Powerful equipment is necessary for radiographic examination of the horse's vertebral column, because exposures of up to 150 kV and 500 mA may be required in large horses.[66] Exposure values will vary according to the system employed, but a few suggested radiographic techniques are given in Table 21.4.[67]

One of the major problems encountered in radiography of such a thick subject is the inevitable production of secondary radiation. However, there are a number of ways to minimize scatter. The tube can be mounted on an overhead gantry system and linked to a cassette holder on the far side of the horse. The primary beam can then be automatically directed to the center of the cassette and the beam size can be care-

Table 21.4 Suggested radiographic techniques for imaging the thoracolumbar spine

Vertebral structures or region	Kilovolt (peak)	Milliamps	Grid
Spinous processes			
Withers (T3–T8)	75	30	No
Midthoracic (T9–T15)	70	55	Yes
Thoracolumbar (T16–L4)	85	80	Yes
Articular processes			
Midthoracic (T9–T15)	100 +	200–300	Yes
Vertebral bodies			
Thoracic (T5–T18)	75	55	Yes
Lumbar (L1–L5)	100 +	200–300	Yes

fully collimated to the size of the film. This system makes it possible to use high-ratio and crosshatch grids with confidence to effectively reduce scatter. The fastest possible system of intensifying screens and film (e.g. rare earth screens) should be employed so that exposures can be kept to a minimum. Most radiographic film cassettes contain lead in the backing, but at exposures over 100 kVp, it is advisable to place an additional lead sheet behind the cassette to absorb backscatter. As the scatter is oriented perpendicular to the ground with a film-focus distance of 150 cm, an air gap exists between the spine and the cassette and this helps to reduce the amount of scatter reaching the film. There is a considerable difference in tissue attenuation between the tips of the spinous processes and the vertebral bodies; thus, at least two radiographs of the same region at different exposures must be taken or some form of beam filtration is necessary. Considerable improvement in radiographic quality can be obtained by filtering (dodging) part of the primary beam to help compensate for the marked variation in thickness of the horse's spine.[66]

The horse should be sedated prior to radiography to reduce the degree of movement and to allow the handler to stand well out of range of the beam. Stocks are also useful to prevent movement. Lead markers placed midline on the horse's back are useful for orientation on the radiographs. The horse must be standing completely square, as the spine rotates to some extent if one leg is non-weight bearing. For the dorsal apexes of the spinous processes, the beam should be centered 5 cm ventral to the dorsal skin surface; for the region of the vertebral bodies, it should be centered 15–20 cm below the dorsum depending on the size of the horse. The beam should normally be horizontal but for visualization of the dorsal articular facets in the cranial lumbar region, it is useful to angle the beam from a ventral to dorsal orientation at an angle of 20–30° to avoid superimposition by the transverse processes. As a grid is being used, the cassette must be tilted accurately at the same angle of 20–30°.[67]

Under general anesthesia It is not possible to take radiographs of diagnostic quality of the caudal lumbar (L3–L6) and sacroiliac regions in a standing horse. The horse must be anesthetized and placed on its back in the frog-legged position so that the cassette can be inserted beneath the pelvis for a ventrodorsal view. Even in very large horses (i.e. weighing over 700 kg), exposures above 150 kV are not required, although up to 500 mA have been used on some occasions. To limit scattered radiation, it is necessary to use crossed, high-ratio grids and to put additional lead on the back of the cassette to prevent backscatter.

Normal radiographic anatomy The thoracolumbar spine of the newborn foal has a more pronounced curvature (i.e. dorsally convex) in the midthoracic region than does the adult horse.[67,68] The dorsal spinous processes appear short in relation to the length of the vertebral bodies, and in the midthoracic region they are blunt ended or spatula shaped, with wide interspinous spaces. The vertebral bodies have well-defined cranial and caudal epiphyses, but all the other ossification centers in the vertebral bodies and neural arch have fused before birth. During the first few months of life the thoracolumbar spine straightens out to some extent. In the mid and caudal region there is some alteration in shape of summits as well as a general lengthening and reduction in size of the interspinous spaces. At about 12 months of age, calcification of separate ossification centers on the summits of the cranial spinous processes occurs, and these persist without fusion into old age (i.e. 15 years or older). The tallest point of the vertebral column is at the withers, usually T4–T6. Areas of periosteal irregularity are frequently seen in the midportion of the thoracic spine, but these are of no clinical significance. The spines beneath the saddle region, T11–T17, are considerably shorter and more upright; the anticlinal vertebra is usually T15. Caudal to this, the spinous processes are increasingly slanted forward and the interspinous spaces are considerably narrowed. The summits are variable in shape, but they have cranially directed, often beak-shaped tips.

In the adult the thoracolumbar spine lies horizontal when the horse stands squarely on a level surface. The ventral portions of the vertebral bodies are clearly visible radiographically as far back as T16, because they form the roof of the thoracic cavity. It is difficult to see the articulations of the ribs and the articular and transverse processes unless oblique views are taken. Behind the diaphragm, the lumbar vertebrae as far back as L3 can be defined, as well as the articular and transverse processes. Closure of the vertebral epiphyses occurs at 3–3.5 years of age. In the region of the midback the width of the interspinous spaces varies and some impingement or over-riding of the spinous summits may occur. This is more often seen in Thoroughbreds than in other breeds and seems to be related to the conformation of the back; it is more common in stocky, short-coupled horses. The reduction or obliteration of the interspinous spaces, chiefly in the region from T13 to T18, is associated with local periosteal reaction and focal areas of radiolucency. The spinous summits sometimes overlap one another and become misshapen presumably because of the continued pressure from the adjacent spines. In one survey of clinically normal horses, 34% showed some degree of spinous process impingement.[68] There are few variations noted in the normal radiographic anatomy apart from the changes associated with impingement or over-riding dorsal spinous processes in the midback

region. Other osseous findings (e.g. abnormal spinal curvature, osteoarthritis, vertebral fracture or spondylosis) are incidental or are rarely encountered.

Primary indications for radiography of the pelvis include acute or severe pelvic asymmetries, upper hindlimb lameness and pelvic crepitus or fractures.[69] Ilial wing overlap and the deep anatomic location of the sacroiliac joint make radiographic imaging difficult at best. The radiographic features of chronic sacroiliac joint disease are minimal and include nonspecific increases in the joint space and apparent enlargement of the caudomedial aspect of the sacroiliac joint.[33] Linear tomography has also been used to examine the lumbosacral and sacroiliac regions of horses, but limited access to equipment has restricted its clinical usefulness.[70] Positive findings include widening of the sacroiliac joint and irregular joint outlines with osteophyte formation at the caudal aspect of the joint. Osseous changes are common bilaterally, but may be more pronounced on the clinically affected side.[70]

Scintigraphic examination

A useful adjunct to clinical diagnosis in recent years has been the advent of nuclear scintigraphy for horses.[71–74] The technique involves intravenous injection of a radionuclide and detection of 'hotspots' of increased radioactivity in the bone phase by use of a gamma camera. Scintigraphy is helpful in detecting over-riding or impinged spinous processes, vertebrae fractures, osteoarthritis, spondylosis, stress fractures of the wing of ilium and some sacroiliac osteoarthritis. Scintigraphy is particularly valuable in identifying bony lesions at sites not accessible with conventional radiography.

The radiopharmaceutical most commonly used for equine scintigraphy is 99 m technetium-labeled methylene diphosphonate (^{99m}Tc-MDP). A weight-dependent dose between 3 and 6 GBq (100–150 mCi) of ^{99m}Tc-MDP is injected intravenously and images of the bone phase are obtained 2–3 hours later. Due to the initial high renal and bladder radioactivity, vascular phase and soft tissue phase images of the thoracolumbar spine cannot be obtained. Damaged skeletal muscle can be detected by abnormal soft tissue uptake of ^{99m}Tc-MDP during bone-phase imaging, but usually only if the horse has been strenuously exercised before the scintigraphic examination.[75]

For a complete examination, the horse should be imaged from both the left and the right; otherwise some subtle lesions, for example those located at the articular processes, can easily be missed. A high-resolution, low-energy, parallel-hole collimator should be used; this gives a geometrical resolution of 4.4 mm at a distance of 5 cm from the collimator face. For the caudal thoracic and lumbar regions, the camera is positioned obliquely at an angle of 50–65° to the horizontal. This allows the distance between the camera and spine to be minimized. Positioning the camera horizontally above the spine results in superimposition of all the vertebral structures. The camera can be oriented perpendicular to the floor for views of the cranial thoracic spine. When the camera is positioned over the lumbar spine, the image quality may be improved by shielding the kidney using a lead sheet.

The images are acquired on the basis of either counts or time. One million counts or more are optimal for maximal resolution of the caudal regions of the equine back and the pelvis. This large number of counts requires several minutes of immobility on the part of the horse, however, and thus generally cannot be achieved without general anesthesia. Movement of the standing horse can be minimized by appropriate sedation and quiet handling of both the horse and camera. Blinders and cotton earplugs for the horse may help. Nuclear medicine software that is able to correct for motion is now available and this compensates for the slight swaying of the horse and respiratory movements.

Normal scintigraphy findings In normal horses, regions of bone close to the skin surface such as the tuber sacrale and tuber coxae appear 'hotter' (i.e. increased radiopharmaceutical uptake) than adjacent bone structures, as there is less soft tissue attenuation. Other superficial sites that appear slightly 'hot' are the apices of the spinous processes, particularly at the withers. In good-quality images, the individual vertebra can be clearly distinguished. The spinous processes and articulations have a slightly higher uptake, but this should be equal for all joints in the region. On lateral oblique views, each rib is located cranial to its respective vertebra. As an aid to orientation, on left lateral views the 16th rib usually overlies the cranial pole of the right kidney.

Any scintigraphic abnormality appears as increased radiopharmaceutical uptake (a 'hotspot'), whereas areas of diminished uptake are difficult to detect due to poor image resolution. The most common sites for increased uptake are at the apices of the spinous processes, the articular processes or the sacroiliac region.

Nuclear scintigraphy is considered by some authors to be an accurate and diagnostically useful technique for identifying acute and chronic sacroiliac joint injuries.[53] Subjective evaluation or quantitative analysis of bone scans are typically able to identify asymmetric radioisotope uptake over the affected tuber sacrale. However, presumed normal horses, without a history of hindlimb or sacroiliac joint injuries, may also have asymmetric uptake over the tuber sacrale. A dorsal view of the sacrum is considered the most diagnostic image for evaluating and comparing the sacroiliac joints.[53] However, there is usually extensive overlap of uptake in the tuber sacrale and the sacroiliac joints on the dorsal view. Oblique views of the ilial wings are recommended to confirm left-to-right asymmetries in radioisotope uptake and to separate the tuber sacrale dorsally from the sacroiliac joint region ventrally,[76] although oblique views may be difficult to interpret due to inconsistent camera positioning on the left and right sides. The thick overlying gluteal musculature may also attenuate radiopharmaceutical uptake from an affected sacroiliac joint. Stress fractures of the ilial wing may be difficult to differentiate from sacroiliac joint injuries due to the common location and extension of the incomplete fracture line into the sacroiliac joint.[53,77,78]

Ultrasonographic examination

There has been considerable interest in recent years concerning the value of ultrasonography for evaluation of the

epaxial structures, particularly the supraspinous and dorsal sacroiliac ligaments.[35,79]

Supraspinous ligament A 7.5 or 10 mHz linear array transducer is used to examine the supraspinous ligament that runs dorsal to the thoracic and lumbar spinous processes. It is necessary to clip the hair over an area of approximately 20 cm in width extending from the withers to the base of the tail. The ligament has an echogenic, striated appearance similar to tendon. It is thinner and wider in the caudal withers region and becomes narrower and thicker in the lumbar region. It is always thinner as it runs over the spinous processes. The dorsal convex surface of the spinous processes can be clearly seen and impinged or over-riding spinous processes can be identified by visualizing narrowed interspinous spaces. There may also be evidence of false joint formation between impinging spines. The echogenicity of the ligament may vary somewhat and a more clearly defined fibrous pattern seen in the caudal thoracic and lumbar regions. In the withers (T6–T9) it is sometimes possible to see hyperechogenicity that may cast acoustic shadows. These are associated with the secondary centers of ossification on the dorsal tips of the spinous processes. A little caudal to this (T9–T12) it is possible to see hypoechoic areas that may be associated with cartilage metaplasia adjacent to the ligament insertion into the dorsal spinous process. This does not usually have any clinical significance.

Dorsal sacroiliac ligament The dorsal portion of the dorsal sacroiliac ligament can be visualized with a 7.5–10 mHz linear array transducer as it runs from the tuber sacrale to the summits of the sacral spinous processes.[80] The sacroiliac region is first viewed on midline in transverse section. The tuber sacrale are seen as hyperechoic convex lines on either side of the sacral spinous processes. The transducer is then moved laterally over the tuber sacrale so that the dorsal portion of the dorsal sacroiliac ligament appears as a crescent-shaped echogenic structure. Longitudinal views of the dorsal sacroiliac ligament are then examined. The ligaments are examined for alterations in echogenicity and fiber orientation, but particularly for any increase in size.

Additional pelvic and vertebral structures It is possible to examine the dorsal surface of the iliac wing and caudal margin of the sacroiliac articulation to identify dorsal cortex irregularities associated with incomplete and complete ilial wing fractures.[81,82] Denoix has elegantly demonstrated the visualization of the thoracolumbar articular processes, transverse processes, lumbosacral and caudal lumbar intervertebral disk spaces and the sacroiliac joint.[35] The ventral sacroiliac ligament and the ventral joint margins of the sacroiliac joint can also be visualized on transrectal ultrasonography.[79] Ventral periarticular remodeling of the sacroiliac joint has been observed with transrectal ultrasound approaches. Muscle injuries are more difficult to detect ultrasonographically, although in severe cases of muscle strain an increased echogenicity with thickening of the connective tissue septae within the muscle may be identified.

Thermographic examination

Thermography has been used successfully as an aid to diagnose back problems. However, it is important to have the right equipment and to establish normal thermal profile parameters. Even so interpretation of infrared thermography imaging can be difficult. A single thermal study has little or no prognostic value. Von Schweinitz concludes:

> Thermal imaging reveals important information about the neural outflow of the spine in terms of sympathetic tone. The thermal findings are a compilation of local tissue factors and vasomotor tone requiring care in interpretation. The relevance of disturbed vasomotor tone, especially persistent vasoconstriction, is well established in chronic back pain syndromes in man. Many of these syndromes involve disturbing sensory faults (e.g. allodynia, burning, aching) which can neither be directly communicated by our patients nor readily described by any other current diagnostic test.[83]

Thermography provides quick, safe and non-invasive assessment of the whole patient. It takes into account a major aspect of homeostasis and prompts one to investigate all other thermally abnormal sites. With current diagnostic technologies, it often provides the only objective evidence confirming cases of equine back disease. Routine use of thermal imaging in equine poor performance syndromes confirms that thoracolumbar and sacral neuromuscular disease is a common condition.[83] Thermography has been used to diagnose muscle strain or inflammation in the sacroiliac and croup regions.[84] Horses with sacroiliac joint injuries are expected to have protective muscle spasms in the adjacent musculature. Palpation of muscle sensitivity has been correlated with abnormal thermographic images in most cases.[84]

Magnetic resonance imaging (MRI) and computed tomography (CT)

These are emerging modalities that have not yet been applied to the problems involving the thoracolumbar spine. However, the detail and quality of both skeletal and soft tissue structures elsewhere in the horse's body mean that once the technological difficulties have been overcome there is great potential for improved diagnostic ability for the thoracolumbar and lumbosacral spine.

Specific pathologic conditions

Clinical signs associated with spinal muscle pathology include atrophy, focal swelling and palpable tenderness of the epaxial muscles. Spinal muscle biopsies help to evaluate suspected back disorders, but are best used with a complete physical examination and imaging procedures. Spinal ligament injuries affect the supraspinous and sacroiliac ligaments. Osseous pathology has been observed at the vertebral processes, intervertebral articulations and sacroiliac joints in horses. Degenerative changes are common in many articular processes, intertransverse, lumbosacral and sacroiliac

articulations. Osseous spinal lesions tend to affect multiple vertebral locations.

Vertebral anomalies and deformities

Developmental variations in the morphology of thoracolumbar vertebral bodies, processes and joints in horses are known to occur, but usually result in secondary rather than primary back problems.[14–16,28,51] Congenital abnormalities that affect the normal spinal curvature include scoliosis, lordosis and kyphosis. In newly born foals signs of scoliosis and lordosis are sometimes seen in association with other in utero postural deformities (e.g. limb contractures, bent face and torticollis). These may be severe and necessitate euthanasia or be mild when they show an apparent complete recovery. The condition of kyphosis (i.e. roach-back) is most frequently seen during the period of active growth after weaning although the underlying cause does not appear to be in the vertebral column. The problem may be associated with a progressive straightening of the hindlimb conformation during a growth spurt or perhaps be secondary to a stifle or hock problem (e.g. osteochondrosis). The condition of congenital lordosis (i.e. dipped or sway-back) has been associated with hypoplasia of the cranial and caudal intervertebral articular processes in the cranial thoracic region T5–T10.[85] There is overextension of one or more of these articulations leading to the ventral curvature of the midthoracic spine. In older horses acquired lordosis is sometimes seen, particularly in brood mares after a number of pregnancies, but usually no clinical problems are associated with it.

All these vertebral deformities predispose to some weakness of the thoracolumbar spine, leading to poor performance and soft tissue injuries. Diagnosis can be confirmed by radiography revealing abnormal curvature of the vertebral column, principally in the cranial thoracic region (T5–T10) with lordosis, mid- to caudal thoracic region with scoliosis and the cranial lumbar region (L1–L5) with kyphosis.

Soft tissues injuries

Muscle strain

Damage to the epaxial tissues is undoubtedly the most common cause of back injury in the horse.[4] The main action of the longissimus muscle is to extend the back (i.e. to dorsiflex) or, if acting singly, to laterally bend the spine. The primary role of these muscles is to control the stiffness of the back rather than to actively assist locomotor movements. Strain or injury to all or part of the longissimus muscles most frequently occurs during ridden exercise because of a slip, fall or poorly executed jump. It may be caused through fatigue or inadequate fitness. The clinical signs are an acute onset of poor performance often accompanied by a change of temperament. Local swelling and heat of the muscles may occur, particularly in the lumbar region. The back is kept rigid and there is a restriction in the hindlimb gait at exercise, often with a wider than normal rear limb stance. There may be difficulty in maintaining normal tracking action of the hindlimbs. Disunited canter and frequent breaking of stride are also frequently seen. Stiffness of the hindlimb and back is seen particularly in short turns, but no clear signs of lameness are evident. There is obvious pain on palpation and a marked reduction in flexibility of the thoracolumbar spine. In the acute stages some elevation (i.e. 2–4 times baseline levels) in the plasma levels of muscle-derived enzymes (CK and AST) will be noted after mild exercise. If the sublumbar muscles are involved pain will be easily elicited on rectal palpation.

Classic signs of exertional myopathy (i.e. rhabdomyolysis) are not difficult to differentiate from muscle strain of the back. However, the atypical low-grade form of exertional myopathy is more difficult to diagnose as it can occur after varying amounts of exercise, but is more commonly seen in horses on a high-protein diet and in highly strung fillies or mares in excellent bodily condition. Diagnosis can usually be confirmed by determination of muscle-derived enzymes after exercise. In exertional myopathy, levels will be increased greater than five times over baseline values.

Polysaccharide storage myopathy (PSSM) has been recently diagnosed from longissimus muscle biopsies in showjumpers, dressage and draft horses.[44] The horses showed typical signs of a soft tissue back injury and biopsies from the longissimus lumborum muscles revealed high glycogen levels with abnormal deposits of amylase-resistant polysaccharide. This study indicates that muscle biopsy may be an important diagnostic aid in some chronic back problem cases.

Ligamentous damage

Clinical conditions affecting the spinal ligaments include mild, moderate or severe sprains. Severe injuries are characterized by complete ligamentous disruption and joint laxity (i.e. joint luxation). A fairly common site of thoracolumbar injury in Thoroughbred gallopers and jumpers is the supraspinous ligament which runs all the way down the middle of the back and is adherent to the summits of the thoracic and lumbar dorsal spinous processes. It is made up of a continuous ligament to which the multiple tendon insertions of the longissimus muscles contribute. The composite structure is subject to strain in the same way as the muscle injuries just described. The clinical signs are essentially similar, but tend to persist for longer and the ultimate prognosis is less favorable. The cranial lumbar region is the most common site of injury. The ligament is often visibly thickened above the spinous summits and pain is easily elicited on palpation. Reduced lateral flexion of the thoracolumbar spine is seen in one or both directions. By taking low-exposure radiographs, the soft tissue thickening and some focal radiodensity in the ligament may be seen in long-standing cases. Detached flakes from the spinous summits are also noted on occasion and are associated with periosteal irregularity and sclerosis on the dorsal surfaces of the spinous summits. This may also be seen in the caudal withers' regions, but care must be taken not to confuse elevated periosteum with a vestigial center of ossification on the dorsal tips of the T3–T12 spines. Diagnosis can be assisted by ultrasonographic examination.[35,36] The prognosis for supraspinous ligament strain is usually guarded, largely because of the likelihood of recurrence. Some

horses do recover but go on to develop signs of a 'cold back', which is defined as temporary stiffness and a dipped back, without affecting their competitive performance.

Other soft tissue lesions

These include such disorders as skin lesions (e.g. wounds, scars, warbles, pruritic conditions), which may cause secondary signs of back pain. Pressure or chaffing from an ill-fitting saddle, particularly in endurance competitions, may also be observed.

Thoracolumbar osseous pathology

Spinal disorders and sacroiliac joint injuries have been identified as significant causes of chronic poor performance in horses.[4,33,86] In humans, the most common known sources of back pain are related to the intervertebral disks, zygapophyseal joints and sacroiliac articulations.[87] Intervertebral disk disease is uncommon in horses, but significant and widespread degenerative changes of the thoracolumbar zygapophyseal joints and sacroiliac articulations have been reported, even in active race horses.[52]

Articular pathophysiology

The zygapophyseal joints are synovial articulations that undergo joint capsule pathology and joint degeneration similar to other synovial joints. Articular degeneration usually progresses through three phases of pathology: dysfunction, instability and degeneration. Joint dysfunction is characterized by restricted joint motion, localized pain and inflammation, and abnormal paraspinal muscle hypertonicity. Restricted articular motion stimulates local biochemical alterations and the release of inflammatory products. The inflammatory process can alter the intra-articular environment and further contribute to joint capsule pathology and periarticular fibrosis. Muscle hypertonicity may restrict joint motion and contribute to adhesion formation. Joint immobilization also produces bone demineralization, capsular adhesions and loss of ligamentous strength. Restoring joint motion can lead to normal joint function, depending on the amount and duration of the immobilization. Joint motion is essential for the prevention of joint contracture and adhesion formation. Progressive joint immobilization is characterized by initial musculotendinous contractures, followed by capsular and periarticular adhesions and eventual intra-articular adhesions.

Joint degeneration progresses as the dysfunctional joint is unable to distribute normal biomechanical stresses. The instability phase of joint degeneration is characterized by cartilaginous, meniscal, capsular and ligamentous deformation and degeneration. Abnormal joint and paraspinal tissue biomechanics induce additional subchondral bone changes and joint derangement. Reduced or asymmetric motion in one vertebral motion segment may induce compensatory hypermobility in adjacent vertebral segments due to injuries to the joint capsule or ligamentous laxity. The increased joint mobility results in joint instability, joint derangement and secondary muscle hypertonicity. Joint instability also affects the neurologic influences of proprioception and the central neuromotor control of movement and posture. Potential radiographic findings of articular instability may include osteophyte formation or vertebral instability (i.e. listhesis). The spinal degenerative phase is characterized by attempts at stabilization of the degenerative tissues. Chronic joint immobilization can lead to fibrocartilaginous replacement of the joint cavity and eventual ankylosis. Radiographic signs of advanced osteoarthritis and osteophyte formation, spinal ligament ossification and spinal ankylosis can be visualized at this stage.

Articular process degenerative joint disease

As with any synovial articulation, loss of motion or aberrant joint physiology can be a primary source of pain.[21] Jeffcott states that degenerative joint disease of the articular processes (i.e. zygapophyseal joints) is common in older horses but

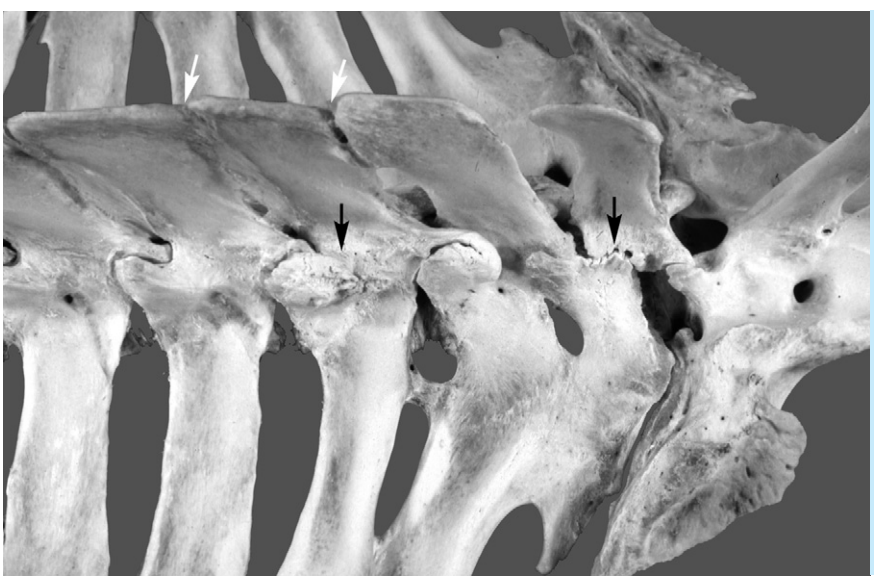


Fig. 21.11
Dorsolateral view of the lumbosacral vertebral region (L2–S2) of a 4-year-old racing Thoroughbred that fractured the right front sesamoids during a race. Varying degrees of spinous process impingement (white arrows), vertebral lamina stress fractures (black arrows), articular process ankylosis (L4–L6) and bilateral intertransverse joint ankylosis (L5–L6) are present.

probably not clinically significant.[88] However, Denoix reports that zygapophyseal joint pathology at the thoracolumbar junction and lumbar vertebral region is one of the most common spinal disorders associated with back pain.[89] In a necropsy survey of 36 Thoroughbred race horses, severe articular process degenerative changes were reported in 25% of specimens (Fig. 21.11).[52] Articular surface lipping, osteophytes, periarticular erosions, intra-articular erosions and ankylosis (in order of increasing severity) were noted. Articular surface lipping and periarticular erosions of the articular processes were common at the thoracolumbar junction and cranial lumbar spine. Intra-articular erosions and ankylosis were restricted to the caudal lumbar vertebral segments, where vertebral mobility is normally limited.[90] Additional studies may help to show that the zygapophyseal joints are a clinically significant source of back pain in horses, as has been shown in humans.[87]

Impinged or over-riding spinous process

Spinous process overlap, without any evidence of osseous impingement, has been noted in horses.[52] In humans, isolated spinous process deviation is a common finding and can be related to vertebral rotation (i.e. scoliosis) or developmental asymmetries in the neural arch, but rarely is it associated with spinous process fracture or malposition of the entire vertebra.[91] Impinged or over-riding spinous processes (i.e. kissing spines) are reported to be the most common osseous cause of back pain in horses.[4]

Spinous process impingement in the thoracic spine occurs most commonly between T13 and T18, reportedly related to altered spinous process morphology.[51,92] Thoroughbreds have a higher prevalence of spinous process impingement or overriding compared with other breeds due to misshapen dorsal apices and narrower interspinous spaces.[4,51] Competitive jumping or dressage horses reportedly have a higher prevalence of thoracolumbar spinous process impingement related to ventroflexion or demanding spinal maneuvers.[4] However, dorsoventral vertebral mobility in the caudal thoracic spine has not been reported to differ from other adjacent vertebral regions, therefore increased dorsoventral movement may not fully account for the vertebral distribution of spinous process impingement.[90,92] Additional weight-carrying requirements have also been implicated because this vertebral region is covered by the saddle while being ridden,[41] although thoracolumbar spinous process impingement has been reported in Standardbreds and an extinct equine species, *Equus occidentalis*, which presumably have not had extraneous weight placed on their backs.[93] Aging has not been found to be a factor in the pathogenesis of thoracolumbar spinous process impingement.[4,51,92]

The diagnosis of impinged or over-riding spinous processes is difficult since apparently normal horses often have a high prevalence of osseous changes radiographically.

Vertebral lamina stress fractures

Stress fractures are usually characterized by bone-specific predilection sites, periosteal and endosteal callus, an incomplete fracture line that may progress to complete fracture, tendency to occur bilaterally, a predominance in athletes undergoing strenuous or repetitive activities, and a patient history of periodic, recurrent, low-grade lameness.[78,81,94] In a necropsy sample of Thoroughbred race horses, 50% (18 of 36) of specimens had incomplete fractures and focal periosteal proliferation of the vertebral lamina, characterized as vertebral stress fractures (see Fig. 21.11).[77] Incomplete fractures of the vertebral lamina occurred consistently at the cranial aspect near the junction of a cranial articular process and the spinous process. Most vertebral stress fractures were continuous with vertical articular clefts of the cranial articular processes, which may provide a site for stress concentration and may contribute to the etiopathogenesis of equine vertebral stress fractures.[95] Thoracolumbar articular process morphology may also contribute to the development of vertebral lamina stress fractures. The articular processes of the caudal thoracic and lumbar portions of the spine (T16–L6) are deeply interlocking and restrict axial rotation.[16,92] Complete articular process fractures in this vertebral region are thought to result from excessive axial rotation.[92] Most specimens had one vertebra affected unilaterally, but several specimens had multiple vertebral lamina stress fractures and some were bilateral. Bilateral complete fractures of the vertebral lamina were noted in one specimen, so that the dorsal L6 vertebral arch and spinous process could be removed.

Spondylosis

Spondylosis is a degenerative disease of the vertebral joints that produces large osteophytes that bridge the ventral vertebral bodies. The exact cause of vertebral body osteophytes is unknown but biomechanical and biochemical mechanisms have been proposed.[96] Abnormal joint loading produces microtrauma and degeneration of the annulus fibrosis and periarticular tissues. Portions of the annulus fibrosis and ventral longitudinal ligaments become ossified and produce partial bridging of the involved joints. As the osteophytes increase in size, nerve roots may be compressed at the intervertebral foramen or spinal cord compression occurs if the proliferation extends dorsally into the vertebral canal. The cycle of altered joint biomechanics and inflammatory mediators may continue until complete ankylosis and obliteration of the joint occurs. The forming vertebral osteophytes and the ankylosed vertebral bodies are susceptible to fracture due to the reduced ability to absorb or transfer normal locomotor forces through the ossified ligaments and fused vertebral joints. Several vertebral bodies are usually involved, especially in advanced stages.

Vertebral fractures

Spinous process fractures of the withers (T2–T9) are usually due to falling over backwards and landing on the highest point of the back. Conservative care is usually recommended. Proper saddle fit is difficult following fracture due to lateral displacement of the multiple fracture fragments. Spinous

process fractures do not typically cause spinal cord compromise.[97]

Vertebral end-plate fractures occur more commonly in foals and are usually related to a fall or significant trauma. Vertebral body compression fractures have been reported in the thoracolumbar vertebral region (T1–T3, T9–T16 and T18–L6) and are frequently due to physical trauma, electric shock or lightning strike.[97–100] Depending on the severity of the vertebral fracture, minimal fracture displacement is usually found. A complete neurologic examination will help to localize the fracture site if spinal cord compromise is present.[101,102] Isolated hindlimb paresis or paralysis with normal forelimb function suggests a spinal cord lesion caudal to T2.

Sacral fractures are a common cause of cauda equina injury. Horses that forcefully back into a solid object or fall backwards can fracture the sacrocaudal vertebral region and produce abnormal perineal neurologic signs. Careful palpation may help to localize a site of pain or vertebral asymmetry.

Neurologic diseases

Conditions that are primarily neurologic in origin must always be considered in differential diagnosis of a back problem. However, there are few disorders that can be specifically related to the thoracolumbar vertebral column.

Ataxia

The most common group of conditions are those that cause ataxia and proprioceptive deficits. These conditions include cervical vertebral stenosis (CVS or wobbler disease), equine protozoal myeloencephalitis (EPM), equine degenerative myeloencephalopathy (EDM) and equine herpesvirus 1 vasculitis (EHV-1). Some of the signs in these conditions will be similar to back problems mainly because of ataxia or incoordination resulting in stiffness or splinting of the back muscles. The hind action with varying degrees of proprioceptive deficit will cause stiffness (hypomelia), weakness and toe dragging. Horses with EPM may also exhibit some lameness and neurogenic atrophy of skeletal muscles. Other causes of ataxia that are usually seasonal are associated with ingestion of certain types of grass (e.g. rye grass, Bermuda and Dallis grass). For more information see Chapter 24.

Lower motor neuron diseases

The condition of stringhalt can produce severe and bizarre signs affecting the hindlimbs.[103] However, in milder cases stiffness and exaggerated action of one or both hindlimbs may be seen. The specific etiology of this condition is not known, but morphologically it appears to be distal axonopathy.[104] Another long-established but little understood condition is that of 'shivering'. It is assumed to be of neurologic origin, but its etiology is completely unknown. The clinical signs involve muscle fasciculations of the back and hindquarters, particularly if a hindlimb is picked up and fully flexed. The condition rarely affects performance and does not appear to be the cause of a genuine back problem. 'Shivers' may also be confused with polysaccharide storage myopathy (see Chapter 6).

Other neurologic diseases

Lyme disease (borreliosis) may need to be considered in some locations where various species of ticks are present. The infective agent is a spirochete, *Borrelia burgdorferi*, which may cause neurologic signs of lethargy or aggression due to low-grade meningitis. Musculoskeletal pain is usually due to polyarthritis or intermittent lameness. Serological confirmation (i.e. IFA, ELISA and Western blot) is possible and response to treatment with amoxicillin or tetracycline for 2 weeks may support a diagnosis of Lyme disease.

Sacropelvic pathology

The ante-mortem diagnosis of sacroiliac joint injury in horses is difficult and often based on a diagnosis of exclusion.[53] Based on a review of the literature, osteoarthritis of the sacroiliac joint is the most prevalent disease process affecting horses with sacroiliac joint pain or dysfunction, although its clinical significance remains uncertain.[33,52,63,105] Degenerative changes tend to be bilaterally symmetric and localized to the medial aspect of the sacroiliac joint (Fig. 21.12).

Sacroiliac ligament desmitis has been documented ultrasonographically in the dorsal portion of the dorsal sacroiliac ligament.[36,79,80] A diagnosis of sacroiliac ligament desmitis is based on loss of normal echogenicity on a short-axis view and a decrease in parallel fiber pattern on the long-axis view. Complete sacroiliac ligament disruption is most likely due to substantial trauma, such as flipping over backwards or catastrophic musculoskeletal injuries associated with race training.[52] However, few cases of complete rupture of the sacroiliac ligaments have been reported in the veterinary literature.[52,106]

The pathogenesis of apparent spontaneous or insidious differences in tuber sacrale height needs to be further researched.[33] The presumed diagnosis of sacroiliac joint subluxation based solely on the presence of tuber sacrale height asymmetry is inappropriate.[56] Variable degrees of tuber sacrale height asymmetry occur frequently and may be due to chronic asymmetric muscular or ligamentous forces acting on the malleable osseous pelvis and not direct sacroiliac ligament injury.[107] Horses with chronic sacroiliac problems and presumed sacroiliac joint subluxation have not had identifiable changes in the sacroiliac ligaments at necropsy.[33] In addition, Standardbred trotters with substantial tuber sacrale height asymmetries did not have significant increases in sacroiliac pain compared to horses with lesser degrees of asymmetry.[108] An ante-mortem diagnosis of sacroiliac joint luxation can only be supported if an acute change in tuber sacrale height asymmetry due to substantial trauma has been documented or if sacroiliac joint instability (i.e. crepitus or independent tuber sacrale movement) is evident during physical examination.

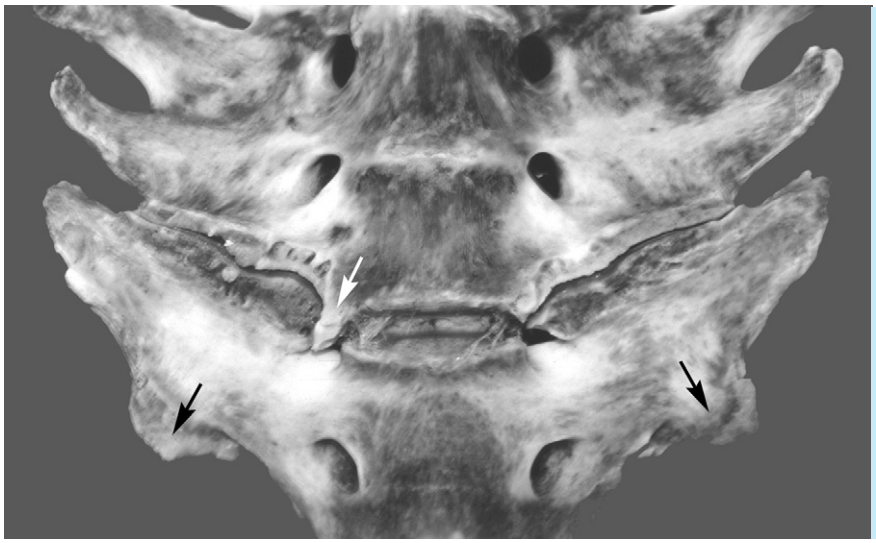


Fig. 21.12
Ventral view of the lumbosacral vertebral region (L5–S2) of a 23-year-old Thoroughbred used for dressage. The horse had a clinical history of psoas muscle soreness and chronic pain localized to the lumbosacral junction. Bilateral intertransverse joint ankylosis (L4–L6), a large osteophyte at the right ventral lumbosacral intervertebral foramen (white arrow) and proliferative changes of the sacral articular surface of the sacroiliac joints (black arrows) are present.

Table 21.5 Techniques used in the treatment of back problems in horses

Category	Specific methods
Rest	Stall rest
	Paddock turnout
	Restricted or controlled exercise
Management	Replace or reflock saddle
	Therapeutic saddle pads
	Change stable and work routine
	Attempt reschooling or try another training approach
	Graduated exercise program
	Assess or modify rider's equitation
Pharmaceuticals	NSAIDs (oral, parenteral or local injection)
	Corticosteroids (oral or local injection)
	Muscle relaxants
	Sclerosing agents (local injection)
	Sweats or counterirritants
	Hormonal therapy
	RVI injections
Surgery	Compound or comminuted fracture of the withers
	Impinged dorsal spinous processes
Physiotherapy	Heat (hot packs, infra-red heat lamp, poultice, short-wave diathermy)
Thermal	Therapeutic ultrasound
Mechanical	Hydrotherapy and swimming
Electrical	Electrical muscle stimulation
	Magnetic therapy (static and pulsed)
	Shock-wave therapy
Manual therapy	Osteopathic techniques
Articular techniques	Chiropractic techniques (high velocity, low amplitude)
Soft tissue techniques	Physical therapy techniques (mobilization, soft tissue techniques)
	Manipulation under general anesthesia (MUA)
	Massage therapy
	Stretching exercises
Acupuncture	Dry needle, aquapuncture, low-level laser puncture
	Moxibustion
Nutraceuticals	Chondroitin sulfate
	Glucosamine
	Glycosaminoglycans
	MSM
Botanicals	Western herbs
	Chinese herbs
Homeopathy	Arnica montana

Pelvic stress fractures also need to be ruled out in horses with sacroiliac pain or dysfunction.[41] A high prevalence of occult pelvic stress fractures has been reported in Thoroughbred race horses.[77,78,94,109] Pelvic stress fractures occur in consistent locations on the caudal border of the ilium adjacent to the sacroiliac joint.[76,81,94] The incomplete fracture lines extend into the caudomedial aspect of the sacroiliac joint, which could possibly produce concurrent sacroiliac joint inflammation and degradation. Complete ilial wing fractures (the most common type of pelvic fracture) typically produce a palpably depressed tuber sacrale on the affected side.[78]

Treatment and management

Medical management

The basic principles of medical management are to reduce pain and muscle spasms to permit better healing, followed by a program of rehabilitation and measures to prevent further injury or stress to the back. It is therefore necessary in many cases to use a combination of medications (e.g. NSAIDs, muscle relaxants, corticosteroids, local irritants or analgesics) in addition to physiotherapy or manipulative therapies (Table 21.5).

Non-steroidal anti-inflammatory drugs (NSAIDs)

For acute and severe pain from muscle strain, fractured withers and acute sacroiliac injury, intravenous NSAIDs followed by oral doses are beneficial. Phenylbutazone (1–2 g, p.o., b.i.d.) is still the drug of choice for many equine practitioners. Other NSAIDs include ketoprofen (2.2 mg/kg (1 mL/100 lb), i.v., s.i.d. for up to 5 days) or naproxen (5–10 mg/kg, p.o., b.i.d. for up to 14 days). If severe muscle spasms are present then diazepam (0.08 mg/kg, i.v. or p.o.) may also be administered.[110] In mild or chronic cases, oral naproxen once or twice daily (5–10 mg/kg) is recommended. Phenylbutazone in low doses (1 g, p.o., s.i.d.) for mild aches and stiffness can be beneficial, but may mask signs of developing tendinitis or other musculoskeletal injuries with long-term use.[110] In chronic cases with low-grade bone pathology (e.g. over-riding dorsal spinous processes or osteoarthritis) a course of NSAIDs can be useful in conjunction with a progressive exercise program. Exercise should begin with a graduated program of lunging to build up and loosen the back and hindquarter muscles. Once the horse is fairly fit on the lunge line, riding work may begin. At this time oral phenylbutazone (i.e. 4 g/day for 4 days; 3 g/day for 4 days; 2 g/day for 4 days; 1 g/day for 4 days and 1 g every other day for 8 days) can be given as the exercise is gradually increased.

Muscle relaxants

Muscle relaxants such as dantrolene sodium (2 mg/kg, p.o., s.i.d.) and methocarbamol (15–44 mg/kg, p.o., s.i.d.) have been advocated for many years, but their effectiveness does not seem to be uniform in all horses.[111] These drugs may not have any specific effects other than reducing muscle tension or spasm in order to allow natural healing to progress. Thiocolchicoside (2–4 mg/100 kg, i.m., twice weekly for 4 weeks) and repeated injections of methocarbamol (10 mg/kg, i.v.) have also been advocated in Europe.[112]

Corticosteroids

The systemic use of corticosteroids is rarely indicated for primary back problems because of the possible side effects of laminitis, arthropathy and alimentary problems. NSAIDs are usually more effective and are associated with fewer adverse effects. The use of local injections into the interspinous spaces for the diagnosis or treatment of impinged or over-riding dorsal spinous processes has been successful.[110] The injection mixture includes methylprednisolone acetate, isoflupredone acetate and serapin with approximately 5 mL injected at each interspinous space of concern. Improvement usually takes 2–6 days and repeated treatment is sometimes necessary. Occasionally, a local infection at the injection site can be a complication, which needs to be treated immediately with antibiotics. Denoix & Dyson recommend local injections of corticosteroids (flumethasone, 0.5–1 mg per injection site with a maximum total dose of 4 mg; dexamethasone 1.5–2.5 mg per injection site, with a maximum total dose of 10 mg; methylprednisolone acetate, 40–60 mg per injection site, with a maximum total dose of 200 mg), sometimes in association with muscle relaxants or serapin.[112] Injections of corticosteroids around the sacroiliac joint region have been used quite extensively, but currently there are no well-designed or controlled trials reported in the literature. Larger doses of corticosteroids (20 mL) mixed with serapin have been advocated for sacroiliac joint injections.[110]

Additional medications

This is another controversial area and one where there is really only anecdotal information on efficacy of a range of different preparations. However, they have been widely used in practice, often in combination with acupuncture or physical therapy.

Serapin Serapin is an aqueous solution derived from the pitcher plant (*Sarraseniaceae*), which is said to block selectively the C fibers that carry pain sensation in peripheral nerves. Serapin is used alone or in combination with other drugs (i.e. corticosteroids) and may be used for both soft tissue (muscle and ligament injuries) and osseous problems (e.g. over-riding dorsal spinous processes). Small doses of 1–2 mL of serapin are given at multiple sites.

Sclerosing agents Again a number of proprietary agents have been used particularly around the sacroiliac joint and in the region of the ventral sacroiliac ligament. Horses are reported to improve their performance, but no scientific reports of their use are available.

Iodine For chronic muscle soreness, multiple injections of 2% iodine in oil (Hypodermin or McKay's solution, 3–4 mL, i.m., at multiple sites) within the sore muscle (e.g.

longissimus and middle gluteal muscles) have been recommended.[110] The injection area is massaged and the horse walked out the next day. Light work can then be resumed. Scientific reports on the beneficial action of iodine on muscle soreness are not currently available.

Hormones The estrus-suppressing drug altrenogest (0.044 mg/kg (1 mL/110 lb), p.o., s.i.d.) has been useful in some mares that exhibit apparent back pain when they are in estrus. Also in young Thoroughbreds that show signs of 'cold back' the use of estrone sulfate (0.1–0.15 mg/kg, i.m., every 2 weeks) may be beneficial.

Rubeola virus immunomodulator (RVI) Some practitioners have promoted RVI injections to assist in the reduction of chronic muscle soreness in some horses. RVI (2 mL, SQ, s.i.d. for 6 or more days) is an inactivated rubeola virus that is reported to have immunomodulatory effects that reduce chronic myofascial inflammation. However, the exact mechanism of action and extensive clinical reports are not currently available.

Mesotherapy

Mesotherapy is a technique that has been used for more than 30 years in France.[113] It consists of multiple intradermal injections with fine 5 mm needles into the dermatomes corresponding to the site of the lesion. The mechanism of action apparently involves type I and II nerve fibers coming from the skin which have collateral fibers that can inhibit pain transmission in the spinothalamic fasciculus, from deep structures of the same spinal segment to the thalamus and cerebrum.[112]

Mesotherapeutic injections are made using a mixture of local anesthetic solution (7 mL of lidocaine, 140 mg), short-acting corticosteroid (7 ml of dexamethasone, 15 mg), and muscle relaxant (8 ml of thiocolchicoside, 20 mg). The injections are made at the level of the lesion and caudal to it, taking into account the caudal orientation of the segmental nerves. For example, if treating over-riding dorsal spines between T10 and T15, the treated region extends from T10 to L1. Two to three rows of injections are made on each side of the median plane. The horse is restricted to light work on the lunge for 3 days. Normal training is progressively resumed over 5 days. A substantial improvement is anticipated within 7–14 days. The expected duration of action varies between 3 and 12 months.

Surgical management

There are few surgical indications for treatment of back problems except for impinged or over-riding dorsal spinous processes. In young horses that fracture the dorsal spines in the withers (T3–T10) surgery is not necessary unless the fractures are highly comminuted, when it may be necessary to debride the site to prevent infection or osteomyelitis.

Resection of dorsal spinous processes

Surgery for over-riding spinous processes was first reported by Roberts[114] and since then there have been a number of modifications to the technique.[34,115,116] However, the principle is the same, which is to remove the parts of the spinous processes that impinge. We believe that it is absolutely essential to confirm the correct diagnosis and select the most appropriate spines to alleviate the condition. There are many horses that show radiographic findings of over-riding spinous processes that do not exhibit clinical signs of a back problem.[68] Furthermore, many milder cases of over-riding spinous processes will respond to medical and conservative therapy.[51]

A recent paper reported by far the largest series to date and recorded a good response to surgery in those horses that failed to respond to conservative management.[34] The surgical technique involved placing the horse in lateral recumbency. A midline incision is made through the skin, subcutis and supraspinous ligament. The incision extends from one spinous process cranial to those identified for resection to one process caudal to them. The dorsal 4–5 cm of the dorsal spinous processes are dissected free of the supraspinous ligament, the interspinous ligaments and adjacent muscle tissue. Partial resection of the processes is performed with an oscillating saw to a depth that ensures that there is a minimum gap of 5 mm between the remaining bodies of each process resected. The minimum number of processes are resected in each case (e.g. if two processes are affected then one is removed, and if three are affected only the middle one is removed). One centimeter of the dorsal apex of the adjacent spinous process is also removed so that the change from resected to unresected processes is less abrupt. The supraspinous ligament and muscles are sutured and a simple interrupted suture placed between these sutures. The subcutis is sutured using three metric polyglycolic acid sutures and the skin is closed. The wound is protected by a stent bandage sutured over it. In the series, 72% of horses returned to full work and a further 9% improved sufficiently to be used for some athletic work.[34]

Chiropractic

Mechanism of action

Chiropractic evaluation focuses on evaluating and localizing segmental vertebral dysfunction (i.e. chiropractically defined 'subluxation') which is characterized by localized pain, muscle hypertonicity and reduced joint motion.[117] A thorough knowledge of vertebral anatomy, joint physiology and biomechanics is required for proper chiropractic evaluation and treatment. Alterations in articular neurophysiology from mechanical or chemical injuries can affect both mechanoreceptor and nociceptor function via increased joint capsule tension and nerve ending hypersensitivity.[118] Mechanoreceptor stimulation induces reflex paraspinal musculature hypertonicity and altered local and systemic neurologic reflexes. Nociceptor stimulation results in a lowered pain threshold, sustained afferent stimulation (i.e. facilitation), reflex paraspinal musculature hypertonicity and abnormal neurologic reflexes.

The goal of chiropractic treatment is to restore normal joint motion, stimulate neurologic reflexes and to reduce pain and muscle hypertonicity. Multiple theories have been proposed and tested over the years to explain the pathophysiol-

ogy of vertebral segment dysfunction and its interactions and influences on the neuromusculoskeletal system.[117,119] Chiropractic treatment is thought to affect mechanoreceptors (i.e. Golgi tendon organ and muscle spindles) to induce reflex inhibition of pain and reflex muscle relaxation and to correct abnormal movement patterns.[45,120] Anecdotal evidence and clinical experience suggest that chiropractic is an effective adjunctive modality for the diagnosis and conservative treatment of select musculoskeletal-related disorders in horses. However, therapeutic trials of chiropractic manipulations are often used since we currently have limited formal research available about the effectiveness of chiropractic procedures in equine practice.

During treatment, a 'release' or movement of the restricted articulation is often palpable. An audible 'cracking' or 'popping' sound may also be heard during chiropractic treatment as the applied force overcomes the elastic barrier of joint resistance.[121,122] The rapid articular separation produces a cavitation of the synovial fluid.[123] In humans, radiographic studies of synovial articulations after manipulation have shown a radiolucent cavity within the joint space (i.e. vacuum phenomenon) that contains 80% carbon dioxide and lasts for 15–20 minutes. A second attempt to recavitate the joint will be unsuccessful and potentially painful until the intra-articular gas has been reabsorbed (i.e. refractory period). The static position of the vertebral or sacroiliac joints in humans has been studied before and after manipulation by roentgen stereophotogrammetric analysis, which allows precise measurements of three-dimensional articular movement.[124] Static palpation changes were noted before and after manipulation but no changes were seen with the roentgen stereophotogrammetric analysis. Therefore, soft tissue responses such as joint capsules, muscles, ligaments, tendons and postural neuromuscular reflex patterns should be the focus of future spinal manipulative studies and not articular malpositioning (i.e. bone out of place).[124]

Indications

The principal indications for equine chiropractic evaluation are back or neck pain, localized or regional joint stiffness, poor performance and an altered gait that is not associated with overt lameness. A thorough diagnostic work-up is required to identify soft tissue and osseous pathology, neurologic disorders or other lameness conditions that may not be responsive to chiropractic care. The primary clinical signs that equine chiropractors look for are localized musculoskeletal pain, muscle hypertonicity and restricted joint motion. This triad of clinical signs can be found in a variety of lower limb disorders, but is most evident in neck or back problems. Chiropractic care can help manage the muscular, articular and neurologic components of select musculoskeletal injuries in performance horses. Musculoskeletal conditions that are chronic or recurring, not readily diagnosed or are not responding to conventional veterinary care may be indicators that chiropractic consultation is needed. Chiropractic care is usually contraindicated in the acute stages of soft tissue injury. However, as the soft tissue injury heals, chiropractic has the potential to help restore normal joint motion, thus limiting the risk for future reinjury.[40] Chiropractic care may provide symptomatic relief in early degenerative joint disease if related to joint hypomobility and subsequent joint degeneration. Chiropractic is usually much more effective in the early clinical stages of disease versus end-stage disease where reparative processes have been exhausted.

Contraindications

Chiropractic is not a 'cure all' for all back problems and is not suggested for treatment of fractures, infections, neoplasia, metabolic disorders or non-mechanically related joint disorders. Acute episodes of sprains or strains, degenerative joint disease or impinged spinous processes are also relative contraindications for chiropractic treatment. All neurologic diseases should be fully worked up to assess the potential risks or benefits of chiropractic treatment. Serious diseases requiring immediate medical or surgical care need to be ruled out and treated by conventional veterinary medicine before routine chiropractic treatment is begun. However, chiropractic care may contribute to the rehabilitation of most postsurgical cases or severe medical conditions by helping in the restoration of normal musculoskeletal function. Chiropractic care cannot reverse severe degenerative processes or overt pathology.

Acupuncture

Mechanism of action

Acupuncture involves the insertion of fine needles into specific predetermined locations (i.e. acupuncture points) to produce therapeutic effects.[125] Acupuncture points are often chosen within the same dermatome as the lesion or condition being treated, as well as local tender or painful sites, points cranial or caudal, proximal or distal to the localized lesion.[126] Additional methods of stimulation include acupressure, aquapuncture, electrostimulation and low-level laser therapy. Theoretically, each acupuncture point, or combination of points, has specific therapeutic actions when stimulated.

The primary benefit of acupuncture for back problems is pain management via opioid (i.e. enkephalin and β-endorphin) and non-opioid (e.g. serotonin) pathways.[126] Pain relief is often immediate, but may have variable durations of effectiveness, depending on the type and severity of musculoskeletal dysfunction. Acute injuries often respond rapidly and require fewer treatment sessions, whereas chronic musculoskeletal conditions may require periodic or long-term treatment. Acupuncture is often the treatment of choice for trigger points, which are localized tight, painful bands of muscle at characteristic locations within large muscle groups, particularly the middle gluteal muscle.

Indications

Clinical studies and experimental reports indicate that acupuncture is a safe and effective modality for specific musculoskeletal conditions if used properly.[125] Disease conditions managed by acupuncture include trauma, osteoarthritis and

muscle hypertonicity. Pain is the primary indication for acupuncture in horses with back problems. Acupuncture does not have any known direct effects on reducing joint stiffness, as do manual therapies. Therefore, synergistic effects are often obtained with combined chiropractic and acupuncture treatment that cannot be obtained consistently with either modality by itself. The immediate pre-race use of acupuncture is banned by many racing jurisdictions and athletic organization regulations due to its potential misuse of analgesic properties.

Contraindications

There are few specific contraindications for acupuncture since the majority of medical and surgical conditions have associated indications for acupuncture. Fractures, active infections and bleeding tendencies are relative contraindications. Risks and complications associated with needle placement include infection, puncture of organs or pneumothorax. Solid needles or aquapuncture are often recommended over the thoracolumbar region due to the risk of breaking off a portion of the needle within the epaxial muscles from the action of the thoracolumbar fascia on the needle.

Physical therapy

Mechanism of action

Physical therapy modalities that may have direct application to back problems in horses include devices that apply electrical currents for pain control or neuromuscular rehabilitation; thermal modalities (i.e. superficial and deep heat or cold applications) for influencing inflammatory mediators, collagen extensibility and altering nerve conduction; and mechanical approaches (e.g. massage, vibration, stretching and training exercises) for maximizing musculoskeletal rehabilitation.

Indications

In the absence of trauma or documented pathologic findings, the primary goal of treatment should address restoration of function and prevention of future disability.[40] Management should be systematically and methodically directed toward developing co-ordination and proprioception, flexibility, strength and endurance. The negative effects of immobilization and deconditioning should be minimized with early mobilization and controlled activity. Increased mobility is addressed with joint mobilization and muscle stretching.[127] Altered movement patterns are addressed with co-ordination via proprioceptive retraining, postural re-education, muscle strengthening and endurance training.[40]

The primary indications of physical therapy for back or pelvic problems include localized or generalized pain, joint motion restrictions and altered back muscle tonicity.[128] Pain modulation can be provided by influencing inflammatory mediators, altering pain perception and transmission, and increasing β-endorphin levels. Physical therapy modalities involved in pain control include electrical stimulation (i.e. muscle stimulation, transcutaneous electrical nerve stimulation (TENS)), the application of hot or cold, mechanical vibration and electromagnetic modalities. Soft tissue and articular motion restrictions (i.e. stiffness) can be directly addressed with specific stretching exercises to induce creep and stress relaxation within fibrotic or shortened periarticular soft tissues. With minimal training, horses and their owners can be taught how to do simple but effective passive joint mobilization and active stretching exercises (i.e. carrot stretches) to improve both axial skeleton and limb flexibility. Cryotherapy (i.e. ice packs or ice massage) is indicated in the first 24–48 hours post injury to reduce pain, induce muscle relaxation and reduce inflammation. The application of heat or electrical stimulation can provide increased soft tissue extensibility, reduced inflammation and adhesion formation, and pain control to help facilitate the restoration of normal joint motion.[118]

Abnormal muscle tone can be addressed with modalities that increase or decrease muscle contractility or coactivation and nerve conduction or inhibition. Some of these modalities include hydrotherapy, electrical stimulation and rehabilitative exercises that specifically address issues of reduced flexibility, co-ordination, strength and endurance. In humans, anti-inflammatories and other drugs can be delivered into superficial soft tissues via electrical currents (i.e. iontophoresis) or via mechanical sound waves (i.e. phonophoresis). However, preliminary equine research indicates that a heavy hair coat, thick skin and deep articular structures may limit the overall effectiveness of these novel drug delivery systems for back problems.

Contraindications

Contraindications for massage include active skin lesions, open wounds, acute inflammation or persistent muscle hypertonicity (i.e. exertional rhabdomyolysis).[129] Contraindications for electrical modalities include active skin lesions, open wounds, pain of unknown origin or pain conditions where masking the pain may be detrimental (e.g. pre-race).[130] Contraindications for superficial or deep heating modalities include acute injury or inflammation, open wounds, recent or potential hemorrhage, neoplasms or impaired sensation.[118] Precautions or contraindications for cryotherapy include open wounds, vascular compromise or peripheral vascular disease due to the induced vasoconstriction produced by the ice.[118]

Future areas of research

In horses with back pain, specific functional pathologies that need to be addressed in addition to initial pain relief include trigger points, hypertonic muscles, weak muscles, abnormal movement patterns and joint dysfunction. Compared to their human counterparts, veterinarians and equine athletes often have a very limited selection of options for the treatment of musculoskeletal disorders. Currently, we do not have objective measurement or rehabilitation tools to specifically assess soft tissue or articular pain, reduced flexibility and joint stiffness,

muscle hypertonicity, trigger points or alterations in proprioception or co-ordination associated with musculoskeletal or nerve dysfunction. Normal kinematics of the thoracolumbar spine have been investigated[8,9,11,131,132] but continued work needs to be done to assess segmental vertebral motion and its response to specific and defined articular and soft tissue injuries. Objective measures of spinal stiffness have been investigated[133] but the effects of pain, muscle hypertonicity, articular process osteoarthritis and concurrent lameness have not been explored.

Functional outcome measures assess how well a horse is able to do the job asked of it (e.g. speed, flexibility, co-ordination, strength and endurance). Quantitative assessments of pain include the use of a 0–10 pain scale, algometry or pain pressure threshold measurements, and mapping areas of pain. A 0–10 visual analog scale or pain scale is easy to use and provides a semi-objective means of following pain, dysfunction, performance or any other musculoskeletal parameter either immediately before and after treatment or over several days or weeks of treatment. Measurements can be compiled independently by both the owner and the veterinarian, with similarities or differences evaluated.

Other areas of musculoskeletal treatment that need further scientific investigation include well-defined, scientifically validated strength and endurance training programs tailored for the unique athletic demands of the various equestrian events. It is hoped that new insights into measuring musculoskeletal dysfunction and the pathophysiology of chronic pain syndromes will assist in assessing the effectiveness of many of the traditional and complementary modalities currently applied to horses with the rationale of reducing morbidity and improving overall performance in our elite equine athletes.

References

1. Lupton. Mayhew's illustrated horse management. London: Allen; 1876.
2. Youatt W. The horse: With a treatise on draught. London: Baldwin and Cardock; 1831.
3. British Equine Veterinary Association. Survey of equine disease. Vet Rec 1965; 77:528–538.
4. Jeffcott LB. Disorders of the thoracolumbar spine of the horse – a survey of 443 cases. Equine Vet J 1980; 12(4):197–210.
5. Jeffcott LB. Back problems in the horse – a look at past, present and future progress. Equine Vet J 1979; 11(3): 129–136.
6. Cauvin E. Assessment of back pain in horses. In Practice 1997; 19:522–533.
7. Licka T, Peham C. An objective method for evaluating the flexibility of the back of standing horses. Equine Vet J 1998; 30(5):412–415.
8. Pourcelot P, Audigié F, Degueurce C, et al. Kinematics of the equine back: a method to study the thoracolumbar flexion-extension movements at the trot. Vet Res 1998; 29: 519–525.
9. Audigié F, Pourcelot P, Degueurce C, et al. Kinematics of the equine back: flexion-extension movements in sound trotting horses. Equine Vet J 1999; 30(Suppl):210–213.
10. Denoix J-M. Spinal biomechanics and functional anatomy. Vet Clin North Am Eq Pract 1999; 15(1):27–60.
11. Licka TF, Peham C, Zohmann E. Treadmill study of the range of back movement at the walk in horses without back pain. Am J Vet Res 2001; 62:1173–1179.
12. Faber M, Johnston CJ, Schamhardt HC, et al. Basic three-dimensional kinematics of the vertebral column of horses trotting on a treadmill. Am J Vet Res 2001; 62:757–764.
13. Haussler KK, Bertram JEA, Gellman K. *In-vivo* segmental kinematics of the thoracolumbar spinal region in horses and effects of chiropractic manipulations. Am Assoc Eq Pract 1999; 45:327–329.
14. Getty R. Sisson and Grossman's the anatomy of the domestic animals, 5th edn. Philadelphia, PA: Saunders; 1975.
15. Stecher RM. Lateral facets and lateral joints in the lumbar spine of the horse: a descriptive and statistical study. Am J Vet Res 1962; 23(96):939–947.
16. Townsend HGG, Leach DH. Relationship between intervertebral joint morphology and mobility in the equine thoracolumbar spine. Equine Vet J 1984; 16(5):461–465.
17. Denoix J-M. Aspects fonctionnels et approche sémiologique des régions lombo-sacrale et sacro-iliaque chez le cheval. Swiss Vet 1991; 8:89–106.
18. Jeffcott LB, Dalin G. Natural rigidity of the horse's backbone. Equine Vet J 1980; 12(3):101–108.
19. Giles LGF. Anatomical basis of low back pain. Baltimore, MD: Williams and Wilkins; 1989.
20. Bogduk N, Twomey LT. Clinical anatomy of the lumbar spine, 2nd edn. Melbourne, Australia: Churchill Livingstone; 1991.
21. Cramer GD, Darby SA. Basic and clinical anatomy of the spine, spinal cord and ANS. St Louis, MD: Mosby-Year Book; 1995.
22. Nickel R, Schummer A, Sieferle E, et al. The anatomy of the domestic animals: volume 1. The locomotor system of the domestic mammals, 5th edn. New York: Springer-Verlag; 1986.
23. Budras K-D, Sack WO, Röck S. Anatomy of the horse: an illustrated text, 2nd edn. London: Mosby-Wolfe; 1994.
24. Rutherford KMD. Assessing pain in animals. Animal Welfare 2002; 11:31–53.
25. Jeffcott LB, Dalin G, Drevemo S, et al. Effect of induced back pain on gait and performance of trotting horses. Equine Vet J 1982; 14(2):129–133.
26. Jeffcott LB. Diagnosis of back problems in the horse. Compend Cont Ed Pract Vet 1981; 3(4):S134–S143.
27. Martin BB Jr, Klide AM. Physical examination of horses with back pain. Vet Clin North Am Eq Pract 1999; 15(1):61–70.
28. Rooney JR. Congenital equine scoliosis and lordosis. Clin Orthoped Rel Res 1969; 62(Jan/Feb):25–30.
29. Lerner DJ. Congenital kyphoscoliosis in a foal. J Am Vet Med Assoc 1978; 172(3):274–276.
30. Adams SB, Steckel RR, Blevins WE. Discospondylitis in five horses. J Am Vet Med Assoc 1985; 186:270–272.
31. Hillyer MH, Innes JF, Patteson MW, et al. Discospondylitis in the adult horse. Vet Rec 1996; 139:519–521.
32. Rooney JR, Delaney FM, Mayo JA. Sacroiliac luxation in the horse. Equine Vet J 1969; 1:287–289.
33. Jeffcott LB, Dalin G, Ekman S, et al. Sacroiliac lesions as a cause of chronic poor performance in competitive horses. Equine Vet J 1985; 17(2):111–118.
34. Walmsley JP, Pettersson H, Winberg F, et al. Impingement of the dorsal spinous processes in two hundred and fifteen horses: case selection, surgical technique and results. Equine Vet J 2002; 34(1):23–28.

35. Denoix J-M. Ultrasonographic evaluation of back lesions. Vet Clin North Am Eq Pract 1999; 15(1):131–160.
36. Gillis C. Spinal ligament pathology. Vet Clin North Am Eq Pract 1999; 15(1):97–101.
37. Herrod-Taylor EE. A technique for manipulation of the spine in horses. Vet Rec 1967; 81:437–439.
38. Marks D. Back pain. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia, PA: Saunders; 1997; 6–12.
39. Stashak TS. Adams' lameness in horses, 5th edn. Philadelphia, PA: Lippincott Williams and Wilkins; 2002.
40. Liebenson C. Rehabilitation of the spine. Baltimore, MD: Williams and Wilkins; 1996.
41. Steckel RR, Kraus-Hansen AE, Fackelman GE, et al. Scintigraphic diagnosis of thoracolumbar spinal disease in horses: a review of 50 cases. Am Assoc Eq Pract 1991; 37:583–591.
42. Cox JH, Murray RC, DeBowes RM. Diseases of the spinal cord. In: Kobluk CN, Ames TR, Geor RJ, eds. The horse: diseases and clinical management. Philadelphia, PA: Saunders; 1995; 443–467.
43. Valberg SJ, Hodgson DR. Diseases of muscle. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St. Louis, MO: Mosby; 2002; 1266–1291.
44. Quiroz-Rothe E, Novales M, Aguilera-Tejero E, et al. Polysaccharide storage myopathy in the M. longissimus lumborum of showjumpers and dressage horses with back pain. Equine Vet J 2002; 34(2):171–176.
45. Gatterman MI. Foundations of chiropractic. St Louis, MO: Mosby-Year Book; 1995.
46. Chaitow L. Palpation skills. New York, NY: Churchill Livingstone; 1997.
47. Fischer AA. Pressure algometry over normal muscles: standard values, validity and reproducibility of pressure threshold. Pain 1987; 30:115–126.
48. Fischer AA. Application of pressure algometry in manual medicine. Man Med 1990; 5:145–150.
49. Tunks E, McCain GA, Hart LE, et al. The reliability of examination for tenderness in patients with myofascial pain, chronic fibromyalgia and controls. J Rheumatol 1995; 22:944–952.
50. Dung HC. A simple new method for the quantitation of chronic pain. Am J Acupuncture 1985; 13(1):57–62.
51. Jeffcott LB. Radiographic features of the normal equine thoracolumbar spine. Vet Radiol 1979; 20:140–147.
52. Haussler KK, Stover SM, Willits NH. Pathology of the lumbosacral spine and pelvis in Thoroughbred racehorses. Am J Vet Res 1999; 60(2):143–153.
53. Tucker RL, Schneider RK, Sondhof AH, et al. Bone scintigraphy in the diagnosis of sacroiliac injury in twelve horses. Equine Vet J 1998; 30(5):390–395.
54. Kessler RM, Hertling D. Assessment of musculoskeletal disorders. In: Hertling D, Kessler RM, eds. Management of common musculoskeletal disorders: physical therapy principles and methods, 2nd edn. Philadelphia, PA: Lippincott; 1990; 68–71.
55. Adams OR. Subluxation of the sacroiliac joint in horses. Am Assoc Eq Pract 1969; 15:198–207.
56. Cassidy JD, Townsend HGG. Sacroiliac joint strain as a cause of back and leg pain in man – implications for the horse. Am Assoc Eq Pract 1985; 31:317–333.
57. Luukkainen R, Nissila M, Asikainen E, et al. Periarticular corticosteroid treatment of the sacroiliac joint in patients with seronegative spondylarthropathy. Clin Exp Rheumatol 1999; 17:88–90.
58. Maugars Y, Mathis C, Berthelot JM, et al. Assessment of the efficacy of sacroiliac corticosteroid injections in spondyloarthropathies: a double-blinded study. Br J Rheumatol 1996; 35:767–770.
59. Rooney JR. The horse's back: biomechanics of lameness. Equine Pract 1982; 4(2):17–27.
60. Hardy J, Marcoux M. L'Arthrose sacro-iliac chez le cheval Standardbred. Med Vet Quebec 1985; 15:185–189.
61. Snyder JR. Selected intra-articular injections in the horse. Proceedings of the 7th Congress on Equine Medicine and Surgery, Geneva, Switzerland, 2001; 115–123.
62. Engeli E, Haussler KK, Erb HN. A diagnostic injection technique of the sacroiliac joint in horses. 12th Annual ACVS Veterinary Symposium: Equine Proceedings, San Diego, CA, 2002;7.
63. Dalin G, Jeffcott LB. Sacroiliac joint of the horse. 1. Gross morphology. Anat Histol Embryol 1986; 15:80–94.
64. Dyce KM, Sack WO, Wensing CJG. Textbook of veterinary anatomy, 2nd edn. Philadelphia, PA: Saunders; 1996.
65. Butler JA, Colles CM, Dyson SJ, et al. The spine. In: Clinical radiology of the horse. Oxford: Blackwell Science; 1993; 355–398.
66. Jeffcott LB. Back problems in the horse – a method of clinical examination. Vet Rec 1979; 1(Suppl 5):4–15.
67. Weaver MP, Jeffcott LB, Nowak M. Radiology and scintigraphy. Vet Clin North Am Eq Pract 1999; 15(1): 113–129.
68. Jeffcott LB. Radiographic examination of the equine vertebral column. Vet Radiol Ultrasound 1979; 20:135–139.
69. Butler JA, Colles CM, Dyson SJ, et al. The pelvis and femur. In: Clinical radiology of the horse. Oxford: Blackwell Science; 1993; 399–421.
70. Jeffcott LB. Radiographic appearance of equine lumbosacral and pelvic abnormalities by linear tomography. Vet Radiol 1983; 24(5):201–213.
71. Ueltschi G. Bone and joint imaging with 99mTc labeled phosphates as a new diagnostic aid in veterinary orthopedics. J Am Vet Radiol Soc 1977; 18:80–84.
72. Devous M, Twardock A. Techniques and applications of nuclear medicine in the diagnosis of equine lameness. J Am Vet Med Assoc 1984; 184:318–325.
73. Lamb CR, Koblik PD. Scintigraphic evaluation of skeletal disease and its application to the horse. Vet Radiol Ultrasound 1988; 29:16–27.
74. Steckel RR. The role of scintigraphy in lameness evaluation. Vet Clin No Am Eq Pract 1991; 7:207–239.
75. Morris EA, Seeherman HJ, O'Callaghan MW, et al. Scintigraphic identification of skeletal muscle damage in horses 24 hours after strenuous exercise. Equine Vet J 1991; 23:347–352.
76. Hornof WJ, Stover SM, Koblik PD, et al. Oblique views of the ilium and the scintigraphic appearance of stress fractures of the ilium. Equine Vet J 1996; 28(5):355–358.
77. Haussler KK, Stover SM. Stress fractures of the vertebral lamina and pelvis in Thoroughbred racehorses. Equine Vet J 1998; 30(5):374–381.
78. Pilsworth RC, Shepherd MC, Herinckx BMB, et al. Fracture of the wing of the ilium, adjacent to the sacroiliac joint, in Thoroughbred racehorses. Equine Vet J 1994; 26(2): 94–99.
79. Denoix J-M. Ligament injuries of the axial skeleton in the horse: supraspinal and sacroiliac desmopathies. Dubai International Equine Symposium 1996; 273–286.
80. Tomlinson JE, Sage AM, Turner TA, et al. Detailed ultrasonographic mapping of the pelvis in clinically normal horses and ponies. Am J Vet Res 2001; 62: 1768–1775.

81. Shepherd MC, Pilsworth RC. The use of ultrasound in the diagnosis of pelvic fractures. Equine Vet Educ 1994; 6(4): 223–227.
82. Reef VB. Diagnosis of pelvic fractures in horses using ultrasonography. Vet Radiol Ultrasound 1992; 33:121.
83. von Schweinitz DG. Thermographic diagnostics in equine back pain. Vet Clin North Am Eq Pract 1999; 15(1): 161–177.
84. Turner TA. Thermography as an aid in the localization of upper hindlimb lameness. Pferdeheilkunde 1996; 12(4): 632–634.
85. Rooney JR, Prickett ME. Congenital lordosis of the horse. Cornell Vet 1967; 57(3):417–428.
86. Wagner PC. Diseases of the spine. In: Mansmann RA, McAllister ES, eds. Equine medicine and surgery, 3rd edn. Santa Barbara, CA: American Veterinary Publications; 1982; 1145–1158.
87. Bogduk N. The anatomical basis for spinal pain syndromes. J Manip Physiol Ther 1995; 18(9):603–605.
88. Jeffcott LB. The horse's back – muscle, soft tissue and skeletal problems. Their diagnosis and management. Dubai International Equine Symposium 1996; 337–359.
89. Denoix J-M. Diagnosis of the cause of back pain in horses. In: Lindiven A, ed. 1st Conf Equine Sports Med & Sci. Wageningen Pers, Wageningen, The Netherlands; 1998; 97–110.
90. Townsend HGG, Leach DH, Fretz PB. Kinematics of the equine thoracolumbar spine. Equine Vet J 1983; 15(2):117–122.
91. van Schaik JPJ, Verbiest H, van Schaik FDJ. Isolated spinous process deviation: a pitfall in the interpretation of AP radiographs of the lumbar spine. Spine 1989; 14(9):970–976.
92. Townsend HGG, Leach DH, Doige CE, et al. Relationship between spinal biomechanics and pathological changes in the equine thoracolumbar spine. Equine Vet J 1986; 18(2):107–112.
93. Klide AM. Overriding vertebral spinous processes in the extinct horse, *Equus occidentalis*. Am J Vet Res 1989; 50(4):592–593.
94. Stover SM, Ardans AA, Read DH, et al. Patterns of stress fractures associated with complete bone fractures in racehorses. Am Assoc Eq Pract 1993; 39:131–132.
95. Haussler KK, Stover SM, Willits NH. Developmental variation in lumbosacropelvic anatomy of Thoroughbred racehorses. Am J Vet Res 1997; 58(10):1083–1091.
96. Clyne MJ. Pathogenesis of degenerative joint disease. Equine Vet J 1987; 19:15–18.
97. Jeffcott LB, Whitwell KE. Fractures of the thoracolumbar spine of the horse. Am Assoc Eq Pract 1976; 22:91–102.
98. Wagner PC. Surgical treatment of traumatic disease of the spinal column. In: Auer JA, ed. Equine surgery. Philadelphia, PA: Saunders; 1992; 1093–1098.
99. Rhoads WS, Cox JH. What is your diagnosis? J Am Vet Med Assoc 1997; 210(6):755–756.
100. DeBowes RM, Wagner PC, Gavin PR, et al. Vertebral compression fracture in a foal following electric shock. J Vet Orthop 1981; 2(2):14–19.
101. Moyer WA, Rooney JR. Vertebral fracture in a horse. J Am Vet Med Assoc 1971; 159(8):1022–1024.
102. Chiapetta JR, Baker JC, Feeney DA. Vertebral fracture, extensor hypertonia of thoracic limbs, and paralysis of pelvic limbs (Schiff-Sherrington syndrome) in an Arabian foal. J Am Vet Med Assoc 1985; 186(4):387–388.
103. Huntington PJ, Jeffcott LB, Friend SCE, et al. Australian stringhalt. Epidemiological, clinical and neurological investigations. Equine Vet J 1989; 21:266–273.
104. Slocombe RF, Huntington PJ, Friend SCE, et al. Pathological aspects of Australian stringhalt. Equine Vet J 1992; 24(3):174–183.
105. Townsend HGG. Pathogenesis of back pain in the horse. Equine Sports Med 1987; 6:29–32.
106. Rooney JR. Sacroiliac luxation. Mod Vet Pract 1979; 60:45–46.
107. Haussler KK. Anatomy of the thoracolumbar vertebral region. Vet Clin North Am Eq Pract 1999; 15(1):13–26.
108. Dalin G, Magnusson L-E, Thafvelin BC. Retrospective study of hindquarter asymmetry in Standardbred Trotters and its correlation with performance. Equine Vet J 1985; 17(4):292–296.
109. Shepherd MC, Pilsworth RC, Hopes R, et al. Clinical signs, diagnosis, management and outcome of complete and incomplete fracture to the ilium. Am Assoc Eq Pract 1994; 40:177–180.
110. Marks D. Medical management of back pain. Vet Clin North Am Eq Pract 1999; 15(1):179–194.
111. Marks D. Notes on treatment and management on thoracolumbar pain in the horse. Am Assoc Eq Pract 1985; 30:353–357.
112. Denoix J-M, Dyson SJ. The thoracolumbar spine. In: Ross M, Dyson S, eds. Diagnosis and management of lameness in the horse. Philadelphia, PA: Saunders; 2003; 509–521.
113. Denoix J-M. Personal communication. 2000.
114. Roberts EJ. Resection of thoracic or lumbar spinous processes for the relief of pain responsible for lameness and some other locomotor disorders of horses. Am Assoc Eq Pract 1968; 14:13–29.
115. Jeffcott LB, Hickman J. The treatment of horses with chronic back pain by resecting the summits of the impinging dorsal spinous processes. Equine Vet J 1975; 7(3):115–119.
116. Steckel RR, Krasu-Hansen AE, Fackelman GE, et al. Clinical aspects of thoracolumbar spinal disease in horses: a review of 50 cases. Am Assoc Eq Pract 1991; 36:583.
117. Leach RA. The chiropractic theories: principles and clinical applications, 3rd edn. Baltimore, MD: Williams and Wilkins; 1994.
118. Cameron MH. Physical agents in rehabilitation. Philadelphia, PA: Saunders; 1999.
119. Haldeman S. Principles and practice of chiropractic, 2nd edn. Norwalk, CT: Appleton and Lange; 1992.
120. Cassidy JD, Lopes AA, Yong-Hing K. The immediate effect of manipulation versus mobilization on pain and range of motion in the cervical spine: a randomized controlled trial. J Manip Physiol Ther 1992; 15(9):570–575.
121. Brodeur R. The audible release associated with joint manipulation. J Manip Physiol Ther 1995; 18(3): 155–164.
122. Reggars JW, Pollard HP. Analysis of zygapophyseal joint cracking during chiropractic manipulation. J Manip Physiol Ther 1995; 18(2):65–71.
123. Herzog W, Zhang YT, Conway PJW, et al. Cavitation sounds during spinal manipulative treatments. J Manip Physiol Ther 1993; 16(8):523–526.
124. Tullberg T, Blomberg S, Branth B, et al. Manipulation does not alter the position of the sacroiliac joint. Spine 1998; 23(10):1124–1129.
125. Altman S. Small animal acupuncture: scientific basis and clinical applications. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine: principles and practice. St Louis, MO: Mosby; 1998; 147–167.
126. Fleming P. Equine acupuncture. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine:

principles and practice. St Louis, MO: Mosby; 1998; 169–184.
127. Porter M. Stretching for the horse. In: Porter M, ed. The new equine sports therapy. Lexington, KY: The Blood-Horse; 1998; 31–42.
128. Porter M. Physical therapy. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine: principles and practice. St Louis, MO: Mosby; 1998; 201–212.
129. Porter M, Bromiley MW. Massage therapy. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine: principles and practice. St Louis, MO: Mosby; 1998; 213–216.
130. Bromiley MW. Physical therapy for the equine back. Vet Clin North Am Eq Pract 1999; 15(1):223–248.
131. Faber M, Schamhardt HC, van Weeren R, et al. Basic three-dimensional kinematics of the vertebral column of horses walking on a treadmill. Am J Vet Res 2000; 61(4):399–406.
132. Haussler KK, Bertram JEA, Gellman K, et al. Segmental *in vivo* vertebral kinematics at the walk, trot and canter: a preliminary study. Equine Vet J 2001; 33:160–164.
133. Haussler KK. Dorsoventral spinal mobility in horses: chiropractic treatment versus control group comparisons. 2nd International Symposium on Rehabilitation and Physical Therapy in Veterinary Medicine, Knoxville, TN, 2002; 207–208.

CHAPTER 22

Prevention of orthopedic disease in athletic horses

Antonio Cruz

Introduction

The science of injury prevention in equine sports medicine is still underdeveloped. Although there exists valuable and scientifically obtained information regarding the characterization of horses' gaits and the influence of conformation and environment (shoeing, surface, etc.) on the incidence of injuries, it appears that practical recommendations towards injury prevention are not very commonly implemented nor regulated within the equine industry across the world. Largely, riders and trainers may still believe that traditional training methods and good horsemanship will produce sound horses and the implementation of scientific findings in the daily equestrian routine has not found a resounding echo amongst equestrians. In contrast, in the human literature there are a large number of studies pertaining to injury prevention, mostly driven by the rising cost of healthcare and liability associated with sport-induced injuries. In addition, the approach to training human elite athletes is mostly multidisciplinary, including exercise physiologists, kinesiologists, physicians, physiotherapists, nutritionists and biomechanical engineers.

In the last decade a significant thrust has occurred in the area of sport-induced injuries in horses. As a result there is a body of information describing risk factors, incidence of injuries and preventive measures for exercise-induced injuries. Despite a higher number of horses enrolled in equestrian disciplines other than racing, most of the investigative efforts have been directed to the racing industry due to the greater socioeconomic impact that it represents. The racing industry also, concerned about horse welfare and its public perception, has funded most of this research as an effort to improve racing conditions. In the United Kingdom a comprehensive approach to preventing race horse injuries[1] has been warmly welcomed by the racing industry. A close partnership amongst owners, trainers, jockeys, veterinarians, epidemiologists and regulatory bodies is producing relevant information regarding the incidence of race horse injuries and associated risk factors and should serve as a role model for other racing jurisdictions and equestrian disciplines (Fig. 22.1).

The identification of injuries and risk factors and the understanding of injury pathophysiology are the first steps towards preventing orthopedic injuries. In most cases injuries occurring in performing horses are highly correlated with their equestrian discipline. Each athletic activity places stresses in specific anatomic regions. The identification of injury patterns associated with different equestrian sports (Table 22.1) has led veterinarians to recognize lesions promptly to prevent further damage. For instance, condylar fractures are recognized mainly in race horses or pastern fractures in barrel racing Quarter Horses.

Recognizing musculoskeletal structures at risk, such as cannon bone, superficial digital flexor (SDF) tendon or suspensory ligament (SL), has prompted the study of their

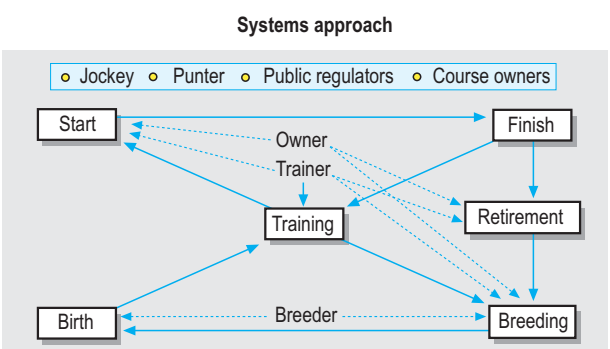


Fig. 22.1
A systems approach to reducing musculoskeletal injuries. (Courtesy of Professor KL Morgan, University of Liverpool, UK.)

Table 22.1 Common injuries seen in horses by sport activity. A soundly conformed horse with adequate and balanced feet is essential to prevent many of these injuries

Activity	Common injuries
Flat racing	Bucked shins, stress fractures (humerus, tibia, pelvis), condylar fracture, osteochondral (chip) fragmentation (carpus/fetlock), SDF tendinitis, suspensory breakdown, P1 fracture, DJD
Harness racing	Bucked shins, stress fractures, condylar fracture, osteochondral (chip) fragmentation (carpus/fetlock), SDF tendinitis, suspensory breakdown, DJD
Hurdle racing	Catastrophic fracture, interosseous muscle desmopathy
Barrel racing	SDF tendinitis, P2 fracture (hind leg)
Rodeo	Navicular disease, 'Ringbone', bone 'spavin', P2 fracture
Cutting/reining	Navicular disease, interosseous muscle desmopathy, bone 'spavin', stifle injuries
Team roping	Bone 'spavin', interosseous muscle desmopathy, P2 fracture, back/pelvic problems
Showjumpers/ eventers	Interosseous muscle desmopathy, SDF tendinitis, stifle/fetlock injuries, P1 fractures, back problems
Dressage	Interosseous muscle desmopathy, SDF tendinitis, back problems
Polo ponies	SDF tendinitis, proximal interosseous muscle desmopathy, back problems, fetlock DJD
Endurance	Myopathies, SDF tendinitis

biomechanical behavior under different conditions. However, the scientific study of incidence of injury and associated risk factors has occurred to a large extent only in the racing industry. In racing horses there is information available through different studies in different racing jurisdictions (Table 22.2). A comparison amongst these studies must be done carefully due to the different study designs and conditions under which they were carried out. We must accept that in the current competition environment we will not succeed in totally eliminating injuries. The goal is therefore not to eliminate them, but to significantly reduce their risk and incidence to a level that is just the result of unforeseen accidents. It is important to define an injury, measure the extent of its risk and to identify modifiable factors associated with such risk. These risk factors can then be seen as highly preventable, preventable, non-preventable or unforeseen risks.

In other equestrian disciplines the prevention of orthopedic injuries is mainly based on the practice of good horsemanship combined with generally applied physiology and biomechanics as well as good old common sense developed through previous experiences. The use of different training surfaces and programs, exercise intensity, jump or course design is based mostly on tradition and experience rather than on scientific findings of the biomechanical behavior of the horse's locomotor system under different circumstances. Most of the research efforts have been made to characterize horse locomotion and loads transmitted to the appendicular skeleton during different types of exercise. A comprehensive universal analysis of injury incidence and risk factors in equestrian disciplines other than racing is lacking at the present time.

The making of a champion athlete capable of outperforming its competition in extreme conditions, sustaining minimal or no injuries, starts long before it is born. In the equine industry, earnings are the measure of success. To generate earnings a horse must enter competition and the sounder and fitter the horse, the higher the likelihood of success. Although selection of breeding stock is based on a few traits, such as speed, it is also possible that those successful horses that become part of the breeding pool are not only transmitting the desired trait but perhaps some superior biomechanical qualities, likely associated with conformation.[2]

This chapter will focus on the training and performing horse but we must recognize that choosing the optimal genetic lines, normal pregnancy and adequate management of the horse during growth and development can provide the future trainer with an outstanding 'diamond in the rough'. Genetics, nutrition and exercise play a crucial and somewhat unknown role in the development of an athlete. All of them need to be investigated more fully to determine the optimal management of a growing horse to prevent performance-limiting injuries.

Thoroughbred, Standardbred, Arabian or Quarter Horse racing generates a significant economic activity in many countries.[3] There are several modalities of racing. In North America most of the racing is flat and harness racing while in other countries other modalities such as steeplechasing, hunterchase or hurdling exist. Most of the scientific work related to characterization and prevention of exercise-associated injuries has been carried out in race horses. Aspects of horse selection, management, training and competition have been investigated. Race horses are usually started into training at an early age (1–3 years of age), as most of the competition occurs when the horse is 2 or 3 years old. Considerable debate has centered round the optimal training age as the North American system has been criticized for starting horse training at a very early age.[4,5] The central point of disagreement has been the perceived notion that horses trained at an early age tend to have an increased risk of catastrophic injury and certain industry groups have lobbied to change actual training practices. In order to understand the risk of training a young race horse, several investigations have focused on the effects of early exercise in musculoskeletal development.

The training period represents a time of intensive psychological and physical challenges for a horse. Training not only achieves the development and maintenance of cardiovascular fitness and musculoskeletal strength but it also improves the neuromuscular co-ordination and mental aptitude of the horse. One of the objectives of training is to decrease the risk of injury during athletic competition by adapting the musculoskeletal and cardiovascular systems to the rigors of competition. The term 'functional adaptation' is used to describe the response of the body to accommodate an imposed

Table 22.2 Studies reporting injury risk factors and potential strategies to diminish them. Note that most of the studies are conducted in race horses under different racing jurisdictions. Comparison amongst studies must be done with caution as study design will vary (MS, musculoskeletal; N/A, no preventive measures offered; QH, Quarter Horses; TB, Thoroughbreds)

Risk factor	Injury	Pop.	Country	Prevention strategies	Reference
Speed, distance	Bucked shins	TB	USA	Increase speed, decrease distance, introduce high-speed sprints	43
Age at first race, racing history, race distance, sand gallops, woodchip gallops, zero gallop work	Catastrophic	TB	UK	Introduce schooling races, shorten National Hunt racing distance, gallop at least 1 furlong for every 7 furlongs cantered	1
Track conditions	Fracture	TB	Japan	Decreased sharp turns, change banking %, change vertical profile, change composition of ground	31
Firm turf tracks Heavy dirt tracks	Fracture	TB	Japan	Regulate racing according to track conditions	37
Location on the track	Fracture	TB	Japan	Map hardness distribution on track and water track to maintain adequate water content, automatic rakes to remove sand accumulation and eliminate excessive water content on the track surface	38
Increased cumulative high-speed exercise	Catastrophic	TB	USA (California)	Decreased cumulative high-speed exercise	52
Pre-existing injury	MS injury	TB	USA (Kentucky)	Pre-race inspection	29
Pre-existing injury	MS injury	QH	USA (Texas)	Pre-race inspection	53
Jockey's use of whip	Fracture	TB	Japan	Regulate use of whip	38
Toe-grabs	Fracture	TB	USA (California)	Ban use of toe-grabs	54
Suspensory injury	Condylar fracture	TB	USA (California)	Monitor health of suspensory ligament	51
Age of training	Tendon damage	TB	UK	Start early training/conditioning of tendon	5
Racetrack, racing surface, total number of starts, season, number of seasons raced and age of the horse	Fracture	TB	USA (New York)	Regulate racing schedule of individual horse, limit racing seasons	34
Barrier position, type of race, and change in distance from previous race	Fracture	TB	Australia	N/A	39
Racetrack, class of race, and race length	MS injury	QH	USA (Texas)	N/A	53
Sex, number of days since last race and racing surface	MS injury	TB	USA (Florida)	N/A	35
Back half of the file at the end of the first quarter of the race, short races, backstretch and stretch turn, track	MS injury	TB	USA (Kentucky)	N/A	55

Table 22.2-cont'd

Risk factor	Injury	Pop.	Country	Prevention strategies	Reference
Pre-existing stress fracture	Complete humeral fracture	TB	USA (California)	Pre-race inspection	56
Trainer; hoof angle and conformation	MS injury	TB	USA (Minnesota)	Rigorous regulation of training licencing process, optimization of hoof angles	57
Underlying disease process	Fracture	TB	USA (New York)	Pre-race inspection	58
Track (Saratoga), turf, more seasons of racing, more starts per year, racing in a later race, non-summer races, and younger age	Fracture	TB	USA (New York)	Implement track design changes	34
Soft and heavy ground, winter season	Fall	TB (Steeplechasing)	UK	Regulate competition according to ground characteristics	1
Fence height	SDF tendon injury	Show jumpers	The Netherlands	Reduction in fence height	23

mechanical environment in a way which optimizes the mass and distribution of the tissues.[6] It is important to understand that this adaptation occurs in a timeframe that varies with different tissues.

Specific activity-oriented training will help develop the relevant muscle groups and strengthen the skeleton and other supporting structures in areas of higher demands, according to the type and intensity of a specific exercise. It will also develop the co-ordination required to maintain an adequate balance during the different stages of competition and the competitive attitude required to succeed at equestrian disciplines. Maintaining an adequate body balance will ensure the proper loading of the musculoskeletal system and will decrease the incidence of orthopedic injuries.[7] Intense training also separates horses with moderate physical aptitude from those with outstanding physical and psychological qualities, which will finally enter elite athletic competition. Training programs should focus on speed, strength, precision (mental focus) and stamina. It is during training that the musculoskeletal system is allowed to adapt to a particular exercise intensity characterized by cyclic loading to increase the fatigue life and therefore minimize the risk of injury. During training an evolution in the intensity and complexity of exercise occurs which allows the supporting musculoskeletal structures to develop the necessary strength to sustain performance. In addition, other less well-investigated factors, such as proprioceptive adaptation, will adjust to provide an adequate body and joint balance such that the loading conditions under which performance occurs do not result in an injury.

Musculoskeletal changes occurring during training are time dependent and vary with exercise intensity, age of the horse and quite possibly with each individual horse. Therefore, training programs must adjust to these biological characteristics of different tissues to optimize their results. In race horses most of the injuries occur during training.[8,9] Since training management will determine conditions such as shoe wear, foot angles, training speed, cumulative distance and frequency, racing intervals and racing surface, training constitutes the largest single element influencing risk of athletic injuries. Training regulations vary with racing jurisdictions and no formal education or rigorous testing is required to become a trainer in many racing jurisdictions. Trainers have the ability to affect a horse's performance and they are largely responsible for the success that a horse may enjoy. In a study carried out by Verheyen and Wood at the Animal Health Trust in Newmarket, England, where data were collected on 1178 horses in training and 13 trainers, it was found that fracture risk was significantly affected by trainer.[10] Training methods are jealously guarded by many trainers afraid of disclosing their methodology. However, the enforcement of regulations regarding training guidelines needs to be investigated as a method to reduce injury risk.

Functional adaptation of the musculoskeletal system

The adaptive response of bone may be summarized in Wolf's Law and its behavior is well described and understood.[11,12] Bone responds to loads (exercise) by depositing new bone in those areas where the loads imposed are higher. The bone response occurs at a certain rate determined by bone remodeling, which involves osteoclastic and osteoblastic activity. Intense repetitive loading, which occurs at a faster rate than bone remodeling, will increase the risk of bone damage and

catastrophic fracture.[13] McCarthy & Jeffcott evaluated the third metacarpal bone responses to treadmill exercise and found that exercised horses had less cortical porosity, larger subperiosteal osteogenesis and increased bone stiffness, showing a significant adaptive response.[14]

Responses of suspensory ligament and proximal sesamoid bones to exercise have also been evaluated. In a study by Bramlage et al, two groups of six horses each, trained versus untrained, were tested for the load to failure response of the suspensory apparatus. The load to failure was higher in trained horses (1340 kg versus 1100 kg) and most of the trained horses (83%) suffered rupture of the suspensory apparatus by sesamoid fracture, showing also a response to exercise.[15]

Tendon functional adaptation is less well defined. Superficial digital flexor tendon responds to exercise by increasing the cross-sectional area, decreasing echogenicity and increasing the modulus of elasticity.[16] Exercise also induced histomorphologic changes in the SDF tendon by diminishing crimp angle and length in its central region in relation to the periphery, where the crimp angle was greater than in control (unexercised) horses. In this study, the authors concluded that the changes observed in the core region of the SDF tendon of exercised horses were indicative of microtrauma.[17,18] From these studies it appears that although there are some changes associated with exercise, it is difficult to determine if they are responses to microtrauma or adaptations to exercise.

It has been hypothesized that the adaptive capacity of tendon is reduced with increased age. To test this hypothesis, a series of experiments were conducted to evaluate the effects of exercise in young horses. The results are summarized in a paper by Smith et al.[5] The authors conclude that immature tendon can respond to exercise by synthesizing and maintaining the integrity of the matrix, while mature tendon has a limited response capacity. It is therefore possible that exercising the horse as a foal may allow for a functional adaptation response, which provides the horse with a tendon that is more resistant to injury (Fig. 22.2). Additional evidence of a hypertrophic response to exercise at an early age is offered by Kasashima et al.[19] This opens up the possibility of using early training as a measure to reduce the incidence of tendon injuries at a later time. The necessary training strategies and the optimal age at which to achieve such a goal require further investigation before making practical recommendations.

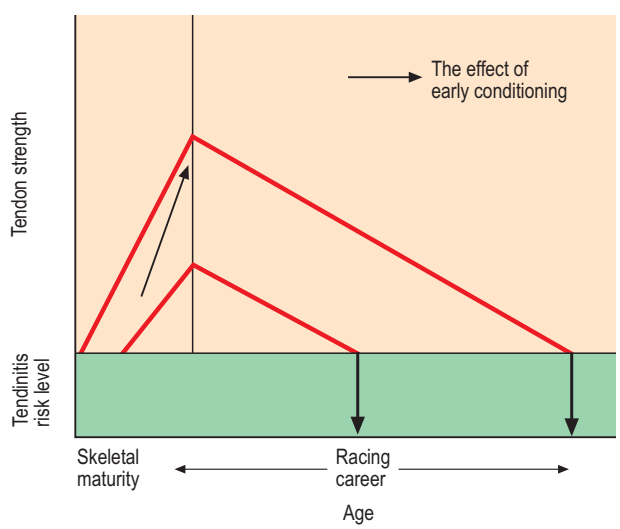


Fig. 22.2
Effect of early conditioning resulting in increased tendon strength and diminishing incidence of tendinitis. (Courtesy of Dr Roger Smith, The Royal Veterinary College, North Mimms, UK.)

As the horse gets older, exercise induces histomorphologic changes in the digital flexor tendons that do not seem sufficient to sustain the demands associated with high-speed racing. Since the mechanical behavior of the tendon in response to loads has been well defined,[20] exercising conditions, which repetitively overcome the tendon's biomechanical properties, will likely result in pathologic damage or even tendon breakdown. During galloping at racing speed the strain sustained by the SDF tendon has been calculated to be about 16%.[21] Under experimental conditions SDF tendons reached failure point at strains of 12–20%.[20,22] The high rate of tendon injuries in race horses may therefore be associated with the inability of current training programs or the tendon itself to modify their biomechanical properties to tolerate the high loads occurring during exercise.

In jumping horses, forelimb tendon injuries are an important cause of lameness and wastage.[23] The study of the effect of jump height in landing forces in these structures has revealed that fence height significantly increases the forces in the SDF tendon but not in the deep digital flexor (DDF) tendon or SL. In vitro experiments have shown the rupture forces of the DDF and SDF tendons to be around 13 and 12 kN respectively.[23,24] In addition, peak force in the SDF tendon slightly exceeds the in vitro failure force.[23] Comparison between in vitro and in vivo experiments must be done carefully but there is evidence to suggest that the in vivo peak landing force of the SDF approaches in vitro rupture forces. From this study it was concluded that the higher the fence, the higher the landing force on the SDF, therefore increasing the risk of SDF injury. The effect of jump height cannot be evaluated by itself as the quality of the horse, jumping technique and fatigue have been shown to have an effect on the forelimb landing forces. In a study by Schamhardt et al, experienced horses could clear higher fences than inexperienced horses with minimal effect on the ground reaction forces at landing.[25] In trotting horses, for example, SL loading increases during fatigue by an increase in fetlock hyperextension.[26] Therefore proper conditioning, training and selection of a horse with natural aptitude to clear fences are also important to limit the incidence of injuries in this equestrian discipline. Trainers and riders must be coached and understand that to push a horse beyond its capabilities will significantly increase the risk of musculoskeletal injury.

The equine industry must ensure that the conditions under which a horse is exercised do not impose further stress on the soft tissue structures. Since certain performing conditions such as fatigue, inadequate surfaces or shoeing,

Table 22.3 Studies reporting incidence of injuries and the main findings during the study, by year of study and country (OR, odds ratio; TB, Thoroughbreds; QH, Quarter Horses)

Country	Population	Year	Main findings	Reference
UK	Race horses (flat and National Hunt)	96–98	Fatal injuries 0.29% of all starts, non-fatal injuries 0.76% National Hunt > flat racing Injuries ↑ as surfaces became firmer Lowest incidence of injuries on turf surfaces	1
UK	Race horses (flat and National Hunt)	90–99	55% on injuries: lower limb fracture and tendon breakdown Risk factors: ↑ age, surface firmness and race distance	1
USA (New York)	Thoroughbreds	1986	Fracture injuries: dirt > turf Other injuries: dirt = turf 2 yr olds had more fracture injuries than other injuries	33
USA (Minnesota)	Thoroughbreds	1987	57% soft tissue injuries, 36% bone injuries, 7% other ↑ breakdown in horses > 4 yr old OR: Dirt (1.6) vs turf	32
USA (New York)	Thoroughbreds	1991	OR: Dirt (3) vs turf Risk of injury ↓ with racing season and no. of starts Risk of breakdown ↑ with horse's age	34
USA (New York)	Thoroughbreds	86–88	Risk factors: track, dirt > firm track, ↑ with track distance Worst surfaces: muddy dirt and firm turf OR: Hindlimbs severe injury (4) vs forelimb	61
USA (Kentucky)	Thoroughbreds	92–93	Injury prevalence per start: 0.33% Catastrophic injuries: left forelimb, sesamoid, third metacarpal Injuries: 90.2% affected forelimb, 44.7% affected suspensory apparatus	55
USA (California)	All race horses	90–92	Fatal injuries: 42% (racing), 39% (training) QH: fatal injuries 82% (racing) TB: fatal injuries 48% (racing) TB (racing injuries): prox. sesamoids and third metacarpal QH (racing injuries): prox. sesamoids and carpal bones	50
USA (California)	Thoroughbreds (post-mortem)	92–94	Toe-grabs ↑ risk of injury OR Low toe-grabs for fatal injury (1.8), for suspensory app. failure (6.5), for condylar fracture (7) OR regular toe-grabs for fatal injury (3.5), for suspensory app. failure (15.6) for condylar fracture (17.1)	54
South Africa	Thoroughbreds	93–94	8.1% of available training days were lost (72.1% due to lameness) Wastage amongst trainers: 0.1 to 23.7%	59

Table 22.3 cont'd

Country	Population	Year	Main findings	Reference
USA (Kentucky)	Thoroughbreds	94–96	87% of injuries in the lower limb (carpus to fetlock) 94.4% of injuries in the forelimbs (left > right) Risk factors identified: age > 5 yr old; stumbling; changing leads; interfering with another horse; > 60 days interval between races; positive pre-race inspection findings	29
Australia	Thoroughbreds	85–95	0.24% incidence of breakdown injuries per start 0.04% of fatal injuries per start Risk factors identified: ↑ horse age; Change distance from previous race; lower class of race; barrier position	39
Australia	Standardbreds	92–95	Injury rate ↓ 22% after elevating banks from 4.8° to 5.7°	60
USA (California)	Thoroughbreds (post-mortem)	94–96	↓ difference between toe and heel angle ↓ risk of suspensory app. failure ↑ toe angle helps diminish risk of suspensory app. failure	54
USA (Kentucky)	Thoroughbreds	96–97	Incidence of injury: 0.44% Risk factors: abnormality of suspensory ligament during pre-race inspection; claiming race < 25,000$; < 7 furlongs distance	29
USA (Texas)	Quarter Horse	95–98	Catastrophic injuries: 0.8/1000 starts Non-catastrophic: 2.2/1000 starts 73% of injuries in distances of 330–400 yards	53
USA (Florida)	Thoroughbreds	95–98	Injury incidence: 1.2/1000 starts Turf injury incidence: 2.3/1000 starts Dirt injury incidence: 0.9/1000 starts Risk factors: geldings; > 33 days since last race; turf surface	34
USA (California)	Thoroughbreds	98	Risk factors: pre-existing subclinical suspensory injury; toe-grabs	33
UK	Thoroughbreds	2000–01	78% of fractures occurred during training Fracture rate: 1.18/100 horses/month; 50% are stress fractures; 20% affect 3rd Mtc.; 30% affect pelvis; 20% affect knees Fracture risk is affected by trainer	1

improper conditioning or metacarpo(tarso)phalangeal hyperextension may be associated with an increase in the load sustained by structures of the appendicular skeleton, it would seem logical to avoid or modify conditions that would promote such motion without jeopardizing other structures.

Once we have recognized the adaptive nature of the musculoskeletal system, and the value of training in taking advantage of this, it is important to analyze which risk factors are involved in orthopedic injuries in exercising horses.

Risk factors

It has been shown that many of the injuries occurring in race horses are not the result of random accidental events but the end-point of a chronic process associated with the overuse of the body's biomaterials.[27] The most common biological structures injured in equine disciplines are the bones, tendons and ligaments of the appendicular skeleton. In order to prevent

the wear of these structures to the point of breakdown, it is of paramount importance to understand the concept of fatigue and the biomechanical behavior of those structural components under different conditions.

Fatigue of a material refers to a process by which the material reaches the breakdown point by cyclic loading above the endurance limit, similar to repetitively bending a paper clip until it breaks.[28] Fatigue represents a significant risk factor for musculoskeletal injuries and avoiding the onset of fatigue should significantly decrease the risk of a catastrophic injury.[13] Muscle fatigue reduces the muscle's ability to store energy and neutralize the stresses imposed on the bone, potentially resulting in a fracture. Fatigue of the cardiovascular system may lead to exhaustion and a reduced ability to quickly respond to changes in the body's spatial orientation. Accurate and timely control of body movements is essential to prevent body injuries resulting from high inertial forces associated with high-speed exercise. An inadequate response to motion changes may place uncommon forces on supporting structures which may not be prepared to support them. These forces could overwhelm a musculoskeletal structure, resulting in breakdown. For instance, stumbling during racing has been linked to the occurrence of catastrophic injuries in Thoroughbred horses.[29] The gait co-ordination required in certain sports trains a specific set of psychomotor skills and muscle activity. The sudden change imposed on a system by an inaccurate motion could potentially jeopardize certain supporting structures, increasing the risk of musculoskeletal injury. The severity of this injury will vary depending on the forces applied.

There are several studies identifying injury risk factors associated with racing (Table 22.3). It is a difficult challenge to define the incidence of injuries and to identify the different risk factors in each equestrian discipline. Most of the scientific efforts have been directed to the investigation of catastrophic injuries occurring to race horses. Although these are devastating incidents, they only represent a minimal part of the industry wastage due to musculoskeletal problems. Other less 'visible' problems, such as tendon or suspensory ligament damage and arthritis, have a larger impact on the economics and welfare of horses.[30] It must be understood that many equestrian disciplines, and in particular racing, represent an activity where horses reach and sustain exercise intensities capable of overwhelming the musculoskeletal system's response capacity, potentially ending in a severe or catastrophic injury. Musculoskeletal injuries represent an occupational hazard for the athletic horse. Veterinarians, trainers and riders must remain vigilant and proactive to design strategies to reduce incident rates amongst exercising horses.

Characterization of sport horse injuries has occurred over time and considerable advance has been made in describing injury patterns, risk factors, treatment modalities and outcomes. This has helped us to understand the pathophysiology of athletic injuries and to put in place the necessary mechanisms to prevent or minimize the risk of injuries. There is a trend towards seeing injuries as an inherent risk to the sport horse but it has been shown that implementation of the appropriate measures will reduce injury rates significantly.[31]

In North America, the main investigation into the causes of equine racing injuries was established by the California Horse Racing Board in 1990, although other studies, such as the racetrack breakdown pilot study in Minnesota[32] or those conducted in New York,[33,34] Florida[35] and Kentucky,[36] have contributed to our current body of knowledge. In other countries where racing constitutes an important sport activity, similar studies have been undertaken, such as in Japan,[37,38] the UK[1] and Australia.[39] Because of the different racing conditions in different parts of the world, it is difficult to extrapolate results across continents. However, one thing is clear: musculoskeletal injuries represent the leading cause of wastage in the racing industry across the world.

Early detection of subtle injuries leads to effective prevention of further injury and catastrophic breakdown and it has been suggested that adequate monitoring of horses is critical to prevent further damage to an already injured structure.[29] Minimally invasive techniques are currently being developed to identify biomechanical changes related to exercise and identify high-risk horses.

As veterinarians investigate the trend of training-related injuries, further study of the methods of training will likely reveal a cause–effect relationship. In this respect, the excellent work carried out by Nunamaker's group at the University of Pennsylvania is important, investigating the pathophysiology of the 'bucked shin' complex, where a clear relationship has been found between methods of training and the occurrence of 'bucked shins'.[13] It has been reported that 70–92% of race horses will develop 'bucked shins' at some point in their careers.[40,41] An investigation showed that 'bucked shins' are produced by an excessive cycling of the dorsal cortex of the metacarpus and its pathophysiology is discussed in Chapter 17. Modification of training regimes by introducing shorter high-speed (breeze) workouts has decreased the incidence of 'bucked shins'.[42]

The most common orthopedic injuries suffered by performing horses as a result of exercise are indicated in Table 22.1.

Soft tissue injuries

The main soft tissue structures affected during exercise are the SDF tendon, the SL and the accessory ligament (AL) of the DDF tendon. Although they seldom produce a catastrophic breakdown, a study has shown their importance in the North American racing industry.[43] In the UK a 30% incidence of tendinitis has been reported,[44] although a more recent report quotes an incidence of 43% amongst National Hunt horses.[45]

Considering that the SDF tendon strain associated with racing approximates the strain associated with tendon failure, it is not surprising that some horses will eventually damage their tendons as the safety margin at peak performance is very small.[46] During post-mortem examinations of clinically normal equine flexor tendons, the morphology, biochemistry and histology of the tendon were investigated.

Abnormal macroscopic appearance, increase in total sulfated glycosaminoglycans, increase in total proportion of type III collagen and decrease in collagen-linked fluorescence were the main findings. The results suggested that this was a healing response to microdamage.[47] It has also been postulated that tendon fiber microdamage often precedes catastrophic tendon breakdown.[48] The response to galloping exercise was evaluated in another study. Young Thoroughbreds were exercised for 18 months and compared to a group exercised only with walking. Crimp angle and length were evaluated. The results indicated that galloping exercise modifies normal age-related changes in crimp morphology consistent with microtrauma.[18] The effects of different training regimes have not been investigated at this time. Since the healing response of tendons is a slow process, in those horses that have suffered from tendinitis, it is crucial to monitor tendon health and to allow proper healing to occur before reintroduction to exercise.

Before the introduction of tendon ultrasonography, one of the problems associated with tendon injuries was reinjury of the affected tendon, caused by premature return to exercise. Today we recognize that appropriate monitoring of tendon healing should be done by ultrasound and return to exercise should ideally be delayed until there is ultrasonographic evidence of healing. Sonographic indications of early tendinitis include an enlargement of cross-sectional area and a decrease in tendon echogenicity. The recent advances in ultrasound imaging suggest an important role for it as a method of routine monitoring during training. By combining monitoring and new training strategies, the incidence of tendinitis and associated wastage should be reduced.[49] There is a need for a scientifically based approach to training horses for peak athletic performance with minimal risk of injuries. However, the reduction in tendinitis should not be at the expense of other tissues and therefore the responses of all tissues and systems contributing to high-speed locomotion must be optimized.[5]

Pre-existing pathology has emerged as a culprit for many racing injuries. The California post-mortem study has described stress fractures occurring to humerus, pelvis and tibia previous to catastrophic breakdown.[50] In addition, soft tissue injuries leading to inadequate support of the skeletal system have also been implicated in the occurrence of certain racing injuries. LeJeune and co-workers recently presented the results of an investigation where damage to the medial suspensory ligament branch increased the load placed on the lateral metacarpal condyle, speculating that damage to the suspensory branch may play an important role in the occurrence of condylar fractures.[51] This study seems to support the clinical impression and the results of another study where early detection of soft tissue lesions (pre-race examination) decreased the incidence of severe musculoskeletal injury.[29] Published injury risk factors and prevention strategies are summarized in Table 22.2.

We must persevere with the investigation of the pathophysiology of sport injuries and the identification of risk factors. In addition, the industry has to be willing to compromise or perhaps change the spectacle in order to reduce injury rates. Design of different performing surfaces, jumping courses, racetrack profiles, length of races, speed of races or training programs may need to be reviewed and potentially altered without jeopardizing the essence of the competition.

References

1. Horse Race Betting Levy Board. Proceedings of a Seminar on Preventing Racehorse Injuries. New insights and practical solutions. Oxford, UK: Blue Zebra; 2001.
2. Holsmtrom M. Predicting performance from conformation and gait. Proceedings of a Seminar on Preventing Racehorse Injuries. New insights and practical solutions. Oxford, UK: Blue Zebra; 2001; 12–23.
3. Bailey CJ. Wastage in the Australian throroughbred racing industry: a survey of Sydney trainers. Aust Vet J 1997; 75(1):64–66.
4. Cherdchutham W, Becker C, Smith RK, et al. Age-related changes and effect of exercise on the molecular composition of immature equine superficial digital flexor tendons. Equine Vet J 1999; 31(Suppl):86–94.
5. Smith RK, Birch H, Patterson-Kane J, et al. Should equine athletes commence training during skeletal development? Changes in tendon matrix associated with development, ageing, function and exercise. Equine Vet J 1999; 31(Suppl): 201–209.
6. Smith RKW, Gerard M, Dowling B, et al. Correlation of cartilage oligomeric matrix protein (COMP) levels in equine tendon with mechanical properties: a proposed role for COMP in determining function-specific mechanical characteristics of locomotor tendons. Equine Vet J 2002; 34(Suppl):241–244.
7. Chateau H, Degueurce H, Jerbi N, et al. Normal three-dimensional behaviour of the metacarpophalangeal joint and the effect of uneven foot bearing. Equine Vet J 2001; 33(Suppl):84–88.
8. Bathe AP. 245 fractures in thoroughbred racehorses: results of a 2-year prospective study in Newmarket. Am Assoc Eq Pract 1994; 40:175–176.
9. Japan Racing Association. Preventing accidents to racehorses: studies and measures taken by the Japan Racing Association. Report of the Committee on the Prevention of Accidents to Racehorses 1991. Japan Racing Association; 1991.
10. Verheyen KLP, Wood JLN. Injuries in training. Proceedings of a Seminar on Preventing Racehorse Injuries. New insights and practical solutions. Oxford, UK: Blue Zebra; 2001; 30–37.
11. Firth EC, Delahunt J, Wichtel JW, et al. Galloping exercise induces regional changes in bone density within the third and radial carpal bones of thoroughbred horses. Equine Vet J 1999; 31:111–115.
12. Davies HMS, Gale SM, Baker IDC. Radiographic measures of bone shape in young thoroughbreds during training for racing. Equine Vet J 1999; 30(Suppl):262–265.
13. Nunamaker DM, Butterweck DM, Provost MT. Fatigue fractures in thoroughbred racehorses: relationships with age, peak bone strain and training. J Orthop Res 1990; 8:604–611.
14. McCarthy RN, Jeffcott LB. Effects of treadmill exercise on cortical bone in the third metacarpus of young horses. Res Vet Sci 1992; 52:28–37.
15. Bramlage LR, Bukowiecki CW, Gabel AA. The effect of training on the suspensory apparatus of the horse. Am Assoc Eq Pract 1989; 35:245.
16. Gillis CL, Meagher DM, Pool RR, et al. Ultrasonographically detected changes in equine superficial digital flexor tendons

during the first months of race training. Am J Vet Res 1993; 54(11):1797–1802.
17. Patterson-Kane JC, Wilson AM, Firth EC, et al. Comparison of collagen fibril populations in the superficial digital flexor tendons of exercised and non-exercised thoroughbreds. Equine Vet J 1997; 29(2):121–125.
18. Patterson-Kane JC, Wilson AM, Firth EC, et al. Exercise-related alterations in crimp morphology in the central regions of superficial digital flexor tendons from young thoroughbreds: a controlled study. Equine Vet J 1998; 30(1):61–64.
19. Kasashima Y, Smith RKW, Birch HL, et al. Exercise induced tendon hypertrophy: cross sectional area changes during growth are influenced by exercise. Equine Vet J 2002; 34(Suppl):264–268.
20. Wilson AM, Goodship A.E. Mechanical properties of the equine superficial digital flexor tendon. J Biomech 1990; 24:474.
21. Stephens PR, Nunamaker DM, Butterweck DM. Application of a Hall-effect transducer for the measurement of tendon strain in horses. Am J Vet Res 1989; 50:1089–1095.
22. Riemersma DJ, Schamhardt HC. In vitro mechanical properties of equine tendons in relation to cross-sectional area and collagen content. Res Vet Sci 1985; 39:263–279.
23. Meershoek LS, Schamhardt HC, Roepstorff L, et al. Forelimb tendon loading during jump landings and the influence of fence height. Equine Vet J 2001; 33(Suppl):6–10.
24. Crevier N, Pourcelot P, Denoix JM, et al. Segmental variations of in vitro mechanical properties in equine superficial digital flexor tendons. Am J Vet Res 1996; 57:1111–1117.
25. Schamhardt HC, Merkens HW, Vogel V, et al. External loads on the limbs of jumping horses at take-off and landing. Am J Vet Res 1993; 54:675–680.
26. Johnston C, Gottlieb-Vedi M, Drevemo S, et al. The kinematics of loading and fatigue in the standarbred trotter. Equine Vet J 1999;30(Suppl):249–253.
27. Pool RR, Meagher DM. Pathologic findings and pathogenesis of racetrack injuries. Vet Clin North Am Eq Pract 1990; 6:1–30.
28. Riggs CM. Fractures – a preventable hazard of racing thoroughbreds? Vet J 2002; 163:19–29.
29. Cohen ND, Peloso JG, Mundy GD, et al. Racing-related factors and results of pre-race physical inspection and their association with musculoskeletal injuries incurred in thoroughbreds during racing. J Am Vet Med Assoc 1997; 211:454–463.
30. Jeffcott LB, Rossdale PD, Freestone J, et al. An assessment of wastage in thoroughbred racing from conception to 4 years of age. Equine Vet J 1982; 14:185–198.
31. Oikawa M, Ueda Y, Inada S, et al. Effect of restructuring a racetrack on the occurrence of racing injuries in thoroughbred horses. J Equine Vet Sci 1994; 14:262–268.
32. Haynes PF, Robinson RA. Racetrack breakdown pilot study summary. Am Assoc Eq Pract 1988; 34:673–676.
33. Hill T, Carmichael D, Maylin G, et al. Track condition and racing injuries in thoroughbred racehorses. Cornell Vet 1986; 76:361–379.
34. Mohammed HO, Hill T, Lowe J. Risk factors associated with injuries in thoroughbred horses. Equine Vet J 1991; 23:445–448.
35. Hernandez J, Hawkins DL, Scollay MC. Race-start characteristics and risk of catastrophic musculoskeletal injury in thoroughbred racehorses. J Am Vet Med Assoc 2001; 218:83–86.
36. Cohen ND, Berry SM, Peloso JG, et al. Thoroughbred racehorses that sustain injury accumulate less high speed exercise compared to horses without injury in Kentucky. Am Assoc Eq Pract 2000; 46:51–53.
37. Oikawa M. Epidemiological aspects of training and racing injuries of thoroughbred racehorses and corresponding countermeasures. Japan Racing Association, Japan Racing Journal 2000.
38. Ueda Y, Yoshida K, Oikawa M. Analyses of race accident conditions through use of patrol video. J Eq Vet Sci 1993; 13:707–710.
39. Bailey CJ, Reid CWJ, Hodgson DR, et al. Risk factors associated with musculoskeletal injuries in Australian Thoroughbred racehorses. Prev Vet Med 1997; 32:47–55.
40. Norwood GL. The bucked shin complex in thoroughbreds. Am Assoc Eq Pract 1978; 24:319–336.
41. Stover SM, Pool RR, Morgan JP, et al. A review of bucked shins and metacarpal stress fractures in the thoroughbred racehorse. Am Assoc Eq Pract 1988; 34:129–134.
42. Boston RC, Nunamaker DM. Gait and speed as exercise components of risk factors associated with onset of fatigue injury of the third metacarpal bone in 2-year-old Thoroughbred racehorses. Am J Vet Res 2000; 61(6): 602–608.
43. Wilson JH, Robinson RA, Jensen RC, et al. Equine soft tissue injuries associated with racing. Descriptive statistics from North American racetracks. Proceedings of the Dubai International Equine Symposium 1996; 1–21.
44. Vaughan LC, Mason BJE. A clinico-pathological study of racing accidents in horses: a report of a study on equine fatal accidents on racecourses. Horserace Betting Levy Board. Dorking, England: Bartholomew Press; 1975.
45. Pickersgill C. Epidemiological studies into orthopaedic conditions of the equine athlete. MVM thesis, University of Glasgow, 2000.
46. Wilson AM. The effect of exercise intensity on the biochemistry, morphology and mechanical properties of tendon. PhD thesis, University of Bristol, 1991.
47. Birch HL, Bailey AJ, Goodship AE. Extracellular matrix changes in clinically normal equine superficial digital flexor tendons may account for subsequent tendon rupture. Proceedings of the British Equine Veterinary Association 1993; 32.
48. Pool RR. Pathological changes in tendinitis of athletic horses. Proceedings of the International Equine Symposium Dubai 1996.
49. Oikawa M, Goodship AE. Clinical and investigational advances in the prevention of tendinitis. Equine Vet J 1999; 30(Suppl): 640–641.
50. Johnson B, Ardans A, Stover S, et al. California racecourse postmortem program: a 4-year overview. Am Assoc Eq Pract 1994; 40:167–169.
51. LeJeune SS, Macdonald MH, Taylor KT, et al. Biomechanical investigation of the association between suspensory ligament injury and lateral condylar fractures in thoroughbred racehorses. Proceedings of the 37th Annual Science Meeting of the American College of Veterinary Surgeons 2002; 488.
52. Estberg L, Stover SM, Gardner IA, et al. Cumulative racing-speed exercise distance cluster as a risk factor for fatal musculoskeletal injury in Thoroughbred racehorses in California. Prev Vet Med 1995; 24:253–263.
53. Cohen ND, Dresser BT, Peloso JG, et al. Frequency of musculoskeletal injuries and risk factors associated with injuries incurred in quarter horses during races. J Am Vet Med Assoc 1999; 215:662–669.
54. Kane AJ, Stover SM, Gardner IA, et al. Horseshoe characteristics as possible risk factors for fatal musculoskeletal injury of thoroughbred racehorses. Am J Vet Res 1996; 57: 1147–1152.

55. Peloso JG, Mundy GD, Cohen ND. Prevalence of, and factors associated with, musculoskeletal racing injuries of thoroughbreds. J Am Vet Med Assoc 1994; 204:620–626.
56. Stover SM, Johnson BJ, Daft BM, et al. An association between complete and incomplete stress fractures of the humerus in racehorses. Equine Vet J 1992; 24:260–263.
57. Kobluk CN, Robinson RA, Gordon BJ, et al. The effect of conformation and shoeing: a cohort study of 95 Thoroughbred racehorses. Am Assoc Eq Pract 1989; 35:259–274.
58. Krook L, Maylin GA. Fractures in thoroughbred racehorses. Cornell Vet 1988; 11:1–33.
59. Olivier A, Nurton JP, Guthrie AJ. An epizoological study of wastage in thoroughbred racehorses in Gauteng, South Africa. J S Afr Vet Assoc 1997; 68:125–129.
60. Evans DL, Walsh JS. Effect of increasing the banking of a racetrack on the occurrence of injury and lameness in standardbred horses. Aust Vet J 1997; 75:751–752.
61. Mohammed HO, Hill T, Lowe J. The risk of severity of limb injuries in racing thoroughbred horses. Cornell Vet 1992; 82:331–341.

CHAPTER 23

Pharmacotherapy of joint and tendon disease

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Introduction

The reality of pharmacology is that there are no silver bullets or magical cures. No one drug or therapeutic substance can be placed into a syringe, administered as a powder or given as a pill that will cure all of the musculoskeletal conditions affecting the equine athlete. Pharmacotherapeutic agents are designed to assist the body in the healing process. Combination therapy that utilizes rest, physical therapy, pharmacotherapeutics and possibly surgery is necessary to ensure proper healing and restore function. An effective therapeutic plan is based on careful assessment of patient signalment, the history and duration, location, type and severity of the injury, as well as the economics.

The common denominator in all equine athletic injuries is inflammation. The cellular mediators and biochemical processes associated with inflammation are responsible for the clinical signs of heat, pain, and swelling, as well as ongoing tissue destruction. The goal of pharmacotherapeutic intervention should be to control the cellular mediators and biochemical processes of inflammation, prevent ongoing tissue destruction, relieve pain, restore function and return the horse to normal work conditions with minimal loss of fitness. A sound understanding of the mechanism of action, indications for use, effective dosages, drug interactions, toxicity and expected results for the available veterinary drugs is necessary.

The goal of this chapter is to provide information pertaining to drugs used to treat the equine athlete. The knowledge gained from this chapter should help facilitate the optimum selection and application of pharmacotherapeutic agents in the treatment and maintenance of the athletic horse. This chapter will focus on anti-inflammatory drug therapy and other medications used in the treatment of joint and tendon disease in horses.

Anti-inflammatory drug therapy in horses

Anti-inflammatory medications are commonly administered to horses for the treatment of inflammatory and infectious diseases, and for traumatically or surgically induced injuries of the musculoskeletal system. The most commonly used anti-inflammatory drugs include non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, but other drugs such as polysulfated glycosaminoglycans, dimethylsulfoxide and hyaluronate are also believed to have anti-inflammatory effects. The NSAIDs are commonly administered systemically for their analgesic and inhibitory effects on inflammation, fever and edema. Numerous NSAIDs are available, but phenylbutazone (PBZ) and flunixin meglumine (FLM) are currently the most commonly used. Aspirin (acetylsalicylic acid) has limited use in the treatment of musculoskeletal disease in horses due to its poor analgesic effects. Ketoprofen (KTP), carprofen (CRP), dipyrone, meclofenamic acid (MFA) and naproxen (NPX) are other NSAIDs used in horses.

Although corticosteroids are rarely used systemically to treat musculoskeletal disease in horses, they are commonly administered locally within joints affected by synovitis and arthritis. Knowledge of the mechanism of action, pharmacologic properties, pharmacokinetic behavior and therapeutic

and toxic effects of these medications will enable veterinarians to select the optimum anti-inflammatory pharmacotherapeutic regimen for the treatment of horses affected with musculoskeletal disease.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs represent a class of drugs that inhibit one or more of the pathways involved with the synthesis of prostaglandins (PGs) and thromboxanes (TBXs) from arachidonic acid. The principal mechanism of action is through inhibition of cyclo-oxygenase (COX). Prostaglandins, particularly those of the E-series, are involved in synovial inflammation and depletion of proteoglycan from articular cartilage matrix.[1,2] There is substantial evidence to suggest that PGE_2 is the principal PG involved in joint degeneration. Synoviocytes and chondrocytes synthesize PGE_2 in response to exposure to lipopolysaccharide (LPS) and other inflammatory mediators, and increased concentrations of PGE_2 have been reported in the synovial fluid of horses with osteoarthritis.[3] Additionally, there is also evidence to suggest that PGs may modulate latent matrix metalloprotease release with resultant cartilage matrix degradation.[4,5]

Classification and mechanism of action

Non-steroidal anti-inflammatory drugs are classified, based upon their chemical structure, into carboxylic and enolic acids. A majority of NSAIDs belong to the carboxylic acid group, whereas few are enolic acids. Additionally, NSAIDs can be further divided into five major categories.[6] These categories include pyrazolones (phenylbutazone, dipyrone), salicylic acids (aspirin), acetic acids (etodolac), fenamic acids (meclofenamic acid, flunixin meglumine) and propionic acids (naproxen, ketoprofen, carprofen).[7] The acidic nature of the NSAIDs facilitates their accumulation at sites of inflammation (acidic pH), enabling them to be more effective in inflamed versus normal tissues.[6,8]

Most NSAIDs have a similar mechanism of action and physical and chemical properties.[9,10] NSAIDs inhibit the synthesis of PGs and TBXs from arachidonic acid by inhibiting COX. All NSAIDs, other than aspirin, are competitive COX antagonists; this mechanism of action requires the continued presence of the active drug to exert the effect. Aspirin is an irreversible antagonist that deactivates COX by acetylation. Because platelets are non-nucleated and thus do not have the capacity to synthesize new COX, it has a profound effect on platelet function.

A relatively recent discovery expanding knowledge of the COX pathway is that there are at least two COX isomers, namely the constitutive (COX-1) and inducible (COX-2) isoforms.[6] The COX-1 isomer is believed to be the 'housekeeping' enzyme responsible for basal synthesis of PGs necessary for physiologic functions, including maintenance of vasomotor tone (intestinal mucosal and renal blood flow), prevention of platelet aggregation and adhesion and maintenance of gastric cytoprotection.[6] The COX-2 isomer is responsible for increased eicosanoid synthesis associated with inflammation and is induced by LPS, cytokines and other inflammatory mediators. The affinity for the two COX isoforms varies among NSAIDs. Some are more potent inhibitors of COX-1, while some are relatively equipotent for their effects on COX-1 and COX-2, and others have a greater selectivity for COX-2. A COX-1/COX-2 ratio is useful to measure the selectivity of an NSAID for the COX isomers.[6] Unfortunately, many of the NSAIDs currently used in horses have a ratio ≥ 1, which means they inhibit COX-1 as much or more than the COX-2. A COX-1/COX-2 ratio < 1 is preferable in order to maximize the anti-inflammatory effects of the NSAID while minimizing the potential for toxic side effects.

Many of the actions attributed to NSAIDs are dose dependent. Greater doses are necessary to reduce inflammation than are required to actually inhibit eicosanoid synthesis. At lower doses, many NSAIDs inhibit PG-mediated fever, pain and vasomotor tone.[9,10] However, the dose required to decrease edema formation and leukocyte accumulation at inflammatory sites is substantially greater than the dose required to reduce PG synthesis. Therefore, the NSAIDs currently available are likely to be more effective in inhibiting pathologic processes involving PGE_2 (pain, fever), compared with those involving other mediators.

Greater doses of NSAIDs also inhibit non-PG dependent processes, such as enzyme activity, transmembrane ion flux and proteoglycan synthesis by chondrocytes.[9] Ketoprofen was originally reported to also block the lipoxygenase (LPX) pathway, thus reducing synthesis of leukotrienes from arachidonic acid. However, studies using carrageenan-induced inflammation in subcutaneous tissue chambers in horses revealed that ketoprofen decreased PGE_2 synthesis, but not leukotriene B_4 synthesis.[11,12] Thus, these studies have demonstrated that ketoprofen does not inhibit the LPX pathway in horses.

Research into the development of NSAIDs with dual COX and LPX inhibitory activity should offer a more balanced approach to inhibiting the synthesis of arachidonic acid-derived inflammatory mediators. Because COX inhibition may cause preferential metabolism of arachidonic acid via LPX, a dual COX-LPX inhibitor may improve the anti-inflammatory effects of NSAIDs. Additionally, the development of more specific COX-2 inhibitors with a COX-1/COX-2 ratio < 1 will help improve the therapeutic effectiveness of these compounds while minimizing their potential toxic side effects.

Potency and selectivity of NSAIDs in horses

An in vitro study evaluating the potency and selectivity of commonly used NSAIDs in horses revealed that FLM and

indomethacin were more potent than PBZ and CRP in inhibiting prostacyclin and thromboxane synthesis.[12] Flunixin meglumine and indomethacin appeared to be selective COX-1 inhibitors in the horse whereas PBZ and CRP were non-selective COX inhibitors. Carprofen was the weakest COX-2 inhibitor tested. Preliminary in vitro selectivity assays indicate that etodolac, a potential COX-2 inhibitor, is approximately 5–10-fold selective for COX-2 in horses.[14] However, etodolac was nowhere near as selective as some of the experimental COX-2 inhibitors that have been tested in horses.[13] Etodolac was shown to be as effective as PBZ at reducing LPS-induced synovitis and lameness in horses, and it exhibited relative COX-2 selectivity in that it inhibited PGE_2 but not $TBX\text{-}B_2$.[15]

Pharmacokinetics

Absorption

Peak plasma concentrations and the onset of action for NSAIDs after oral administration vary with the timing of administration with regard to eating. Mean time to peak plasma concentration for PBZ (4.4 mg/kg p.o.) in ponies with access to hay was delayed 6–12 hours, compared with fasted ponies.[16] Phenylbutazone and other NSAIDs appear to bind to hay and other digesta, thus delaying time to peak plasma concentration. Fermentative digestion of roughage in the large intestine releases the bound drug, which possibly contributes to the propensity of NSAIDs to cause ulcerative disease in the large intestine.[9] The time to reach peak plasma concentration and the elimination half-life can be dramatically prolonged by the timing of administration relative to feeding. This has important clinical implications with regard to the therapeutic efficacy of an orally administered NSAID as well as potential problems related to horses in sanctioned competitive events.

There are conflicting data regarding the effects of feeding versus fasting on the absorption of MFA.[6,17] Horses with free access to feed had delayed absorption, decreased maximal plasma concentration and delayed time to peak concentration, compared with fasted horses, administered FLM. Although it may not be practical, NSAIDs should be administered to horses that have not eaten for at least 2 hours before and are withheld from feeding for 2 hours after dosing in order to control absorption, time to peak plasma concentration and elimination half-life.

Metabolism and elimination

Most NSAIDs undergo hepatic metabolism and either renal or biliary excretion. NSAIDs administered to lactating mares are not excreted in milk in concentrations yielding measurable plasma levels in foals. Phenylbutazone undergoes hepatic metabolism to yield oxyphenbutazone, the pharmacologically active metabolite, and γ-hydroxyphenylbutazone, an inactive metabolite. The parent compound and the two metabolites are excreted into the urine and, due to their acidic nature, excretion is more rapid in alkaline than acidic urine.[18,19] Aspirin (acetylsalicylic acid) is rapidly deacetylated to salicylate, the active metabolite of the parent drug. A paucity of data regarding metabolism of MFA exists for horses; it is known that conjugation occurs and between 10% and 14% is excreted in the urine after oral administration.[10] Although little is known regarding the elimination of FLM, it does not accumulate in the body and approximately 14% is excreted in urine.[10]

Naproxen undergoes hepatic metabolism and along with its principal metabolite, 2-(6-hydroxynaphthyl)propionic acid, is excreted in the urine in high concentrations.[20] Ketoprofen is used clinically as a racemic mixture of the R(–) and S(+) enantiomers with half-lives of 1.1 hours and 1.5 hours, respectively, after i.v. administration.[21] Ketoprofen accumulates in inflammatory exudates, resulting in substantially prolonged exudate half-lives of 19.7 hours and 22.6 hours for the R(–) and S(+) enantiomers, respectively. Similar to KTP, CRP is used clinically as a racemic mixture of the R(–) and S(+) enantiomers, each with different potencies and pharmacokinetics. There is evidence that the COX inhibitory and anti-inflammatory effects of carprofen are primarily attributable to the S(+) form. However, recent evidence suggests that the R(–) enantiomer may be equipotent to the S(+) form as an analgesic and in some other activities such as inhibition of β-glucuronidase release.[22,23] Coincident with decreases in plasma concentrations, CRP accumulates in inflammatory exudates, resulting in exudate levels exceeding plasma levels from 2 to 48 hours.[24]

Plasma protein binding

NSAIDs are highly (90–99%) bound to plasma proteins; thus, the free active fraction of these drugs is extremely small.[6] Concurrent administration of another highly protein-bound drug (i.e. chloramphenicol, rifampin, barbiturates) can cause displacement of the NSAID, resulting in an increased free active fraction.[6]

Effect of age on pharmacokinetics

The pharmacokinetics of NSAIDs varies with the age of the horse. The plasma half-life of i.v. PBZ (4.4 mg/kg) was longer for 8–10-year-old adult horses and ponies (5.5 hours) than for 3-year-old ponies (3.9 hours).[16] NSAIDs have substantially different pharmacokinetic profiles in neonatal (< 24 hours of age) foals compared with adult horses. In general, neonates have a reduced ability to eliminate NSAIDs, compared with adult horses, after a single i.v. dose.[25–27] The large volumes of distribution of NSAIDS in neonatal foals may necessitate larger initial doses; however, the relatively long half-lives suggest that the dosing interval should be extended to prevent accumulation of these drugs with resulting potential toxic side effects.

Effect of dose on pharmacokinetics

Unlike most NSAIDs, PBZ can have dose-dependent kinetics, with the half-life increasing from 4 to 8 hours when adminis-

tered at a dose of 10 mg/kg.[28] This effect is likely due to saturation of hepatic enzymes responsible for PBZ metabolism. Taken together, the effect of dose and age on the pharmacokinetics of PBZ emphasizes the need for caution in the dose and dosing interval when administering this drug to older horses, especially those that are systemically ill or dehydrated.

Tissue kinetics

Phenylbutazone, like many NSAIDs, has dramatically different kinetic values for tissue compared with plasma.[6] The acidic nature and high protein binding of NSAIDs causes them to accumulate at sites of inflammation. For example, the plasma half-life for PBZ is between 4 and 8 hours, whereas the half-life in exudates is approximately 24 hours.[8] Ketoprofen accumulates in inflammatory exudates and thus the half-lives of the R(–) and S(+) enantiomers are prolonged from 1.1 hours and 1.5 hours to 19.7 hours and 22.6 hours, respectively.[29] Similarly, CRP accumulates in exudates and yields substantially greater concentrations than in plasma between 2 and 48 hours after administration.[24]

Drug interactions

Concurrent administration of chloramphenicol reduces the clearance and increases the half-life of PBZ, which may accentuate both therapeutic and toxic effects. A single dose (25 mg/kg i.v.) of chloramphenicol prior to PBZ administration resulted in a significant decrease in the elimination rate and this effect was accentuated by additional dosing of chloramphenicol.[30] Rifampin induces hepatic biotransformation processes and has been shown to increase the elimination rate of PBZ in horses.[30]

There are anecdotal reports that when PBZ is administered to horses anesthetized with thiobarbiturates, increased depth and duration of anesthesia may occur due to competitive plasma protein binding.[31,32] A study evaluating administration of PBZ (8.8 mg.kg IV) 9 minutes after thiamylal (11 mg/kg i.v.) demonstrated no effects of PBZ on thiamylal pharmacokinetic parameters or depth or duration of anesthesia.[33] However, there were changes in PBZ pharmacokinetics, including increased serum concentrations and decreased percentage protein-bound PBZ. In another study, administration of PBZ (6.6 mg/kg i.v.) for 4 days prior to thiamylal anesthesia did not

Table 23.1 Recommended dosage regimens for non-steroidal anti-inflammatory drugs in horses†

Drug	Route	Formulation	Dose	Duration	References
Acetylsalicylic acid (aspirin)	PO	Tablets, powder	25–35 mg/kg BID 5–50 mg/kg SID		35 36
Dipyrone	IV, IM	Injectable	5–22 mg/kg 11.1 mg/kg QID		35 10
Flunixin meglumine	IV, IM	Injectable	1.1 mg/kg SID-BID 0.25 mg/kg TID	≤ 5 days	35 35, 36
	PO	Granules, paste	1.1 mg/kg SID-BID		10,35
Ketoprofen	IV	Injectable	2.2 mg/kg SID		7
Meclofenamic acid	PO	Granules	2.2 mg/kg SID then QOD	5–7 days	10, 17, 35, 36
Naproxen	PO	Granules	10 mg/kg BID then SID	≤ 14 days	10, 35–37
Phenylbutazone	PO	Tablets, powder	4.4 mg/kg BID 2.2 mg/kg BID 2.2 mg/kg SID	1 day 4 days 2 days	10, 17, 35, 36
	IV	Injectable	2.2–4.4 mg/kg SID 4.2 mg/kg SID	≤ 5 days ≤ 4 days	10, 35, 36 10
Carprofen	IV	Injectable	0.7 mg/kg SID		24, 38
	PO	Tablets	0.7 mg/kg SID		
Eltenac	IV	Injectable	0.5 mg/kg SID	3 days	39
Etodolac	IV	Injectable	23 mg/kg BID		14

PO = per os, IV = intravenous, IM = intramuscular, SID = once daily, BID = twice daily, TID = three times daily, QID = four times daily, QOD = every other day

† Dosages are based on normal horses; may need to adjust dosages if horses are ill, dehydrated, volume depleted, or if administering NSAIDs in combination. Ponies may require lower dosages.

Modified from Kallings P. Nonsteroidal anti-inflammatory drugs. Vet Clin North Am Equine Pract 1993; 9: 523–541.

have a significant effect on recumbency time.[30] Therefore, it seems unlikely that perianesthetic administration of PBZ would alter the intensity or duration of anesthesia. It also seems unlikely that thiamylal administration would have a clinically important effect on the disposition of PBZ.

A study evaluating the pharmacokinetics of steady-state PBZ and single-bolus gentamicin administered together revealed that gentamicin pharmacokinetics are altered by concomitant PBZ therapy. However, no effect of gentamicin was found on the pharmacokinetics of PBZ.[34] Gentamicin was administered as a 2.2 mg/kg i.v. bolus on the fourth day of once-daily treatment with PBZ (4.4 mg/kg i.v.). Phenylbutazone induced a 49% increase in the rate of gentamicin return to the central compartment from peripheral tissues and the half-life and volume of distribution of gentamicin decreased 23% and 26%, respectively. There were no changes in PBZ pharmacokinetics induced by gentamicin. Because PBZ induces changes in the rate and extent of distribution and elimination of gentamicin, caution should be exercised when using this drug combination in horses.

Dosage regimen

The dose, interval and route of administration for NSAIDs commonly used in horses are given in Table 23.1.[7,10,14,17,24,35–39]

Therapeutic uses

NSAIDs are indicated in horses with inflammatory conditions of the musculoskeletal system including myositis, tendinitis, desmitis, laminitis, osteoarthritis, synovitis/tenosynovitis, osteitis/osteomyelitis, septic arthritis and surgically or traumatically induced injury. They are commonly administered perioperatively to control postoperative pain and fever and prevent excessive edema formation.

Although the mechanism of action is the same, there are apparent differences in the efficacy of different NSAIDs depending upon the type of condition being treated. For example, clinical and experimental data suggest PBZ is more efficacious in providing analgesia for most horses with musculoskeletal disease, whereas FLM is more effective in providing visceral analgesia in horses with colic.[40] These differences in effect may be due to the specificity of certain NSAIDs for different COX isomers or for COX within different tissues. Ketoprofen is reported to be effective in decreasing inflammation and pain associated with musculoskeletal disease and colic.[41–43] Acetylsalicylic acid (aspirin) is rarely used as an anti-inflammatory drug in horses because of its extremely short half-life and low potency. However, it is frequently administered to horses with thromboembolic disorders to decrease platelet aggregation.[10,44] Dipyrone is a potent antipyretic agent, but has only mild analgesic properties.[40] Other currently less commonly used NSAIDs include CRP, MFA and NPX. Newer, more specific COX-2 inhibitors, such as etodolac, are currently being developed and evaluated in horses.[13,15,45,46]

Analgesic effects

NSAIDs appear to mediate their analgesic effect in part by their inhibitory effects on COX, thus preventing or modulating PGE_2 synthesis locally at sites of inflammation.[9] However, because there are several clinically effective NSAIDs that are relatively weak COX inhibitors, anti-inflammatory mechanisms other than inhibition of PG synthesis are believed to be involved. PGE_2 is believed to bind to sensory nerve receptors and promote the discharge of impulses with a consequent increase in pain.[9] Prostaglandin E_2 also sensitizes nerve endings to the effects of numerous physical and chemical stimuli. Overall, PGs amplify peripheral pain by decreasing the nociceptor threshold.[9] Although PGE_2 does not cause pain itself, it can amplify the nociceptive pathway by affecting the pain-inducing properties of other mediators such as histamine and bradykinin.[9] It also seems to affect the body's ability to distinguish between different types of nociceptive stimuli. There is evidence to suggest that PGs are involved in nociceptive pathways within the spinal cord and that NSAIDs have at least some action in inhibiting this cascade. NSAIDs do not exert a direct effect on normal pain perception, but rather reduce hypersensitivity to pain caused by inflammation and this effect is mediated by a reduction in PGE_2. The analgesic effects of NSAIDs apparently can be dissociated from the anti-inflammatory effects and require a lower dose. The analgesic effects of NSAIDs are variable depending upon the source of pain and the specific drug. There are limited controlled clinical trials or experimental studies comparing the analgesic effects of commonly used NSAIDs in horses with musculoskeletal disease.

A study evaluating the analgesic effects of PBZ, FLM and CRP administered at the end of surgery, prior to anesthetic recovery, demonstrated that there were no differences in the pain scores or number of horses requiring additional analgesia among the three groups of horses.[47] In horses requiring additional analgesia after surgery, there was a significant difference in the time after surgery between the groups receiving FLM and PBZ. Horses treated with FLM required additional drug 12.8 ± 4.3 hours after surgery whereas those given PBZ required it at 8.4 ± 4.6 hours after surgery. Horses treated with CRP were intermediate in requiring additional drug 11.7 ± 6.9 hours after surgery. A study evaluating and comparing the inhibition of peripheral pain by FLM and CRP in horses demonstrated that there was no demonstrable analgesic effect for either drug when tested using an external skin stimulation test for nociception.[48] However, when the heating element model of nociception was used, a 1.1 mg/kg i.v. dose of FLM failed to inhibit peripheral pain whereas a dose of 0.7 mg/kg i.v. of CRP inhibited the peripheral pain response for approximately 24 hours.[48]

In another study evaluating the analgesic effects of PBZ in horses after arthroscopic surgery, no difference was shown between PBZ-treated and placebo-treated horses regarding plasma β-endorphin or catecholamine concentrations.[49] However, horses treated with PBZ had a lower total postoperative pain severity index, which suggests that perioperative treatment with PBZ did exert some analgesic effects.[49]

Pretreatment of horses with PBZ prior to carrageenan-induced synovitis was more effective in reducing lameness, joint temperature, synovial fluid volume and synovial fluid PGE_2 concentrations than pretreatment with KTP.[50] Additionally, KTP administered at the PBZ equimolar dose (3.63 mg/kg) to horses with chronic laminitis reduced chronic hoof pain and lameness to a greater extent that did 2.2 mg/kg PBZ. This effect was still present 24 hours after drug administration.[51] Therefore, it was recommended that a dosage rate of 1.65 times the recommended therapeutic dose is more potent than PBZ in alleviating chronic hoof pain and lameness in horses.

In a study of experimentally induced carpitis in horses, the effects of eltenac reached a plateau at a dose of 0.5 mg/kg, but its effects were not different from those of FLM administered at a dose of 1.1 mg/kg.[39] Both drugs at these doses caused a reduction of carpal circumference, joint hyperthermia and carpal pain and increased carpal flexion angle and stride length, demonstrating their analgesic, antipyretic and anti-inflammatory effects.

Anti-inflammatory and chondroprotective effects

Inflammation can lead to pain and edema formation. Inhibition of PG synthesis perioperatively can reduce the inflammatory response secondary to surgery or the primary disease, thus decreasing pain and edema. NSAIDs are commonly administered perioperatively to horses for these reasons. For example, PBZ is often administered for several days after arthroscopic surgery in horses with synovitis secondary to osteochondral chip fractures or osteochondrosis in order to decrease synovitis arising from primary joint disease and from the surgery.

Prostaglandins of the E-series seem to be involved with increased metabolic activity in cartilage, whereas those of the F-series are chondroprotective.[9] Prostaglandin E_2 is responsible for the majority of bone resorption associated with osteomyelitis.[9] NSAIDs are therefore useful in acute synovitis and osteomyelitis to decrease PG-mediated synthesis of destructive enzymes and reduce cartilage degradation and bone resorption. However, prolonged administration can accelerate cartilage degeneration. In general, NSAIDs have a suppressive effect on proteoglycan synthesis.[52] In vivo and in vitro studies have investigated the chondroprotective and potentially deleterious effects of NSAIDs, often with contradictory and confusing results. Additionally, the clinical relevance of these effects is not fully known. NSAIDs appear to have a varying ability to inhibit catabolic events in cartilage matrix with several noted differences in their inhibitory effects on the activity of degradative enzymes. Some of the potential beneficial effects of NSAIDs may not result from direct inhibition of these degradative enzymes, but rather suppression of other inflammatory mediators involved in cartilage degeneration.

A study evaluating the effects of orally administered PBZ to horses on proteoglycan synthesis and chrondrocyte inhibition of IL-1β in articular cartilage explants revealed that administration for 14 days caused a significant decrease in proteoglycan synthesis.[53] The investigators concluded that PBZ should be used judiciously in athletic horses with osteoarthritis because prolonged administration could suppress proteoglycan synthesis and potentiate cartilage damage.

Both the R and S enantiomers and the racemic mixture of CRP attenuated the increased IL-6 production induced by LPS in equine synoviocytes whereas the S enantiomer had a similar effect on chondrocytes.[54] Neither enantiomer of the racemic mixture suppressed the LPS-induced IL-1 production in synoviocytes or chondrocytes.

A study evaluating the effect of FLM, tolfenamic acid and both the R and S enantiomers of KTP on the response of equine synoviocytes to LPS demonstrated that all four compounds inhibited β-glucuronidase in a concentration-dependent manner, with tolfenamic acid being the most potent.[55] Tolfenamic acid and FLM caused an increased production of IL-6 induced by LPS, but only at their highest concentration (1000 μmol/L). Flunixin, tolfenamic acid and the S enantiomer of KTP caused a significant and concentration-dependent increase in IL-1 release. All four drugs caused a marked, concentration-dependent inhibition of PGE_2 synthesis. These findings suggest that by removing the regulator role of PGE_2 on IL-1 synthesis, the long-term use of NSAIDs in horses with arthropathies could potentially enhance cartilage degeneration. In another study evaluating the effect of commonly used NSAIDs on LPS-stimulated equine synovial membrane explants, it was demonstrated that PBZ, FLM, KTP and CRP suppressed PGE_2 production without causing a detrimental effect on viability of function as measured by hyaluronan synthesis.[56]

Administration of PBZ (4.4 mg/kg p.o. every 12 hours) for 30 days caused a significant decrease in mineral apposition rate in the tibia and appeared to decrease the healing rate of unicortical defects in horses.[57]

Antipyretic effects

Cytokines such as TNF, IL-1 and IL-6 increase in response to LPS and other inflammatory stimuli and result in the increased production of PGE_2 in the hypothalamus. The net effect of this hypothalamic increase in PGE_2 is to reset the body's thermal set point at a higher temperature, resulting in fever. NSAIDs inhibit endogenous PGE_2, which raises the threshold level of the thermoregulatory center in the hypothalamus[9], thereby preventing or limiting the febrile response. Different NSAIDs seem to have varying antipyretic effects; empirically, dipyrone seems to be the most effective antipyretic in horses. The antipyretic effects of NSAIDs are observed with doses that inhibit PG synthesis, which is usually much lower than those needed for anti-inflammatory effects.

Antiendotoxic effects

NSAIDs are effective in inhibiting endotoxin-induced prostanoid release and thus are used to pretreat horses

predisposed to develop endotoxemia or to treat horses with suspected endotoxemia to prevent endotoxic shock. Some horses with infectious conditions of the musculoskeletal system such as septic arthritis/tenosynovitis, septic cellulitis, myositis and other potential infectious conditions involving Gram-negative bacteria are predisposed to the adverse effects of endotoxemia. Flunixin meglumine reportedly is more effective in ameliorating the cardiovascular effects of endotoxin, whereas PBZ is more selective in blocking the inhibitory effect of endotoxin on gastrointestinal motility.[58] Pretreatment with FLM (0.25 mg/kg i.v.) decreases the synthesis of TBX-B_2 and 6-ketoprostaglandin $F_{1\alpha}$, the stable metabolites of TBX-A_2 and prostacyclin respectively, and improves hemodynamic status in experimentally induced endotoxemia in equids. Flunixin meglumine prevents endotoxin-mediated pregnancy loss in mares during the first 60 days of gestation only if administered in the early stages of endotoxemia (often before clinical signs are present).[59]

Hemostatic and antithrombotic effects

Aspirin and other NSAIDs are sometimes used in horses for treatment or prophylaxis of diseases with a thromboembolic component, including thrombophlebitis, laminitis, navicular disease, intestinal ischemia and non-strangulating infarction. Aspirin is recommended because of its irreversible inhibition of platelet COX leading to inhibition of TBX-A_2 synthesis, which is a proaggregatory and vasoconstrictor substance released during blood clotting.[9,10] A single oral dose of aspirin (20 mg/kg) prolongs bleeding time and decreases platelet adhesiveness in horses.[60] Aspirin (19 mg/kg) causes complete blockade of serum TBX-B_2 synthesis for 7 days; 74% inhibition remains at 24 days.[44] This indicates that aspirin causes complete, irreversible inhibition of platelet COX and this action probably extends to megakaryocytes in the bone marrow.[44] In vitro studies of equine platelets demonstrate that FLM, PBZ and NPX also have potent antiaggregatory properties.[61] Flunixin meglumine and PBZ cause reversible inhibition of platelet COX, with serum TBX-B_2 concentrations returning to normal within 48 hours.[44] Because microthrombi and platelet–platelet or platelet–neutrophil aggregates have been shown to form during laminitis,[62] some clinicians administer aspirin to horses as a preventive or therapeutic agent; however, the efficacy of this treatment is unknown.

Laminitis

Horses with acute gastrointestinal tract disease, other infectious or inflammatory diseases and horses with severe lameness are predisposed to the development of laminitis. Therefore, NSAIDs are often considered crucial in horses for the prevention and/or treatment of laminitis. Providing analgesia disrupts the pain–vasoconstriction cycle induced by the release of catecholamines and other vasoconstrictive substances. This may help attenuate the decreased digital blood flow and laminar perfusion characteristic of the early stages of acute laminitis. Phenylbutazone is believed by many to be more effective in reducing pain associated with laminitis; however, FLM, MFA and KTP are also effective.[9,10,41] Aspirin may also be useful in decreasing platelet aggregation in the laminar microvasculature, which should improve laminar blood flow. A PBZ equimolar dose of KTP (3.63 mg/kg), which is 1.65 times the recommended therapeutic dose, was more potent than PBZ in alleviating chronic hoof pain and lameness.[41] Whether or not the commonly used NSAIDs are effective in reducing the inflammatory cascade involved in laminitis or whether they simply provide analgesia by inhibiting PGE_2 synthesis is currently unknown. Regardless, they are a vitally important component of the medical management of acute laminitis.

Clinical applications

Clinical and experimental evidence suggests that PBZ be used at 4.4 mg/kg once daily or 2.2 mg/kg once to twice daily for its analgesic and anti-inflammatory properties in musculoskeletal disease.[6] Additionally, clinical experience suggests PBZ also exerts anti-inflammatory effects in reducing surgical wound edema; however, this has not been demonstrated experimentally. Clinically, dipyrone is not a very effective analgesic for musculoskeletal pain and is usually administered i.v. in horses principally for its antipyretic effects. Aspirin is a poor analgesic, but its irreversible effect on platelets at low doses makes it potentially useful for horses with laminitis and navicular disease. Meclofenamic acid is apparently most useful for treatment of chronic musculoskeletal pain. In a clinical trial, MFA was shown to improve lameness in 78% of horses with navicular disease, 76% with chronic laminitis and 61% with osteoarthritis.[63] Another clinical trial comparing 7-day treatment regimens of MFA (2.2 mg/kg) to PBZ (4.4 mg/kg) in horses with navicular disease and osteoarthritis demonstrated that 60% of those treated with MFA responded favorably compared with 36% treated with PBZ.[10]

Flunixin meglumine is effective and useful in the treatment of lameness in horses, but because of its high cost in comparison to PBZ, it is usually not the first NSAID administered. In one clinical trial of horses with various musculoskeletal diseases, FLM alleviated clinical signs in 74%.[64] Naproxen is somewhat unique in the relative closeness of the doses required for its analgesic and anti-inflammatory effects. When administered at a dose of 4–8 g/day for 7 days, NPX markedly improved lameness and stride length in horses with experimentally induced myositis.[65] Naproxen was also reported to be particularly effective in the treatment of inflammatory swelling and lameness.[66] Clinically, 90% of horses with myositis treated with NPX responded favorably within 5 days. Ketoprofen has been shown to decrease synovial fluid PGE_2 concentrations, joint effusion and lameness in a carrageenan-induced synovitis model in horses.[51] Some veterinarians prefer KTP to FLM or PBZ in the treatment of musculoskeletal inflammation and pain in foals due to its decreased propensity for gastrointestinal ulceration. Carprofen has been shown to decrease inflammatory exudate

PGE_2 levels for up to 8 hours and ex vivo TBX-B_2 generation for 15 hours after a single i.v. dose.[24] Additionally, it reduced the swelling in an experimental model of soft tissue inflammation in the necks of ponies. Carprofen has also been shown to alleviate cutaneous pain caused by application of a heating element for 24 hours and was equally effective to PBZ and FLM for postoperative analgesia.[47] Ketoprofen and CRP are particularly effective in decreasing inflammation-associated edema and joint effusion in horses.[10,51]

Combination NSAID therapy

Because all NSAIDs have a similar mechanism of action, it is believed that there is no apparent benefit of administering NSAIDs in combination. However, combination NSAID therapy is becoming increasingly common. Although it is true that all NSAIDs inhibit COX, it is currently unknown if there is greater affinity of NSAIDs for COX in certain tissues. Likewise, it is assumed that there is a differential affinity of the COX isoforms by the same NSAID. Thus, because NSAIDs have a similar mechanism of action, combination therapy can increase the potential for toxicity. Therefore, it is important to adjust the dose of each NSAID if administered in combination and it is imperative to maintain hydration in order to reduce the potential for toxicity.

Combination NSAID therapy may be useful perioperatively in certain horses. For example, those with ischemic bowel requiring intestinal resection and anastomosis are predisposed to the development of endotoxemia, postoperative ileus, laminitis and thrombophlebitis. Flunixin meglumine appears to be superior in blocking the effects of endotoxin on hemodynamic variables and decreasing eicosanoid synthesis.[67–71]

Phenylbutazone is anecdotally reported to be more effective in controlling pain in horses with laminitis and has been shown to be more selective in decreasing the inhibitory effects of endotoxin on intestinal motility.[58] Aspirin, often administered for its antithrombotic effects, may help prevent or reduce laminitis, thrombophlebitis and intestinal adhesion formation. Concurrent administration of FLM (1.1 mg/kg i.v.) and PBZ (2.2 mg/kg i.v.) does not alter the disposition or clearance of either drug; therefore, it should not result in increased concentrations of either drug.[72] However, concurrent administration of FLM and PBZ prolongs the pharmacologic effect (TBX-B_2 suppression) and may increase the potential for toxicity.[72] Experimental or controlled clinical studies are necessary to evaluate the therapeutic efficacy and toxicity of combination NSAID regimens before they can be recommended.

Adverse effects of NSAIDs

Inhibition of the COX pathway accounts not only for the therapeutic effects of NSAIDs, but also for the potential toxic effects. Gastrointestinal ulceration and renal papillary necrosis associated with NSAIDs are believed to occur secondary to decreased PGE_2 synthesis, which is important in maintaining mucosal blood flow and other cytoprotective effects and renal medullary blood flow. There may be breed, age and idiosyncratic differences in the susceptibility to NSAID toxicity. For example, ponies are reportedly more susceptible than horses to the toxic effects of PBZ[73] and young animals are also believed to be especially sensitive to the adverse effects of NSAIDs.[74–77] Horses that are aged, systemically ill and/or dehydrated also appear to be predisposed to the toxic effects of NSAIDs. The toxic potential of the three most commonly used NSAIDs in horses was greatest for PBZ, less for FLM and least for KTP.[7] Naproxen did not cause clinically apparent toxicity in horses at three times the recommended dose.[20] Although data are scarce, MFA and CRP seem to have minimal toxic effects when used at the recommended dosing regimen.[6,38] Therefore, veterinarians should use caution when selecting and administering NSAIDs to young, aged, systemically ill or dehydrated animals because of a greater susceptibility to the toxic side effects.

Gastrointestinal tract ulceration

Administration of NSAIDs in excessive doses, for prolonged periods or in the presence of dehydration or volume depletion can lead to a number of serious side effects. Gastrointestinal ulceration (gastric glandular and small and large intestinal mucosa) is a relatively common side effect of NSAID administration in horses. Additionally, horses administered NSAIDs (especially PBZ orally) can develop ulcerations of the oral mucosa as a result of a local irritant effect, which could account for the effects observed on the cecal and large colon mucosa of horses treated with orally administered PBZ. Phenylbutazone binds to hay, which delays its absorption. Once the hay reaches the large intestine (cecum and colon), PBZ is released after digestion and fermentation, resulting in relatively high concentrations that could have a local irritant effect on the cecal and colonic mucosa. However, this local irritant effect cannot account for all of the toxic effects since similar lesions are noted in horses with parenterally administered NSAIDs.

The ulcerogenic effects of NSAIDs are believed to result from an NSAID-mediated decrease in mucosal PGE_2, leading to vasoconstriction, hypoxia and necrosis. Prostaglandins are normally cytoprotective in the gastrointestinal tract. Prostaglandin E_2 and PGI_2 decrease the volume, acidity and pepsin content of gastric secretions and also stimulate bicarbonate secretion by epithelial cells, produce mucosal vasodilation, increase mucus production and stimulate turnover and repair of gastrointestinal epithelial cells.[78] NSAIDs disrupt these normal cytoprotective effects in the gastric mucosal barrier and contribute to the development of gastric glandular mucosal ulceration. Gastrointestinal ulceration is often accompanied by secondary anemia, hypoproteinemia and hypoalbuminemia owing to blood and plasma protein loss. Additionally, horses with NSAID toxicity often demonstrate neutropenia, which has been suggested to be due to suppression of granulopoiesis in the bone marrow. However, this effect is most likely secondary to intestinal inflammation, disruption of the mucosal barrier and subsequent absorption of endotoxin into the circulation.

In recent studies, PBZ did not decrease gastric or intestinal mucosal PG concentrations in horses 48 hours after

administration.[79] There is evidence to suggest that PBZ causes direct injury to the intestinal microvasculature.[79] Juvenile horses are especially predisposed to the ulcerative effects of these drugs on the gastric mucosa, while adult horses are more commonly affected with right dorsal colon ulceration, resulting in abdominal pain, diarrhea and a protein-losing enteropathy.[7] Most reported cases of ulcerative colitis have been in adult horses administered PBZ but other NSAIDs can contribute to the development of this disease. The relative ulcerogenic effect of three commonly used NSAIDs in clinically normal adult horses is PBZ > FLM > KTP.[7]

Non-selective COX-1 inhibitors or those with combined COX-1 and COX-2 inhibitory effects delay the recovery of ischemic-injured intestinal mucosa.[45] This finding demonstrates that constitutively synthesized PGs are important for mucosal recovery. Etodolac, a potential COX-2 inhibitor in horses, partially inhibited PG synthesis, but had no effect on recovery of ischemic-injured equine jejunal mucosa in vitro, which is in contrast to FLM, which almost fully inhibited PGs and inhibited mucosal recovery.[45] Etodolac behaved similar to a COX-2 inhibitor in that it partially inhibited PGE_2 and PGI_2, but had no effect on TBX-B_2, a COX-1 metabolite.[45]

Renal toxicity

Papillary necrosis is the major nephrotoxic effect of NSAIDs observed in horses but tubular nephritis can also occur. Renal synthesis of PGs occurs primarily in the medulla.[80] Conditions resulting in renal vasoconstriction (dehydration, volume depletion, shock) induce PG synthesis and secondary compensatory vasodilation.[80] Under normal circumstances, vasodilatory PGs play a minor role in maintaining renal blood flow and controlling renal function. However, during certain pathophysiological conditions, vasodilatory PG synthesis is required to maintain adequate renal perfusion and function. Renal medullary ischemia is considered the initiating factor in the development of renal papillary necrosis. This occurs when horses are administered NSAIDs either in excessive doses, for prolonged periods, or concomitant with dehydration or volume depletion.[74,75,81] Without concurrent dehydration, PBZ does not reportedly result in renal papillary necrosis.[75] However, concurrent administration of NSAIDs and aminoglycoside antibiotics can also potentiate the risk of nephrotoxicity.[10] If possible, horses that are dehydrated or volume depleted should have their fluid volume normalized prior to beginning NSAID therapy.

Hemostatic effects

Although NSAIDs impair platelet adhesion and can either lead to or exacerbate bleeding tendencies owing to their inhibition of platelet TBX-B_2 synthesis, these are not frequently observed complications in horses.[40]

Decreased wound healing

Administration of NSAIDs has been reported to contribute to an increased incidence of abdominal incisional complications in horses.[82] Although NSAIDs reportedly have no clinically significant effect on wound healing, their use in horses has been reported to contribute to the development of abdominal incisional complications.[82] Experimentally, the administration of FLM (1.1 mg/kg i.v. b.i.d) for 7 days caused decreased strength in skin, linea alba and small intestinal enterotomy wounds at 7 days in ponies.[83] Another retrospective study reported no association between the administration of NSAIDs and the development of abdominal incisional complications.[84] Clinically, the use of NSAIDs does not appear to affect wound healing.

Thrombophlebitis

Perivascular injection of PBZ causes intense phlebitis and tissue necrosis. Administration of excessive doses of PBZ has been demonstrated to cause degeneration and dilation of the walls of small veins and microvascular phlebitis, which may contribute to some of the toxic effects on the intestinal mucosa and kidney.[79] Fifty percent of horses administered PBZ develop pulmonary vascular thrombosis observable at necropsy.[85] The clinical significance of these changes is unknown.

Corticosteroid therapy

Corticosteroids are administered systemically and locally for their anti-inflammatory properties in horses. These drugs are often administered either parenterally or orally for their systemic anti-inflammatory effects or locally within joints for local anti-inflammatory effects. Despite the potential untoward effects on articular cartilage, corticosteroids are commonly administered intra-articularly in horses with non-septic joint disease because of their potent anti-inflammatory properties. Intra-articular injection of corticosteroids into inflamed joints depresses the initial inflammatory events, including capillary dilation, leukocyte margination and migration, inflammatory cell accumulation, enzyme and inflammatory mediator liberation and cytokine, prostaglandin and thromboxane synthesis.[86]

Classification and mechanism of action

Glucocorticoids are produced synthetically and are often classified according to their onset and duration of action, and route of administration.[87] Corticosteroids commonly administered parenterally in horses with rapid onset (< 1 min) and short duration ($t_{1/2}$ = 1–2 h) include prednisolone sodium succinate (Solu-Delta-CORTEF, Upjohn), methylprednisolone acetate (Depo-Medrol, Upjohn) and methylprednisolone sodium succinate (Solu-Medrol, Upjohn). Those corticosteroids with rapid onset (5–45 min) and intermediate duration ($t_{1/2}$ = 3–4 h) include dexamethasone sodium phosphate or dexamethasone in propylene glycol (Azium SP and Azium, Schering). Corticosteroids with slow onset and long duration

include triamcinolone acetonide (Vetalog, Solvay), methylprenisolone acetate (Depo-Medrol), and flumethasone (Flucort, Syntex). Parenteral formulations of corticosteroids with rapid onset are usually used in emergency situations such as anaphylaxis and circulatory shock, whereas those with slow onset and long duration are used for synovitis, arthritis or intralesional therapy. Orally administered corticosteroid formulations are categorized as rapid onset and short duration (prednisone tablets); rapid onset and short-to-intermediate duration (triamcinolone tablets or powder); and slow onset and long duration (dexamethasone tablets or powder).[87] These formulations are usually used for subacute to chronic inflammatory or allergic conditions.

Corticosteroids are 21-carbon molecules that contain three 6-carbon rings and a 5-carbon ring.[88] Pharmacological activity depends upon the presence of a hydroxyl group at the C-11 location. The corticosteroids available for intra-articular use are 11β-hydroxyl compounds that do not require biotransformation and are generally ester salts prepared as suspensions. The duration of effect appears to be inversely correlated with the water solubility of the corticosteroid and the rate of absorption. Triamcinolone is the most insoluble and has the longest duration of action. Other factors believed to determine the duration of action of intra-articular corticosteroids include the rate of hydrolysis of the drug by enzyme in the synovial cavity as well as the binding affinity of the steroid for the steroid receptors in the target cells of the joint.[88]

The local effect of a corticosteroid in the joint is dependent on the rate of hydrolysis within the joint. Methylprednisolone acetate (MPA) is considered a long-acting ester when given i.m. because of the slow rate of absorption from the site of injection with subsequent hydrolysis in the plasma. However, when injected into a joint, it is rapidly hydrolyzed to the active drug (methylprednisolone, MP) with high local synovial fluid concentrations detectable within 2 hours post injection.[89,90] Measurable concentrations of MP were detectable for 5–39 days, whereas MPA was detectable for only 2–6 days post injection. Although MPA was not detectable systemically after intra-articular injection, it was detectable in the synovial fluid for 24 hours. This resulted in depression of endogenous hydrocortisone for 3–4 days, but the adrenal gland remained responsive to corticotrophin.[89]

The biologic potency or activity of corticosteroids is dependent upon many factors, including the total dose administered, the duration of action, duration and frequency of treatment, rate of conversion to biologically active metabolites, crystal size of the suspension and numerous other cell and tissue variables.[88] Corticosteroids exert their effect on cells by binding to plasma membrane and steroid-specific cytosolic receptors of steroid-responsive tissues.[87,91] The corticosteroids apparently passively diffuse into the cytosol of steroid-responsive tissues and bind to cytosolic receptors, which leads to a change in the allosteric nature of the receptor–steroid complex. The activated cytosolic receptors are then translocated to the nucleus where they bind to the steroid response element on nuclear DNA. This results in modulation of gene transcription and mRNA coding for specific proteins that ultimately causes the hormonal effect. Glucocorticoids exert their anti-inflammatory effects via stimulating production of lipocortin, which inhibits the activity of plasma membrane-bound phospholipase A_2 (PLA_2) and thereby inhibits release of arachidonic acid and indirectly the de novo synthesis of inflammatory mediators including PGs, TBXs, LTs and platelet-activating factor. The onset of action at the cellular level is likely immediate, but completion of the necessary steps in this cascade likely takes from a few to several hours, which delays the biologic effect.

Corticosteroids exert their local anti-inflammatory effects by:

- stabilizing lysosomal membranes and the concomitant release of lysosomal enzymes
- decreasing vascular permeability
- inhibiting leukocyte adherence to microvascular endothelium and subsequent diapedesis
- suppressing leukocyte superoxide synthesis
- inhibiting platelet aggregation
- inhibiting PG synthesis by inhibiting the release of arachidonic acid from membrane phospholipids
- reducing inflammatory effects of the healing process that result in fibrosis.[91]

Glucocorticoid receptors have been identified in neutrophils, lymphocytes and eosinophils. Corticosteroids typically have greater effects on cellular rather than humoral processes and on movement rather than function of leukocytes.[88] One of the predominant mechanisms of their anti-inflammatory properties is their inhibitory effect on the migration of neutrophils and macrophages into sites of inflammation. When administered systemically, corticosteroids cause a neutrophilic leukocytosis owing to a prolonged half-life, increased bone marrow synthesis of neutrophils, decreased margination and subsequent egress into sites of inflammation. Corticosteroids also have been shown to exert a dose-dependent effect on neutrophil function but this occurs to a lesser degree than the effect on leukocyte movement. Higher doses inhibit the release of lysosomal enzymes from neutrophils and neutrophilic phagocytosis is similarly suppressed. Poor correlation has been reported between neutrophil numbers and PGE_2 concentrations in synovial fluid after corticosteroid treatment of chronic inflammatory joint disease in people, which suggests a likely alternative source of prostaglandins and/or differential effects of these drugs on cellular function.[92]

Pharmacokinetics

Clearance

Corticosteroid suspensions generally have a relatively short intra-articular half-life. Considerable variation has been reported for the clearance of corticosteroid suspensions from the synovial cavity after intra-articular administration. Triamcinolone acetate has a reported synovial fluid half-life ranging from 1 to 5 days.[93] The median synovial fluid half-life of MPA and MP in the tarsocrural joint space of normal

horses as detected with high-performance liquid chromatography was 10.3 and 10.4 hours, respectively.[94] Another study has demonstrated that MPA can liberate its active principle in the synovial cavity for up to 1 month after intra-articular injection.[89]

Therapeutic uses

Joint disease

Although there is appreciable information in the literature regarding the untoward effects of intra-articular corticosteroid therapy, much of this has been shown more recently to be overgeneralization; there appear to be distinct differences in the effect of steroids on articular cartilage and synovial membrane depending upon the type and dose used. Intra-articular injection of corticosteroids remains a useful treatment for traumatic, degenerative and non-septic joint disease in the horse. Steroids effectively suppress the pain, heat and swelling associated with inflammatory joint disease and thus are effective in treating synovitis and arthritis. Aseptic technique is essential to prevent joint infection.[91]

Several drug formulations are approved for intra-articular administration, such as triamcinolone acetonide (TMA), isoflupredone acetate, betamethasone acetate (BMA), MPA and flumethasone.[87]

Experimental and clinical effects of intra-articular corticosteroids

Numerous in vivo and in vitro experimental and clinical investigations have reported on the therapeutic and deleterious effects of intra-articular corticosteroids in horses.

Methylprednisolone

Intra-articular injection of MPA into the joints of normal horses has shown some regressive effects on articular cartilage.[95,96] However, questions remain regarding the minimal effective dose and the effect this would have in arthritis/synovitis and the effect in joints of exercised horses.

Injection of 100 mg of MPA into the middle carpal joint of horses with experimentally induced osteochondral fragmentation of the distal radial carpal bone did not reduce lameness, but did cause a decrease in synovial fluid PGE_2 concentrations and lowered scores for synovial membrane intimal hyperplasia and vascularity, when compared with polyionic fluid-treated joints.[97] These potential beneficial effects must be weighed against the detrimental findings of articular cartilage erosion and morphologic lesions associated with MPA treatment. The deleterious effects of MPA in this model are in contrast to the favorable effects of TMA on clinical lameness, synovial fluid, synovial membrane and articular cartilage morphologic and biochemical parameters in the same model.[98]

A study of acute synovitis of the radiocarpal and middle carpal joints induced by four injections of lipopolysaccharide (0.5 ng) at 2-day intervals in ponies demonstrated that intra-articular injection of MPA (0.1 mg/kg) concomitant with the last dose of LPS 2 days before euthanasia had substantial effects on proteoglycan, protein and collagen synthesis in harvested cartilage explants.[99] Methylprednisolone alone caused a decrease in proteoglycan synthesis and increased protein and collagen synthesis in cartilage explants. Synovial membrane protein synthesis was also increased by MPA. However, there were no differences in protein or proteoglycan synthesis in explants from horses with synovitis whether or not they were treated with MPA. Acute synovitis appeared to prevent changes induced by intra-articular MPA alone. The effects of intra-articular MPA are different in inflamed versus normal joints.

A study evaluating the effects of LPS-induced acute synovitis and the effects of MPA on transcription of cartilage matrix proteins in ponies demonstrated that articular chondrocytes increase type II procollagen and aggrecan synthesis in response to synovitis and that MPA alters chondrocyte function in both inflamed and normal joints.[100]

In another study, synovial fluid samples were collected weekly from the radiocarpal joints of normal horses and MPA (60 mg) was injected into the radiocarpal joints at 2-week intervals, beginning on week 3, to quantify synovial fluid volume and keratan sulfate, cartilage aggrecan, C-propeptide and cartilage type II procollagen.[101] Synovial fluid volume was significantly reduced by MPA at weeks 4, 6, 7 and 8 but had returned to pretreatment values by week 9, which corresponded to 2 weeks after the last injection of MPA. It is known that corticosteroids suppress synovial membrane hyaluronic acid synthesis in vitro and this may contribute to the reduction in synovial fluid volume in normal joints. Keratan sulfate and cartilage aggrecan were significantly increased in the synovial fluid of joints treated with MPA, when compared with non-treated controls. C-propeptide was significantly decreased in synovial fluid of MPA-treated joints. These results suggest that repeated use of intra-articular MPA leads to potentially deleterious inhibition of procollagen II synthesis and increased release of degradation products of proteoglycan aggrecan from articular cartilage. This study also demonstrated that MPA did not influence articular cartilage aggrecan metabolism in the contralateral joint, which is in contrast to remote-site effects of TMA on articular cartilage GAG content.[98]

In an in vitro study, equine articular cartilage explants were treated with methylprednisolone sodium succinate (MPS) at various concentrations ranging from 0.001 to 10 mg/mL for one day and then in fresh medium without MPS.[102] Proteoglycan synthesis was severely depressed by 10 mg/mL MPS for 24 hours in normal cartilage. Cartilage treated with 5 mg/mL had pyknotic chondrocyte nuclei and empty lacunae. MPS concentrations of 1.0 and 0.1 mg/mL depressed proteoglycan synthesis in normal cartilage but concentrations recovered within 2 days after MPS removal from the medium. Concentrations of MPS of 0.01 and 0.001 mg/mL did not have a significant effect on proteoglycan synthesis in normal cartilage explants. MPS concentrations of 1.0 and 0.1 mg/mL alleviated articular cartilage

degradation in explants cultured in monocyte-conditioned medium, which suggests that it is possible to identify an intra-articular concentration of corticosteroid that will protect articular cartilage from cytokine-induced matrix degradation, but will not have a prolonged or permanent deleterious effect on chondrocyte matrix synthesis.

Equine chondrocytes cultured in monolayer were stimulated with IL-1β and cultured either with or without dexamethasone or MPA.[103] The stimulatory effect of IL-1β on matrix metalloproteinase (MMP) 13 (collagenase 3) gene expression in articular chondrocytes was decreased by dexamethasone, and reduced in a dose-dependent manner by MPA. These in vitro results parallel in vivo studies in other species and indicate that in vivo use of corticosteroids reduces the rate of progression of experimentally induced osteoarthritis.[104–106] In another study, the effects of MPA, BMA and dexamethasone in inhibiting equine MMP-2 and MMP-9 were assessed using gelatinase and casein degradation assays.[107] Betamethasone had no effect on MMP-2 or -9. Dexamethasone and MPA had no effect on MMP-9, but MMP-2 was significantly inhibited at the highest dose tested for dexamethasone (1 mg/mL) and the higher concentrations of MPA (1.2 and 5 mg/mL). Corticosteroids affect MMP levels in disease by preventing synthesis at the transcriptional level, which has been documented in the horse.[108]

Articular cartilage explants and chondrocyte monolayer cultures obtained from young adult horses were cultured to determine the effect of differing concentrations of MPA on chondrocyte function and viability in vitro.[109] Steady-state levels of type II procollagen mRNA decreased without concomitant decreases in type I procollagen expression as the concentration of MPA in the culture medium increased from 1×10^1 to 1×10^8 pg/mL. Cytotoxicity occurred as MPA concentrations increased to 1×10^8 and 1×10^9 pg/ml. The cartilage-specific fibronectin was suppressed in normal and inflamed joints with a single intra-articular injection of 0.1 mg/kg MPA. Collectively, this study demonstrates that MPA suppresses matrix protein markers of chondrocyte differentiation. The investigators speculate that a decreased and altered expression of matrix proteins in chondrocytes likely contributes to corticosteroid-induced cartilage degradation.[109]

An in vitro study evaluating the effect of MPA on proteoglycan and collagen metabolism in cartilage explants from normal equine joints revealed several important findings.[110] Proteoglycans were not lost to the media in response to MPA treatment over a 72-hour period, but there was a decrease in the size of some aggrecan monomers as well as the proteoglycan aggregate. The lowest doses of MPA stimulated protein synthesis and there was a trend for a similar pattern for proteoglycan and collagen synthesis. A protective effect of MPA against proteoglycan degradation in the explants was observed with higher doses (0.04–4.0 mg/mL) as demonstrated by reduced GAG being released into the media. The investigators speculate that MPA may affect post-translational modification of the core protein with the addition of smaller and fewer GAG chains.[110]

Methylprednisolone acetate reduced proteoglycan loss in cartilage explant cultures from the middle carpal joint of horses but this effect was not seen at clinically relevant concentrations.[111] MPA caused a dose-dependent inhibition of proteoglycan synthesis at all concentrations tested but chondrocyte viability was deleteriously affected only at the 2000 μg/mL dose. These results suggest that the therapeutic effect of MPA is not restricted to the anti-inflammatory effects on soft tissues of the joint.

Betamethasone

Horses were administered either 2.5 mL of betamethasone (3.9 mg betamethasone sodium phosphate and 12 mg betamethasone acetate per mL) or an equivalent volume of saline intra-articularly 14 and 35 days after experimentally induced osteochondral fragmentation of the distal radial carpal bone.[112] Some horses were exercised on a high-speed treadmill and others were kept in a box stall, and all horses were evaluated serially and then euthanized 56 days after fragmentation. The BMA did not cause any histologic, histochemical or biochemical evidence of articular cartilage alterations in horses with or without exercise.[112] The exercised horses also had comparable glycosaminoglycan concentrations as the saline-treated control joints. Therefore, the intra-articular injection of BMA in the middle carpal joint did not cause any consistently observable detrimental effects in exercised or non-exercised horses.

Triamcinolone

Recent work has suggested that intra-articular TMA (12 mg) may exert chondroprotective effects in the horse with experimentally induced osteochondral fragmentation.[98] Horses treated with TMA were less lame than horses with osteochondral fragments treated with polyionic fluids and horses without osteochondral fragments injected with polyionic fluids. Joints treated with TMA had less synovial membrane inflammatory cell infiltrate, intimal hyperplasia and subintimal fibrosis. Additionally, TMA-treated joints had better articular cartilage morphologic scores and increased hyaluronic acid concentrations. These findings support a chondroprotective effect of TMA with no observable detrimental effects. Despite previous reports of non-detectable corticosteroid levels in the contralateral joint of horses,[94] there was an observable beneficial remote-site effect in the non-treated joints of these horses. This remote-site effect of TMA in joints contralateral to the treated joints suggests a possible treatment effect perhaps unrelated to detectable levels of the drug and involving a mechanism of action that may not be pharmacologically mediated.[98]

In another report of the effects of intra-articular TMA (12 mg) on subchondral bone in horses with experimentally induced osteochondral fragmentation of the distal radial carpal bone, it was demonstrated that treated horses were significantly less lame than non-treated ones.[113] Additionally, there were no observable detrimental effects of TMA on any parameter measured, indicating there were no deleterious effects on the dynamics of bone remodeling and fragility in horses with experimentally induced osteochondral

fragmentation of the middle carpal joint.[113] However, the investigators mentioned their concern that the treated horses, which were less lame, did not have increased subchondral bone formation as expected from their improved weight bearing and increased loading. They speculate that TMA might have caused a slight reduction in the normal subchondral bone remodeling response.[113]

Dosage regimen

The formulation and dose of corticosteroid suspensions commonly used for intra-articular administration in horses is given in Table 23.2.

Adverse effects of intra-articular corticosteroids

Administration of corticosteroids into joints can have both therapeutic and detrimental effects.[91] The detrimental effects include decreased cartilage elasticity and glycosaminoglycan content with progressive cartilage degeneration; formation of calcium deposits on the surface of hyaline cartilage; cartilage thinning and fissure formation; and decreased synovial fluid viscosity and hyaluronic acid content. The predominant adverse effects include 'steroid arthropathy', postinjection flare, septic arthritis and osseous metaplasia.[91] These deleterious effects have been shown to be both drug and dose dependent.

Because of the intense reduction in inflammation and associated pain caused by intra-articular injection of corticosteroids, there is some concern that horses may overuse an injured, 'pain-free' joint, thus accelerating joint degeneration. This concern has been substantiated by at least some studies showing that corticosteroids can have deleterious effects on chondrocyte metabolism. However, the beneficial effects on reducing inflammation and the associated degradative mediators released from inflammatory cells versus the potential direct deleterious effects must be weighed when considering the use of corticosteroids in an inflamed joint. At high concentrations, corticosteroids inhibit proteoglycan synthesis and have a negative influence on the structure of collagen in the articular cartilage.[95,114] However, there is debate over the clinical importance of decreased proteoglycan content, particularly when lower doses of steroids are used. More recently, BMA or TMA injected into the joints of horses with experimentally induced cartilaginous lesions followed by exercise on a treadmill did not cause any exacerbation of cartilage damage beyond that observed in control animals.[112,113] Therefore, it appears that worsening of cartilaginous damage in horses undergoing strenuous exercise may not be as much of a concern as has been reported previously. This is particularly true when using lower doses of corticosteroids, particularly TMA and BMA.

Corticosteroids can lead to steroid arthropathy by delaying fracture healing and reducing synovial inflammation and associated pain, which enables the horse to continue strenuous exercise, thereby exacerbating the degenerative joint disease.[91] Steroid arthropathy is characterized by an accelerated rate of joint damage, radiographic evidence of severe degenerative joint disease, joint enlargement owing to capsular distension and osteophytic new bone growth, decreased range of motion and crepitation. This condition usually occurs following intra-articular injection of corticosteroids into joints with pre-existing cartilage damage or those not rested appropriately after injection. Recommended doses of corticosteroids injected into a normal joint may not lead to corticosteroid-induced arthropathy, even with strenuous exercise. However, injured joints should be allowed to rest following corticosteroid injection in order to allow the hyaluronic acid content to return to normal levels. Despite the fact that hyaluronic acid content increases with prolonged corticosteroid use, the catabolic effect on cartilage matrix increases the vulnerability of cartilage to traumatic injury. Corticosteroids administered at higher doses or at more frequent intervals than recommended can lead or contribute to steroid arthropathy.

Table 23.2 Corticosteroid suspensions for intra-articular use in horses

Corticosteroid suspension	Trade name	Concentration (mg/mL)	Dose (mg)	Potency relative to hydrocortisone	Relative duration of action
Betamethasone	Celestone soluspan	6*	3–18	30	Medium–Long
Flumethasone	Flucort	0.5	1.25–2.5	120	Short–Medium
Isoflupredone 'acetate'	Predef 2X	2	5–20	50	Short–Medium
Methylprednisolone 'acetate'	Depo-Medrol	40	40–120	5	Long
Triamcinolone 'acetonide'	Vetalog	6	6–18	5	Medium

* Each mL contains 3 mg betamethasone acetate and 3 mg betamethasone sodium phosphate.

Modified from Caron JP. Principles of treatment of joint disease. In: Auer DE, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia, PA: Saunders; 1999: 678–696.

Injection of some corticosteroids can lead to a non-septic inflammatory response ('steroid flare') characterized by heat, swelling and pain.[91] This inflammatory response can begin as early as a few hours following injection and may last from a few hours up to several days. The reaction is believed to be in response to the microcrystalline suspension of the corticosteroid ester, and occurs in approximately 2% of injected joints.[91]

Septic arthritis can occur subsequent to any intra-articular injection secondary to inadvertent contamination of the joint during arthrocentesis.[91] Because corticosteroids suppress the local immune response in the joint following intra-articular injection, the environment is conducive for infection to develop.

Inadvertent deposition of long-acting corticosteroids in periarticular soft tissues can cause idiopathic metaplastic bone formation.[91] This condition does not occur with short-acting steroids, which suggests a reaction to the vehicle in the long-acting formulations. The ossification may take several months to develop and mechanical interference can occur if the lesions become sufficiently large.

Systemic effects of intra-articularly administered corticosteroids

Once intra-articularly administered corticosteroids are absorbed from the synovial cavity they undergo hepatic biotransformation and renal excretion.[88] Corticosteroids administered intra-articularly are absorbed and can have systemic effects, which has been shown by suppression of the endogenous cortisone levels.[89] Serum concentrations of TMA after injection of 6 mg into three joints of horses peaked 4 hours post injection and became undetectable by 48 hours post injection.[115] Only extremely small concentrations of isoflupredone became measurable in serum 24 hours post injection of 4 mg despite concentrations of both drugs remaining detectable in the synovial fluid of treated joints for up to 10 days after injection.[94] Neither drug was detected in the synovial fluid of the contralateral joint despite detectable quantities in serum. Concentrations of the parent drug or metabolites of both MPA and isoflupredone were detected in urine for 24 and 72 hours, respectively. The study demonstrates the rapid elimination of these two corticosteroid preparations from the synovial fluid and serum of horses.

Sodium hyaluronate

Mechanism of action

Hyaluronate (HA) is endogenously synthesized by synoviocytes and chondrocytes. The viscoelasticity of the synovial fluid and the boundary lubrication function of the synovial membrane are directly proportional to the concentration and polymerization of the hyaluronate synthesized and present within the joint.[116–119] HA incorporated into the extracellular matrix of articular cartilage forms the nucleus for proteoglycan aggregates within the equine joint.[120] Exogenous hyaluronate is thought to supplement the actions of depleted or depolymerized endogenous hyaluronate and modulate the increased synthesis of endogenous hyaluronate.[121–130] The half-life of intra-articular HA injected into the normal equine joint is estimated to be 96 hours.[131] The half-life of intra-articular HA injected into the arthritic joints of sheep decreased from 20.8 hours to 11.5 hours.[132] The short half-life suggests that a majority of the exogenous hyaluronate is rapidly cleared from the joint and that a portion remains within the joint associated with the synovial tissues, influencing the metabolic activity of these cells.[131–133]

The anti-inflammatory effects of exogenous hyaluronate have been demonstrated in numerous in vitro studies. These effects include inhibition of macrophage and granulocyte chemotaxis, inhibition of lymphocyte migration, and reduction of granulocyte and macrophage phagocytosis.[132,134–142] HA is thought to interact with the CD44 cell receptor of neutrophils in inhibiting neutrophil-mediated degradation and PGE_2 production; this interaction is concentration and molecular weight dependent.[143] HA has an indirect effect upon articular cartilage mediated through the HA-binding domain of the proteoglycan molecule at the chondrocyte cell surface.[144] High concentrations of intra-articular HA bind the domain and suppress IL-1β and TNF-α induced proteoglycan degradation, thus reducing inflammation and inhibiting cartilage degeneration and early osteoarthritis.[145–148] Although HA has been shown to have no effect on the healing of intracartilaginous and osteochondral joint lesions, a study using partially meniscectomized rabbit stifles demonstrated the ability of high molecular weight HA to inhibit cartilage degeneration and early osteoarthritis in the femoral condyle and tibial plateau of the treated joints.[145,149] Despite research results, clinical reports and anecdotal success, the exact mechanisms by which HA exerts its beneficial effect upon diseased joints remain speculative.

Indications for use

The concentration of synovial fluid HA within normal equine joints does not differ significantly from the concentrations measured in joints affected with acute synovitis or acute and chronic arthritis; however, joints affected by septic arthritis or with radiographic evidence of osteoarthritis had significantly lower concentrations than normal controls.[150,151] The use of HA for the treatment of joint disease in the horse was first reported in 1970.[128] Since that time, clinical reports have supported the use of HA for the treatment of equine joint disease. However, a majority of the evaluations are subjective, the criteria for successful treatment are absent, the duration of post-treatment observation is highly variable and the specific diagnosis for the condition being treated is lacking.[122,124,126,130,131,136,137,152–155] A recent more objective report, utilizing a bilateral osteochondral fracture model created with an arthrotomy, concluded that intra-articular HA had a protective effect on the articular cartilage and resulted in reduced lameness. However, both treated and non-treated limbs returned to preoperative weight-bearing

values.[129,153] In a double-blind study using intra-articular hylan, an HA derivative, gait analysis found no beneficial effect in the treatment of acute amphotericin-induced synovitis.[154]

The most recent investigation evaluated the effect of intravenous HA on carpal joints in exercising horses after arthroscopic surgery and osteochondral fragmentation. The investigators concluded that intravenous HA appears to alleviate signs of lameness by interacting with synoviocytes, and by decreasing the production and release of inflammatory mediators. Treated horses had lower lameness scores, significantly better synovial membrane histologic scores and significantly lower concentrations of total protein and PGE_2 within the synovial fluid when compared to placebo-treated horses. No significant effects were noted for glycosaminoglycan content, synthetic rate or morphologic score in articular cartilage or other synovial fluid measurements.[155]

Hyaluronic acid has been shown to improve tendon healing with naturally occurring tendinitis and was proposed to have prevented scar formation along the damaged tendon tissue.[156] In an experimental study of collagenase-induced tendinitis, peritendinous injections of HA improved tendon healing in areas not associated with a tendon sheath.[157] Intrathecal injections of HA improved tendon healing as measured by ultrasound, increased the HA content of tendon sheath synovial fluid and reduced the number of adhesions formed between the tendon and sheath. Histologically, the HA reduced inflammatory cell infiltrate, improved tendon structure and minimized intratendinous hemorrhage.[158] Another study of collagenase-induced tendinitis examined the effect of subcutaneous peritendinous HA upon lameness, ultrasonographic healing, biochemical indices, biomechanical strength and inflammation.[159] The study did not reveal significant benefits of HA treatment outside the synovial sheath on tendon repair in collagenase-induced tendinitis.[159]

Effective dose

Early in vitro work demonstrated that HA at a molecular weight greater than 5×10^2 kDa stimulated the synthesis of HA in a concentration-dependent manner, and that hyaluronate preparations with a molecular weight below 5×10^2 kDa had little or no effect except at high concentrations when HA synthesis was depressed.[160] Therefore in vitro, the effect of molecular weight has been clearly demonstrated, but the correlation between molecular weight and clinical effect remains less clearly defined. A comparative study, utilizing five sodium hyaluronate products for the treatment of traumatic arthritis, found that horses treated with HA of a molecular weight greater than 2×10^3 kDa were sound significantly longer than those treated with HA with a molecular weight less than 2×10^3 kDa.[161] A study utilizing 77 trotters with moderate to severe joint injuries investigated the comparative effect of HA, polysulfated glycosaminoglycan and a placebo in a double-blind, randomized design. No difference was detected between treatment groups with regard to prevalence or cumulative incidence of soundness; however, the treatment groups did have reduced lameness scores and significantly better results than the placebo.[162] To add to the controversy, another blinded study looked at the clinical effect of HA in the treatment of 69 Thoroughbreds with carpitis and found no therapeutic response or clinically significant difference between HA with molecular weights of 0.13×10^3 kDa and 2.88×10^3 kDa.[163] The molecular weight and manufacturers' dosage recommendations for the currently available HA formulations are given in Tables 23.3 and 23.4, respectively.

The HA formulations currently available for intravenous injection are Legend® (Bayer) in the United States and Hyonate® (Bayer) elsewhere. The manufacturer recommends that Legend® 40 mg sodium hyaluronate (4 mL) be administered i.v. once weekly for a total of three treatments.

Drug interactions

Hyaluronate is frequently combined with corticosteroids for intra-articular treatment of degenerative joint disease in horses. Retrospective studies have shown that intra-articular administration of corticosteroids may suppress effective microbial killing, reducing the immune status within the joints of horses and increasing the potential for low numbers of bacteria to establish an infection within the injected joint.[164–167] A prospective study, utilizing intra-articular HA in carpal joints inoculated with *Staphylococcus aureus*, showed no difference in the development of sepsis between HA-injected joints and controls.[168] Therefore, the potential for septic arthritis and the incidence of 'synovial flare' may be increased for combination drug therapy utilizing corticosteroids.[169]

Toxicity

No contraindications to HA use are noted on the label and acute toxicological studies performed in horses demonstrate no evidence for systemic toxicity secondary to acute and chronic overdose.[170] Intra-articular and intravenous HA at one, three and five times the recommended dose were admin-

Table 23.3 The average molecular weight of currently available sodium hyaluronate formulations for intra-articular use

Trade name	Manufacturer	Average molecular weight in daltons (Da)
Hyalovet	Fort Dodge	$4.0–7.0 \times 10^5$
Hyvisc	Boehringer Ingelheim	2.1×10^6
Synacid	Shering-Plough	$0.15–0.20 \times 10^6$
Hylartin V	Pharmacia & Upjohn	3.5×10^6
HY-50	Bexco Pharma	Not available
Equron	Solvay Animal Health	$1.5–2.0 \times 10^6$
Equiflex	Chesapeake Biological	1×10^6
Legend	Bayer Corporation	3×10^5

Table 23.4 Manufacturers' recommendations for intra-articular use of sodium hyaluronate in horses

Trade name	Concentration	Packaging	Recommended dose
Hyalovet	10 mg/mL	2 mL syringe	20 mg hyaluronate sodium (2 mL) should be administered aseptically in small or medium-sized joints not more than twice weekly for a period not to exceed 4 weeks.
Hyvisc	10 mg/mL	2 mL syringe	22 mg hyaluronate sodium (2 mL) should be administered aseptically in small and medium-sized joints and a double dose or 44 mg hyaluronate sodium (4 mL) once weekly for a total of three treatments.
Synacid	10 mg/mL	5 mL vial	50 mg of hyaluronate sodium (5 mL) should be given intra-articularly in carpal and fetlock joints. Synacid should be injected under strict aseptic conditions and effusion should be removed prior to injection.
Hylartin V	10 mg/mL	2 mL syringe	20 mg sodium hyaluronate (2 mL) should be administered aseptically in small and medium-sized joints and a double dose or 40 mg hyaluronate sodium (4 mL) once weekly for a total of three treatments.
HY-50	17 mg/mL	3 mL syringe	Not available.
Equron	5 mg/mL	2 mL syringe	The dose of Equron in small and medium-sized joints (fetlock, carpal) is 2 mL (10 mg) administered intra-articularly. In larger joints (hock), the dose is 4 mL (20 mg). Depending on the clinical response and medical judgment of the veterinarian, the treatment may be repeated weekly for a total of four treatments. Strict aseptic measures should be taken to prepare the site for injection and during the intra-articular administration of Equron. Care should be used while injecting to avoid scratching the cartilage surfaces. Such trauma can result in diffuse, transient swelling lasting 24–48 hours, but will have no detrimental effect on the ultimate clinical response. For best results, the horse should be given 2 days of stall rest before gradually resuming normal physical activity.
Equiflex	5 mg/mL	5 mL vial	Not available.
Legend	10 mg/mL	2 mL vial	20 mg sodium hyaluronate (2 mL) should be administered aseptically in small and medium-sized joints once weekly for a total of three treatments.

Note: Sterile preparation of the injection site accompanied by the use of a single-dose preparation with the addition of a water-soluble antibiotic is standard practice.

istered at weekly intervals for a total of 9 weeks. Clinical, hematologic and clinical chemistry parameters remained unchanged. Transient slight to mild postinjection swelling of the joint capsule occurred in horses treated with HA, as well as with the saline control. Neither gross nor histological lesions were noted in either the soft tissues or the articular cartilage of the treated and control joints.[170] The safety of using HA in breeding animals has not been established and manufacturers caution against its use in these animals.[171]

Polysulfated glycosaminoglycans

Mechanism of action

Polysulfated glycosaminoglycans (PSGAGs) are highly sulfated polysaccharides derived from the extract of bovine lung and trachea. The principal glycosaminoglycan present in PSGAGs is chondroitin sulfate. PSGAGs are known to inhibit many of the enzymes associated with osteoarthritis and connective tissue degradation. In vitro studies have shown that PSGAGs are capable of inhibiting lysosomal elastase, cathepsins G and B, lysosomal hydrolases, keratin sulfate glycoanhydrolase, serine proteases, neutral metalloproteinase (e.g., proteoglycanase, stromelysin, gelatinase and collagenase), β-glucuronidase, α-glucosidase, β-N-acetylglucosaminidase and hyaluronidase.[132,172–175] In addition, PSGAGs have been reported to inhibit prostaglandin E synthesis, influx of leukocytes into inflammatory sites and the production of superoxide radicals and interleukin-1 and to have a dose-related effect on fibroblast and tenocyte metabolism resulting in increased production of collagen, non-collagen proteins and sulfated glycosaminoglycans.[132,176]

PSGAG has been shown to have a greater affinity for proteoglycans and non-collagenous proteins than for collagen.[173] Fibronectin, which is increased in osteoarthritic cartilage, forms complexes with collagen, which are then stabilized by PSGAG.[173] PSGAGs exert their chondroprotective effect by reducing proteoglycan breakdown, stimulating HA synthesis and enhancing the production of glycosaminoglycan, proteoglycan (glucosamine) and colla-

gen (proline).[176–179] In vitro studies on equine cartilage indicate that PSGAG increases collagen and glycosaminoglycan synthesis, and inhibits glycosaminoglycan and collagen degeneration in normal and osteoarthritic articular cartilage explants and cell cultures.[180] However, in vitro work using smaller PSGAG dosages found a dose-dependent inhibition of proteoglycan synthesis, minimal effect on proteoglycan degradation, no effect on proteoglycan monomer size and no change in monomer aggregation.[181,182] Thus the exact mechanism by which PSGAG exerts its effect remains unclear.

Indications for use

PSGAG is believed to have chondroprotective properties, which make its use preferable when cartilage damage is present in addition to acute synovitis. PSGAGs have been classified as disease-modifying osteoarthritis drugs in that therapy is meant to prevent, retard or reverse the morphologic cartilaginous lesions associated with osteoarthritis.[183]

In vivo work utilizing chemically and physically induced models of intercarpal joint osteoarthritis of horses demonstrated less articular fibrillation and erosion, less chondrocyte death, markedly improved safarin-O staining, but no change in the partial- or full-thickness articular cartilage lesions.[184,185] Investigators concluded, first, that intra-articular PSGAG (250 mg every 7 days for five treatments) could markedly decrease the development of osteoarthritis, but was of no benefit in healing cartilage lesions present at the time of initial therapy, and second, that intramuscular PSGAG (500 mg every 4 days for seven treatments) had an insignificant effect upon physical cartilage defects and only a limited effect upon chemically induced osteoarthritis as evidenced by a slight degree of improvement in safarin-O staining.[184,185] Another study investigated the effect of PSGAG, with or without exercise, on the repair of articular cartilage defects and on the development of osteoarthritis in the carpi of ponies. Investigators concluded that PSGAG was effective in ameliorating clinical, radiographic and scintigraphic signs associated with joint disease, but that repair tissue was more fibrous in the PSGAG-treated joints and the synovium of the PSGAG-exercised joints had a greater degree of cellular infiltration.[186,187]

Negative charges conferred by sulfate groups cause PSGAG to bind to connective tissues.[172,173,175] In rabbits, radioactively labeled PSGAG is distributed to knee joint articular cartilage, patellar cartilage, meniscus and intervertebral disk tissue following intramuscular administration.[172–175] The widespread distribution of PSGAG to connective tissue has proven useful in the treatment of tendinitis. In rabbits with collagenase-induced tendinitis, treatment with PSGAG resulted in diminished loss of tendon mechanical properties, an increased number of large-diameter collagen fibrils, improved organization of repair tissue at the cellular level and suppression of inflammation.[188] In horses with collagenase-induced tendinitis, those treated with PSGAG had earlier sonographic development of echogenic patterns, a more rapid decrease in core defect size and less severe lameness, compared with a control group of untreated horses.[189]

Effective dose

The PSGAGs are most commonly administered by the intramuscular route. Previous work investigating the distribution of radiolabeled PSGAG after intramuscular administration found PSGAG concentrations within the synovial fluid and joint tissues of the carpus consistent with other non-equine studies. No significant difference was found between carpi containing osteochondral fragments and the control joints, suggesting that distribution is not influenced by inflammatory changes. Investigators concluded that intramuscular therapy (500 mg every 4 days) was effective in maintaining anti-inflammatory levels in the joints.[172] Another study, using intramuscular radiolabeled PSGAG in rabbits, demonstrated PSGAG within the superficial digital flexor tendon at concentrations shown to inhibit inflammatory mediators in vitro.[190] Investigators used the label dose for the horse, and concluded that PSGAG may be useful in the treatment of acute tendinitis.[190]

The PSGAG formulations currently available for intra-articular and intramuscular use are Adequan I.A.® (Luitpold) and Adequan I.M.® (Luitpold), respectively. Manufacturers recommend that Adequan I.A.® (250 mg, 1 mL) be injected aseptically into the affected joint once a week for 5 weeks and that Adequan I.M.® (500 mg, 5 mL) be injected aseptically into the muscles of the neck every 4 days for 28 days or seven treatments. The initial treatment with Adequan I.M.® at manufacturer's recommended dose and frequency is often followed with one intramuscular dose every 30 days while the horse is in training. Sterile preparation of the injection site accompanied by the use of a single-dose preparation with the addition of 125 mg of amikacin sulfate (Amiglyde-V®, Fort Dodge) is standard practice for intra-articular administration of Adequan I.A.®.[191]

Drug interaction

PSGAG is frequently combined with corticosteroids for intra-articular treatment of degenerative joint disease in horses. Retrospective studies have shown that intra-articular administration of corticosteroids may suppress effective microbial killing, reducing the immune status within the joints of horses and increasing the potential for low numbers of bacteria to establish an infection within the injected joint.[164–167] A prospective study, utilizing intra-articular PSGAG in carpal joints inoculated with *Staphylococcus aureus*, demonstrated significant increase in the potential for sepsis between PSGAG-injected joints and controls.[168] Previous in vitro work has shown PSGAG-mediated inhibition of the equine complement activity. Inhibition of the complement cascade within the joint may increase the potential for subinfective doses of bacteria to colonize the synovium, resulting in sepsis.[192] Therefore, the potential for septic arthritis and the incidence of 'synovial flare' may be increased with the use of

intra-articular PSGAG alone or in combination with corticosteroids.[193]

There is some concern regarding the potential anticoagulant effect of PSGAG. PSGAG is classified as a heparin analog and has been known to cause local hematomas and heparin-associated thrombocytopenia in humans.[194] Although it has been suggested that PSGAG not be used in conjunction with other NSAIDs or other anticoagulants, there have been no reports of hemarthrosis, thrombocytopenia or coagulopathies in horses despite its widespread use both alone and in combination with NSAID administration.[195]

Toxicity

Toxicology studies were conducted in horses: doses as high as 1250 mg were administered intracarpally to six horses once a week for 18 weeks. This dosage is five times the recommended dosage and 3.6 times the recommended therapeutic regimen. Clinical observations revealed mild, self-limiting swelling and soreness at the injection site in 1.8% of the horses. Dose-related increases in partial thromboplastin time, creatinine and glucose were noted. Toxicological doses as high as 2500 mg were administered intramuscularly to six horses twice a week for 12 weeks. This dosage is five times the recommended dosage and three times the recommended therapeutic regimen. None of the animals in this study showed any adverse effect on clinical, hematologic or clinical chemistry parameters.[193] Studies have not been performed to establish reproductive safety in horses and manufacturers caution against its use in breeding animals.

Chondroitin sulfate

Mechanism of action

Chondroitin sulfate (CS) is the predominant glycosaminoglycan found in adult articular cartilage. CS is similar to polysulfated glycosaminoglycan (PSGAG) in that both contain repeating chains of galactosamine and glucuronic acid disaccharide units, but CS contains only one sulfate group per disaccharide unit compared with the three or four sulfate groups per disaccharide unit for PSGAG.[196] The presence of sulfate groups is critical to the pharmacology and pharmacokinetic activity of both PSGAG and CS.[196] Chondroitin sulfate has been classified as a slow-acting, disease-modifying agent (SADMA) and as a slow-acting drug in osteoarthritis (SADOA).[197–199] It has been shown to inhibit degradative enzymes such as leukocyte elastase and N-acetylglycosaminidase in vitro. However, it must be noted that these inhibitory activities refer to intact polymeric CS molecules and the efficacy of unsulfated monomeric forms and other degradation products is unknown and untested.[200,201]

Chondroitin sulfate marketed for use as a dietary supplement in horses is usually in combination with glucosamine with or without added vitamins and minerals. The bioavailability of oral CS remains speculative and scientific literature provides conflicting results. Absorption of radiolabeled CS has been reported for man, dogs and rats; however, less than 15% of the molecules were absorbed as high molecular weight fractions. Investigators concluded that a majority of the CS was absorbed only after degradation to smaller molecular weight products and the loss of the sulfate group.[202–205] The absence of absorption of oral CS has been reported for several studies in humans and rabbits in which a dimethylene blue assay was unable to detect the presence of smaller sulfated glycosaminoglycan molecules.[205,206]

Large intestinal bacteria utilize CS directly as an energy source while bacterial sulfatases remove the active sulfate groups from the disaccharide units, thus allowing radio-active inorganic sulfate to be present in the body after oral administration of $^{35}SO_4$-labeled CS.[207] This has led some researchers to conclude that CS is not absorbed following oral administration, but rather a low molecular weight desulfated degradation product of the disaccharide polymer is absorbed instead. However, absorption of CS and dermatan sulfate from the gastrointestinal tract has been reported in humans. Treated patients had reduced N-acetylglycosaminidase and granulocyte activity, as well as an increase in HA concentrations.[203] Skeptics would conclude that the existence of a polymer chain and the presence of sulfate groups are necessary for the biologic activity of CS; therefore any positive clinical response to oral administration of CS is secondary to the biologic activity of its low molecular weight degradation products or from the activity of other substances present in the supplement, such as glucosamine.[208]

Indications for use

Several studies report positive responses to oral CS therapy for the management of osteoarthritis in the human knee.[209–214] One human study utilizing oral treatment with *Perna canaliculus* extract for a period of 6 months reported that 19 of the 28 rheumatoid and 15 of the 38 osteoarthritis patients felt that they benefited from the oral therapy.[213] Positive results associated with oral CS therapy have been reported for a rabbit model of osteoarthritis, as well as for a chemically induced canine synovitis model. Dogs with chemically induced synovitis pretreated with CS combined with glucosamine had reduced soft tissue and bone-phase scintigraphic activity as well as reduced lameness scores. However, treatment after the induction of synovitis (without pretreatment) showed no beneficial effects.[215]

Effective dose

A plethora of choices exists regarding oral supplement for the treatment and prevention of joint disease in the horse. Each brand contains varying concentrations of CS with or without glucosamine as key ingredients. These ingredients are then combined with a variety of vitamins, minerals and frequently a 'secret' compound. The supplements are usually recommended as daily top dressing for feed and manufacturers provide a measuring device specific to their product. Because

these products are classified as dietary supplements and neutraceuticals, the efficacy, safety and quality assurance programs put forth by the United States Food and Drug Administration do not apply.

Recommendations regarding effective dose, long-term toxicity, drug interaction and teratogenicity are anecdotal or based on manufacturers' claims.[200,203,205,216–218] One product, Cosequin®, has been clinically and scientifically evaluated. One trial consisted of 25 clinical cases of horses with joint pain treated with oral Cosequin® for a period of 6 weeks.[219] In this study, lameness, response to flexion and stride length improved with Cosequin therapy but there were no controls. In another study utilizing the Freund's complete adjuvant model of inflammatory joint disease, 12 horses were treated with oral Cosequin® for a total of 36 days.[220] Therapy began 10 days prior to induction of arthritis and continued for 26 days afterward. No benefit was observed for lameness, stride length, carpal circumference or response to carpal flexion and synovial fluid protein concentration did not improve.[220] Due to the widespread use and popularity of these products, controlled studies and scientific validation are needed to address the controversy regarding enteral absorption, pharmacokinetics, toxicity, drug interaction and clinical efficacy.

Glucosamine

Mechanism of action

Chondrocytes manufacture glucosamine from glucose as a precursor for the glycosaminoglycan units found within articular cartilage.[221,222] Glucosamine has been classified as a slow-acting, disease-modifying agent, a slow-acting drug in osteoarthritis and as a chondroprotective. When available, glucosamine becomes the preferred substrate over glucose for chondrocyte synthesis of glycosaminoglycans.

Glucosamine is a small, water-soluble molecule that is absorbed from the small intestine and across biological barriers in the body.[223,224] It undergoes gastric dissociation to yield non-ionized glucosamine.[223,224] Glucosamine hydrochloride yields greater quantities of the active non-ionized form of glucosamine than glucosamine sulfate. It is the non-ionized form of glucosamine that directly determines the bioavailability of the glucosamine compounds.[223,224] Labeling with [^{14}C] in rats and the use of specific ion exchange chromatography in dogs and humans have demonstrated almost complete bio-availability with only 5% fecal loss.[223]

In vitro work has shown a dose-dependent increase in the synthesis of hyaluronic acid, glycosaminoglycan and proteoglycan in response to exogenous glucosamine.[222,224] Exogenous glucosamine inhibits superoxide radical generation, lysosomal enzyme production, nitric oxide production, proteoglycan loss, gelatinase activity and collagenase activity in equine cartilage explants exposed to lipopolysaccharide and recombinant interleukin-1β.[225,226] The anti-inflammatory activity of glucosamine is achieved through a prostaglandin-independent mechanism, which is thought to contribute to cartilage preservation as well as provide protection against metabolic impairment induced by NSAIDs.[223,227,228]

In vivo studies have demonstrated uniform incorporation of [^{14}C]-labeled glucosamine into newly synthesized proteoglycans located within articular cartilage.[229,230] The anti-inflammatory effect of glucosamine does not influence or interfere with PG synthesis in rat and dog models and has been shown to improve experimentally induced morphological damage to articular cartilage.[229–231] In rats, glucosamine counteracts metabolic and morphologic chondrocyte damage produced by intra-articular dexamethasone.[232] A study using human subjects affected with osteoarthritis looked at cartilage biopsies taken before and after 4 weeks of treatment with either oral glucosamine sulfate or placebo. Glucosamine therapy correlated with reduced use of joint pain analgesics and improved joint function. Electron microscopy performed on biopsy samples taken before treatment confirmed the presence of chronic osteoarthritis. Electron microscopy performed on biopsy samples taken after 4 weeks of treatment demonstrated evidence for an increase in cartilage matrix production and a mild decrease in inflammatory activity, giving the affected cartilage an appearance more similar to healthy cartilage.[218,232]

Indications for use

Oral supplements, such as glucosamine, were initially developed as an alternative to the practical and financial limitations associated with intra-articular and intramuscular HA and PSGAG. Oral glucosamine administration has been associated with decreased pain and an increased range of motion when compared with placebo in a well-controlled clinical trial in people with osteoarthritis of the knee.[218] Oral glucosamine has been shown to alleviate the symptoms of chronic arthritis with daily dosing over a 6–8-week period.[233] The first of two double-blind studies comparing ibuprofen to oral glucosamine in humans with unilateral osteoarthritis of the knee showed a faster reduction in pain and swelling for ibuprofen during the first 2 weeks, but the difference was found to favor glucosamine at week 8 of therapy.[234] The second study reported a similar difference in response at 2 weeks, but from 3 weeks onwards there was no significant difference in response between ibuprofen and glucosamine, with the exception of a significantly lower incidence of adverse side effects for glucosamine than ibuprofen.[217] Glucosamine proved superior to PBZ in the management of back pain and to a placebo in the treatment of spinal osteoarthritis.[235,236] Researchers investigating combination therapy in humans concluded that the use of oral glucosamine significantly decreased the effective dose of NSAIDs needed to control chronic pain.[237]

Effective dose

Two forms of glucosamine are available for oral administration: glucosamine hydrochloride and glucosamine sulfate. Both disassociate within the stomach, but the hydrochloride

salt yields a greater amount of the active, non-ionized glucosamine, which has direct bio-availability. The oral products currently available for horses are numerous and seem to be increasing on a monthly basis. Unfortunately, there is a dearth of clinical and scientific studies in horses. Information regarding efficacy and dosage for oral glucosamine is anecdotal or based on manufacturers' claims. Given the consistency demonstrated for absorption, distribution and elimination studies in humans, rats and dogs, the assumption is that a similar effective dose rate of at least 10 g per day is necessary to treat a 500 kg horse.[208]

Toxicity

Oral glucosamine is a neutraceutical and as such is not regulated by the United States Food and Drug Administration for purity, efficacy or safety. As a result, safety trials have not been performed prior to these products being released onto the market. To date, investigations into long-term use, placebo controlled, and retrospective evaluation of combination therapy with other medicaments have failed to demonstrate toxicity or adverse effects different from placebo controls associated with the use of oral glucosamine in man.[223,224,236,238,239]

Dimethyl sulfoxide

Mechanism of action

Dimethyl sulfoxide (DMSO), a byproduct of the lumber industry, was originally used as an industrial solvent. DMSO was first employed as a therapeutic agent in the treatment of interstitial cystitis and arthritis during the early 1960s.[240] Since that time, it has been widely used within the equine industry either alone or mixed with corticosteroids to reduce soft tissue swelling, inflammation and edema secondary to acute trauma.[241,242]

The pharmacologic effects of DMSO and its metabolite, dimethyl sulfide, are diverse. DMSO has been shown to possess superoxide dismutase activity. As a result, it can inactivate superoxide radicals, inhibit hydroxyl radical-mediated depolymerization of hyaluronan and suppress PG synthesis by oxygen-derived free radicals.[240,242–245] DMSO is believed to possess analgesic properties secondary to the inhibition of prostaglandins E_2, $F_{2\alpha}$, H_2 and G_2. The analgesic effect of DMSO has been compared to that produced by narcotic analgesics and been found to be efficacious for both acute and chronic musculoskeletal pain.[246]

In addition to its anti-inflammatory effects, DMSO possesses the ability to rapidly and easily penetrate the skin. It serves as a carrier to enhance the penetration of various agents through the skin into underlying synovial, connective and interstitial tissues.[242,246,247] DMSO has been shown to enhance the penetration of percutaneous steroids three-fold and the ability of cortisone to locally stabilize lysosomes 100-fold.[242] In addition, DMSO increases the local antiarthritic effect of hydrocortisone 10-fold when used as a carrier.[248]

DMSO has an antiarthritic effect independent of its ability to promote corticosteroid absorption.[249] Topical application of the gel formulation of DMSO decreased the mean synovial white blood cell concentrations in an equine synovitis model.[250] DMSO has been shown to help resolve tissue inflammation through increased blood flow and promotion of vascular dilation.[242] It causes collagen dissolution, which may help to restore pliability to fibrosed tissues.[242] Topical application of DMSO solution, in rabbits, reduced ankle stiffness in a fracture model of arthritis.[251] Both the anti-inflammatory and antiarthritic effects of DMSO appear to be more effective when used to treat acute versus chronic inflammatory conditions.[246]

Both DMSO and dimethyl sulfide are extensively and rapidly distributed to all areas of the body after oral, intravenous and topical administration.[246] The half-life of the parent compound and its metabolite is 9 hours.[246] DMSO is primary excreted through the kidney, but secondary elimination through the respiratory tract and bile does occur.[246]

Indications for use

DMSO has been used intra-articularly for its anti-inflammatory and free radical scavenging properties in the management of equine inflammatory joint disease.[245,247,252–254] Several equine studies reporting the use of DMSO in intra-articular lavage solutions have shown a decrease in total synovial leukocyte counts and a decrease in synovial inflammatory response in DMSO-treated joints without evidence of gross, histological or histochemical cartilage degradation.[255–257] Juvenile bovine articular cartilage explants repeatedly exposed to a 10% DMSO solution showed a significant time-dependent decrease in the rate of proteoglycan synthesis after 3 or more hours of exposure. Histologically, chondrocyte viability and cartilage matrix water content were decreased.[258] A recent study, evaluating the effect of DMSO on equine articular cartilage metabolism in an explant culture environment, examined proteoglycan synthesis and degradation, lactate metabolism (general indicator of cellular metabolism) and chondrocyte viability after exposure to various concentrations of DMSO for predetermined time intervals.[259] Proteoglycan and lactate metabolism were inhibited in a dose- and time-dependent manner after exposure to DMSO concentrations in excess of 5%. Proteoglycan release and chondrocyte viability were not affected, and the changes in proteoglycan synthesis and lactate metabolism returned to baseline after the exposure period. Investigators concluded that DMSO concentrations in excess of 5% suppress equine articular cartilage matrix metabolism by direct inhibition of chondrocyte metabolism without a decrease in chondrocyte number. Thus DMSO induces a state of metabolic dormancy in the chondrocytes but these effects are reversible and chrondrocyte viability is not affected.[259]

Effective dose

Domoso® (Fort Dodge) is commercially available as a 90% DMSO veterinary gel for topical use. Manufacturer recommendations are for liberal application to skin over affected area 2–3 times per day. The total daily dosage is not to exceed 100 g and the duration of therapy is not to exceed 30 days. Domoso® is also available as a 90% veterinary solution. The recommended dose for the solution is 0.25–1.0 g/kg diluted in saline or 5% dextrose solution at a concentration of not more than 10%. The 10% solution is to be given at a slow rate once daily for 3 days. The solution can be administered orally through a nasogastric tube at a dose of 1.0 g/kg diluted in 1 liter of water.

Current treatment protocol for equine septic arthritis includes joint lavage with lactated Ringer's solution containing 5% to 40% DMSO. Lavage solutions containing DMSO concentrations in excess of 5% have been shown to have detrimental effects upon articular cartilage matrix metabolism. Until further investigation and pharmacokinetic studies can be performed, the concentration of DMSO contained within intra-articular lavage solutions should not exceed 5%.[259]

The manufacturer cautions against the use of non-medical grade DMSO products, which may contain harmful impurities secondary to the distillation process.[246] Washing of the hands and wearing protective rubber gloves before handling DMSO is strongly recommended in order to avoid transcutaneous penetration of potentially harmful substances.

Drug interactions

DMSO possesses anticholinesterase activity and therefore should not be combined or used in conjunction with organophosphates or other cholinesterase inhibitors.[170,246] Death secondary to mercury intoxication has been reported when DMSO was mixed with mercury salts (red blister) and applied topically to the legs of a horse.[246] Caution should be exercised when mixing DMSO with any drug due to enhanced percutaneous absorption and the potential for toxicosis. DMSO potentiates effects of heparin, insulin, corticosteroids and atropine both topically and systemically.[170,246]

Toxicity

When used at the label dose, DMSO is safe. Local effects such as dermal irritation, exfoliation, erythema and vesiculation are common even at recommended dosages and are exacerbated by the use of sweat wraps, blistering agents, heavy bandages and occlusive dressings. These effects are transient and resolve when therapy is discontinued. When in contact with room air, DMSO will self-dilute to a concentration of 66–67%, causing an unpleasant garlic smell and taste to which some individuals are highly sensitive.[170,246]

Hemolysis and secondary hemoglobinuria have been reported to occur in horses following rapid intravenous administration of concentrations in excess of 20%. This effect can be prevented by slowing the administration rate and diluting the DMSO with isotonic fluids to a concentration ≤ 10% or by administering the product orally via a nasogastric tube.[246] DMSO is known to be teratogenic and hepatotoxic in laboratory animal species, including rats and rabbits, and has been shown to cause intravascular erythrocyte hemolysis and nephritis.[260] DMSO should therefore be used with caution in pregnant mares and individuals suffering from dehydration and renal or liver disease.[193,246]

Pentosan polysulfate

Mechanism of action

Pentosan polysulfate (PPS) is derived from beechwood hemicellulose and is similar to PSGAG in that it is highly sulfated. PPS does not possess analgesic activity, but rather works through modification and correction of pathological imbalances associated with osteoarthritis to provide symptomatic relief.[261] Tritiated PPS has been shown to preferentially distribute to the urinary tract after i.v. administration, the large intestine, liver and urinary tract after oral administration and to the articular cartilage and meniscal fibrocartilage after intra-articular administration in rats and rabbits.[262–264] Human studies, using intra-articular administration of tritiated PPS, demonstrated the formation of complexes with the protein components of articular cartilage while similar rat studies showed localization to cartilage and binding with synoviocytes.[264,265] A new calcium derivative of pentosan polysulfate (CAPPS) has been developed that is absorbed more effectively after oral administration than the sodium salt of pentosan polysulfate (NAPPS).[266]

Pentosan polysulfate is a potent inhibitor of human granulocyte elastase, testicular and arterial hyaluronidase, lysosomal chondroitin-4-sulfatase, N-acetylglucosaminidase, cathepsin B_1 and cathepain G.[261,264,267–272] PPS was able to stimulate the synthesis of proteoglycans by bovine chondrocytes cultured in the presence and absence of interleukin-1.[273] PPS in a concentration range of 0.1–1.0 μg/mL was able to stimulate the production of HA by cultured synoviocytes obtained from rheumatoid and osteoarthritic joints with maximum stimulation occurring at concentrations of 0.25 μg/ml.[274,275] PPS at concentrations of 0.1–10.0 μg/mL was shown to consistently stimulate proteoglycan synthesis in an in vitro lapine chondrocyte injury model. Synthesis increased to 25% above control level occurred at 1.0 μg/mL after 2–4 days in culture. This concentration is similar to the concentration achieved in articular cartilage after intramuscular injection of the recommended therapeutic dose; therefore, the in vitro effect could be achieved in vivo.[197,275,276]

An experimental model for joint disease in rabbits demonstrated the ability of oral CAPPS to maintain a ratio of aggrecan to dermatan sulfate similar to normal articular

cartilage.[277] A rabbit atrophy model for arthritis showed that PPS given intramuscularly at 10 mg/kg every other day prevented proteoglycan depletion from articular cartilage.[278] An anterior cruciate transection model and a joint atrophy model for canine osteoarthritis demonstrated significant reductions in active stromelysin levels concomitant with increased levels of tissue inhibitor metalloproteinase in the articular cartilage of treated dogs associated with intramuscular PPS given at 2 mg/kg once weekly.[279,280] A sodium iodoacetate-induced model of arthritis reported amelioration of radiographic and histologic indexes of joint degeneration for chickens treated with 1–5 μg of PPS.[261]

Indications for use

Pentosan polysulfate has been found to abrogate the deleterious effects of chronic administration of hydrocortisone when injected simultaneously into the knee joints of rabbits.[281] An owner- and clinician-blinded study of 40 dogs with osteoarthritis found significant improvement in stiffness, mobility and pain on joint manipulation for dogs treated weekly with intramuscular NAPPS at 3 mg/kg for 4 weeks. The overall responses were measured with a validated scoring system and the effects were evident for a period up to 4 weeks after the first treatment. Placebo-treated dogs did not improve and dogs treated with NAPPS doses of 1 mg/kg or 5 mg/kg did not show any significant effect.[281] NAPPS was evaluated in a randomized prospective study to determine its applicability in the treatment of fragmented coronoid process and osteochondritis dessicans of the elbow compared with conventional surgical management of these disorders in dogs. Dogs treated with intramuscular NAPPS at 3 mg/kg had more rapid improvement of limb function relative to surgically treated dogs as determined by force plate analysis. At 9 months, no detectable difference between NAPPS-treated and surgically treated dogs was detected. Investigators concluded that NAPPS injections are a valid alternative to surgery for the management of fragmented coronoid process and osteochondritis dessicans in dogs.[282]

Effective dose

An open clinical trial in human osteoarthritis patients described improved symptoms of pain, increased function and reduction in the consumption of NSAIDs for up to 12 weeks after intramuscular administration of CAPPS at 2 mg/kg.[283] A double-blind placebo-controlled study of humans with hip or knee osteoarthritis reported that NAPPS administered intramuscularly at 3 mg/kg every 7 days for four consecutive treatments was associated with significantly improved measurements for rest pain, walk pain, early morning stiffness and improved lifestyle scores for up to 3 months when compared with placebo-treated patients.[175] Although there are no published equine studies describing the application of PPS for the treatment of joint disease in the horse, the dosage regimen used corresponds to that recommended for the dog and for humans, i.e. 2–3 mg/kg intramuscularly every 7 days for four treatments, repeated every 3 months as required. Note: this product is not available in North America.

Atropine sulfate

There is anecdotal evidence for the use of atropine in synovial structures of the horse. Atropine is believed to decrease synovial secretions and thus alleviate the gross clinical signs of clinical conditions, such as bog spavin and idiopathic tenosynovitis. Intra-articular and intrasynovial use of atropine alone and in combination with steroids or HA has been reported with the atropine dosages ranging from 4 mg to 20 mg. The primary indication is distension of synovial structures refractory to drainage and intra-articular treatment with either HA or steroids. There are no anecdotal accounts regarding the use of atropine in osteoarthritis or septic arthritis and there are no clinical or scientific studies to support the use of atropine in the synovial structures of the horse.

References

1. Lippiello L, Yamamoto K, Robinson D, et al. Involvement of prostaglandin from rheumatoid synovium and inhibition of articular cartilage metabolism. Arthritis Rheum 1978; 21(8):909–917.
2. Tietz CC, Chrisman OD. The effect of salicylate and chloroquine on prostaglandin-induced articular cartilage damage in the rabbit knee. Clin Orthop 1975; 108:264.
3. May SA, Hooke RE, Peremans KY, et al. Prostaglandin E2 in equine joint disease. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 40.
4. Steinberg JJ, Hubbard JR, Sledge CB. Chondrocyte-mediated breakdown of cartilage. J Rheumatol 1987; May 14:55–58.
5. Mehindate K, al-Daccak R, Aoudjit F, et al. Interleukin-4, transforming growth factor beta 1, and dexamethasone inhibit superantigen-induced, prostaglandin E_2-dependent collagenase expression through their action on cyclooxygenase-2 and cytosolic phospholipase A_2. Lab Invest 1996; 75(4):529–538.
6. May SA, Lees P. Nonsteroidal anti-inflammatory drugs. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 223–237.
7. MacAllister CG, Morgan SJ, Borne AT, et al. Comparison of adverse effects of phenylbutazone, flunixin meglumine, and ketoprofen in horses. Am J Vet Res 1993; 202(1):71–77.
8. Lees P, Taylor JBO, Higgins AJ, et al. Phenylbutazone and oxyphenbutazone distribution into tissue fluids in the horse. J Vet Pharmacol Ther 1986; 9:204–212.
9. Kallings P. Nonsteroidal anti-inflammatory drugs. Vet Clin North Am Equine Pract 1993; 9(3):523–541.
10. Lees P, Higgins AJ. Clinical pharmacology and therapeutic uses of non-steroidal anti-inflammatory drugs in the horse. Equine Vet J 1985; 17(2):83–96.
11. Short CR, Buthrie AJ, Swann GE, et al. The effect of ketoprofen on a soft-tissue inflammation model in Thoroughbred horses. In: Lees P, ed. 6th International

Congress of the European Association for Veterinary Pharmacology and Toxicology, Edinburgh, UK. Oxford: Blackwell Science; 1994.
12. Landoni MF, Lees P. Pharmacokinetics and pharmacodynamics of ketoprofen enantiomers in the horse. J Vet Pharmacol Ther 1996; 19:466–474.
13. Brideau C, van Staden C, Chan CC. In vitro effects of cyclooxygenase inhibitors in whole blood of horses, dogs, and cats. Am J Vet Res 2001; 62(11):1755–1760.
14. Blikslager AT. Relative COX-2 selectivity of etodolac in horses. Personal communication, Raleigh, NC; 2002.
15. Morton AJ, Young NB, Campbell NB, et al. Equine lameness: the role of cyclooxygenase-2. Vet Surg 2002; 31:504–505.
16. Lees P, Maitho TE, Taylor JB. Pharmokinetics of phenylbutazone in two age groups of ponies: a preliminary study. Vet Rec 1985; 116:229–232.
17. Snow DH, Baxter P, Whiting B. The pharmacokinetics of meclofenamic acid in the horse. J Vet Pharmacol Ther 1981; 4:147–156.
18. Moss MS, Haywood PE. Persistence of phenylbutazone in horses producing acid urines. Vet Rec 1973; 93:124–125.
19. Maylin GA. Disposition of phenylbutazone in the horse. Am Assoc Equine Pract 1974; 20:243–248.
20. Tobin T. Pharmacology review: the nonsteroidal anti-inflammatory drugs I. Phenylbutazone. J Equine Med Surg 1979; 6:253–258.
21. Jaussaud P, Bellon S, Beese D, et al. Enantioselective pharmacokinetics of ketoprofen in horses. J Vet Pharmacol Ther 1993; 16:373–376.
22. McCormack K, Brune K. Dissociation between antinociceptive and anti-inflammatory effects of the nonsteroidal anti-inflammtory drugs. Drugs 1991; 41(4):533–547.
23. Villanueva M, Heckenberger R, Strobach H, et al. Equipotent inhibition by R(–), S(+) and racemic ibuprofen of human polymorphonuclear cell function in vitro. Br J Clin Pharmacol 1993; 35:235–242.
24. Lees P, McKellar Q, May SA, et al. Pharmacodynamics and pharmacokinetics of carprofen in the horse. Equine Vet J 1994; 26(3):203–208.
25. Crisman MV, Wilcke JR, Sams RA. Pharmacokinetics of flunixin meglumine in healthy foals less than twenty-four hours old. Am J Vet Res 1996; 57(12):1759–1761.
26. Semrad SD, Sams RA, Ashcraft SM. Pharmacokinetics of and serum thromboxane suppression by flunixin meglumine in healthy foals during the first month of life. Am J Vet Res 1993; 54(12):2083–2087.
27. Wilcke JR, Crisman MV, Sams RA, et al. Pharmacokinetics of phenylbutazone in neonatal foals. Am J Vet Res 1993; 54(12):2064–2067.
28. Lehmann VW, Wintzer HJ, Frey HH. Kinetik einiger analgetisch-anti-inflammatorischer in serum and synovia beim Pferd. Dtsch Tierarztl Wochenschr 1981; 88:218–220.
29. Higgins AJ, Lees P, Taylor JBO, et al. Flunixin meglumine: quantitative determination in and effects on composition of equine inflammatory exudate. Br Vet J 1986; 142:163–169.
30. Burrows GE, MacAllister CG, Tripp P, et al. Interactions between chloramphenicol, acepromazine, phenylbutazone, rifampin and thiamylal in the horse. Equine Vet J 1989; 21(1):34–38.
31. McGrath CJ. Drug interactions. In: Short CE, ed. Principles and practice of veterinary anesthesia. Baltimore, MD: Williams and Wilkins; 1987; 154–157.
32. Short CE. Principles and practice of veterinary anesthesia. Baltimore, MD: Williams and Wilkins; 1987.
33. Young DR, Ewing PJ, Burrows GE, et al. Effects of phenylbutazone on thiamylal disposition and anesthesia in ponies. J Vet Pharmacol Ther 1994; 17:389–393.
34. Whittem T, Firth EC, Hodge H, et al. Pharmacokinetic interactions between repeated dose phenylbutazone and gentamicin in the horse. J Vet Pharmacol Ther 1996; 19:454–459.
35. May SA. Anti-inflammatory agents: nonsteroidal anti-inflammatory drugs. In: Robinson NE, ed. Current therapy in equine medicine 3. Philadelphia, PA: Saunders; 1992; 16–17.
36. Rose RJ, Wright JD. Principles of therapy: anti-inflammatory and antipyretic therapy: nonsteroidal anti-inflammatory drugs. In: Colahan PT, Mayhew IG, Merrit AM, et al, eds. Equine medicine and surgery, 4th edn. Goleta, CA: American Veterinary Publications; 1991; 145–152.
37. Snow D. Non-steroidal anti-inflammatory agents in the horse. Vet Rec 1981; 3(suppl):24–31.
38. McKellar QA, Bogan JA, Fellenberg RL, et al. Pharmacokinetic, biochemical and tolerance studies on carprofen in the horse. Equine Vet J 1991; 23:280–284.
39. Hamm D, Turchi P, Johnson JC, et al. Determination of an effective dose of eltenac and its comparison with that of flunixin meglumine in horses after experimentaly induced carpitis. Am J Vet Res 1997; 58(3):298–302.
40. Moore RM. Nonsteroidal anti-inflammatory drugs. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia, PA: Saunders; 1998; 25–30.
41. Owens JG, Kamerling SG, Stanton SR, et al. Effects of ketoprofen and phenylbutazone on chronic hoof pain and lameness in horses. Equine Vet J 1995; 27(4):296–300.
42. Betley M, Sutherland SF, Gregoricka MJ, et al. The analgesic effect of ketoprofen for use in treating equine colic as compared to flunixin meglumine. Equine Pract 1991; 13(6): 11–16.
43. Longo F, Autefage A, Bayle R, et al. Efficacy of a non-steroidal anti-inflammatory, Ketofen 10%® (Ketoprofen) in the treatment of colic in horses. Equine Vet Sci 1992; 12(5): 311–315.
44. Lees P, Ewins CP, Taylor JBO, et al. Serum thromboxane in the horse and its inhibition by aspirin, phenylbutazone and flunixin. Br Vet J 1987; 143:462–476.
45. Campbell NB, Blikslager AT. The role of cyclooxygenase inhibitors in repair of ischemic-injured jejunal mucosa in the horse. Equine Vet J 2000; 32(suppl):59–64.
46. Campbell NB, Jones SL, Blikslager AT. The effects of cyclooxygenase inhibitors on bile-injured and normal equine colon. Equine Vet J 2002; 34(suppl):493–498.
47. Johnson CB, Taylor PM, Young SS, et al. Postoperative analgesia using phenylbutazone, flunixin or carprofen in horses. Vet Rec 1993; 133:336–338.
48. Schatzmann U, Gugelmann M, Cranach JV, et al. Pharmacodynamic evaluation of the peripheral pain inhibition by carprofen and flunixin in the horse. Schweiz Arch Teirheilk 1990; 132:497–504.
49. Raekallio M, Taylor PM, Bennett RC. Preliminary investigations of pain and analgesia assessment in horses administered phenylbutazone or placebo after arthroscopic surgery. Vet Surg 1997; 26:150–155.
50. Owen JG, Kamerling SG, Stanton SR, et al. Effects of pretreatment with ketoprofen and phenylbutazone on experimentally induced synovitis in horses. Am J Vet Res 1996; 57(6):866–874.
51. Owens JG, Kamerling SG, Barker SA. Pharmacokinetics of ketoprofen in healthy horses and horses with acute synovitis. J Vet Pharmacol Ther 1995; 18:187–195.
52. Hess EV, Herman JH. Cartilage metabolism and anti-inflammatory drugs: osteoarthritis. Am J Med 1986; 81:36–43.

53. Beluche LA, Bertone AL, Anderson DE, et al. Effects of oral administration of phenylbutazone to horses on in vitro articular cartilage metabolism. Am J Vet Res 2001; 62(12):1916–1921.
54. Armstrong S, Lees P. Effects of carprofen (R and S enantiomers and racemate) on the production of IL-1, IL-6, and TNF-alpha by equine chondrocytes and synoviocytes. J Vet Pharmacol 2002; 25(2):145–153.
55. Landoni MF, Foot R, Frean S, et al. Effects of flunixin, tolfenamic acid, R(–) and S(+) ketoprofen on the response of equine synoviocytes to lipopolysaccharide stimulation. Equine Vet J 1996; 28(6):468–475.
56. Moses VS, Hardy J, Bertone AL, et al. Effects of anti-inflammatory drugs on lipopolysaccharide-challenged and -unchallenged equine synovial explants. Am J Vet Res 2001; 62(1):54–60.
57. Rohde C, Anderson DE, Bertone AL, et al. Effects of phenylbutazone on bone activity and formation in horses. J Am Vet Res 2000; 61(5):537–543.
58. King J, Gerring E. Antagonism of endotoxin induced disruption of equine bowel motility by flunixin and phenylbutazone. Equine Vet J 1989; 7(suppl):38–42.
59. Daels PF, Stabenfeldt GH, Hughes JP, et al. Effects of flunixin meglumine on endotoxin-induced prostaglandin $F_{2\alpha}$ secretion during early pregnancy in mares. Am J Vet Res 1991; 52(2):276–281.
60. Judson DG, Barton M. Effect of aspirin on haemostasis in the horse. Res Vet Sci 1981; 30:241–242.
61. Johnstone IB. Comparative effects of phenylbutazone, naproxen, and flunixin meglumine on equine platelet aggregation and platelet factor 3 availability *in vitro*. Can J Comp Med 1983; 47:172–179.
62. Weiss DJ, Evanson OA, McClenahan D, et al. Evaluation of platelet activation and platelet-neurophil aggregates in ponies with alimentary laminitis. AM J Vet Res 1997; 58(12):1376–1380.
63. Conner GH, Riley WF, Beck CC, et al. Arquel (C1–1583). A new non-steroidal anti-inflammatory drug for horses. Am Assoc Equine Pract; 1973; 19:81–90.
64. Houdeshell JW, Hennessy PW. A new non-steroidal anti-inflammatory analgesic for horses. J Equine Med Surg 1977; 1:57–63.
65. Killian JG, Jones EW, Hamm D, et al. The efficacy of equiproxen (naproxen) in a unique equine myositis model. Am Assoc Equine Pract; 1974; 20:201–215.
66. Jones EW, Hamm D. Comparative efficacy of phenylbutazone and naproxen in induced equine myositis. J Equine Med Surg 1978;2:341–347.
67. Moore JN, Garner HE, Shapland JE, et al. Prevention of endotoxin-induced arterial hypoxaemia and lactic acidosis with flunixin meglumine in the conscious pony. Equine Vet J 1981; 13(2):95–98.
68. Moore JN, Hardee MM, Hardee GE. Modulation of arachidonic acid metabolism in endotoxic horses: comparison of flunixin meglumine, phenylbutazone, and a selective thromboxane synthetase inhibitor. Am J Vet Res 1984; 47(1):110–113.
69. Fessler JF, Bottoms GE, Roesel OF, et al. Endotoxin-induced change in hemograms, plasma enzymes, and blood chemical values in anesthetized ponies: effects of flunixin meglumine. Am J Vet Res 1982; 43(1):140–144.
70. Burrows GE. Therapeutic effect of phenylbutazone on experimental acute *Escherichia coli* endotoxemia in ponies. Am J Vet Res 1981; 42(1):94–99.
71. Semrad SD, Hardee GE, Hardee MM, et al. Low dose flunixin meglumine: effects on eicosanoid production and clinical signs induced by experimental endotoxaemia in horses. Equine Vet J 1987; 19(3):201–206.
72. Semrad SD, Sams RA, Harris ON, et al. Effects of concurrent administration of phenylbutazone and flunixin meglumine on pharmacokinetic variables and in vitro generation of thromboxane B_2 in mares. Am J Vet Res 1993; 54(11): 1901–1905.
73. Snow DH, Douglas TA, Thompson H, et al. Phenylbutazone toxicosis in equidae: a biochemical and pathophysiologic study. Am J Vet Res 1981; 42(10):1754–1759.
74. Gunson DE. Renal papillary necrosis in horses. J Am Vet Med Assoc 1983; 182(3):263–266.
75. Gunson DE, Soma LR. Renal papillary necrosis in horses after phenylbutazone and water deprivation. Vet Pathol 1983; 20:603–610.
76. Carrick JB, Papich MG, Middleton DM, et al. Clinical and pathological effects of flunixin meglumine administration to neonatal foals. Can J Vet Res 1989; 53:195–201.
77. Traub-Dargatz JL, Bertone JJ, Gould DH, et al. Chronic flunixin meglumine therapy in foals. Am J Vet Res 1988; 49(1):7–12.
78. Conlon PD. Nonsteroidal drugs used in the treatment of inflammation. Vet Clin North Am Small Anim Pract 1988; 18:1115–1131.
79. Meschter CL, Maylin GA, Krook L. Vascular pathology in phenylbutazone intoxicated horses. Cornell Vet 1984; 74:292–297.
80. Kore AM. Toxicology of nonsteroidal anti-inflammatory drugs. Vet Clin North Am Small Anim Pract 1990; 20(2):419–430.
81. Read WK. Renal medullary crest necrosis associated with phenylbutazone therapy in horses. Vet Pathol 1983; 20:662–669.
82. Turner AS. Local and systemic factors affecting wound healing. Proc Am Assoc Equine Pract 1978; 24:209–218.
83. Schneiter HL, McClure RJ, Cho DY, et al. The effect of flunixin meglumine on early wound healing of abdominal incisions in ponies. Vet Surg 1987; 16:101.
84. Wilson DA, Baker GJ, Boero MJ. Complications of celiotomy incisions in horses. Vet Surg 1995; 24:506–514.
85. MacKay RJ, French TW, Nguyen HT, et al. Effects of large doses of phenylbutazone administration to horses. Am J Vet Res 1983; 44(5):774–780.
86. Caron JP. Principles of treatment of joint disease. In: Auer DE, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia, PA: Saunders; 1999; 678–696.
87. Ferguson DC, Hoenig M. Glucocorticoids, mineralocorticoids, and steroid synthesis inhibitors. In: Adams HR, edr. Veterinary pharmacology and therapeutics, 7th edn. Ames, IA: Iowa State University Press; 1995; 622–637.
88. Trotter GW. Intra-articular corticosteroids. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 237–256.
89. Autefage A, Alvinerie M, Toutain PL, et al. Synovial fluid and plasma kinetics of methylprednisolone and methylprednisolone acetate in horses following intra-articular administration of methylprednisolone acetate. Equine Vet J 1986; 18 (3):193–198.
90. Alvineire M, Toutain PL. Determination of methylprednisolone and methylprednisolone acetate in synovial fluid using high performance liquid chromatography. J Chromatogr 1984; 309:385–390.
91. Harkins JD, Carney JM, Tobin T. Clinical use and characteristics of the corticosteroids. Vet Clin North Am Equine Pract 1993; 9(3):543–562.
92. Bombardieri S, Cattani P, Ciabattoni G, et al. The synovial prostaglandin system in chronic inflammatory arthritis:

differential effects of steroidal and nonsteroidal anti-inflammatory drugs. Br J Pharmacol 1981; 73:893–901.
93. Derendorf H, Mollmann H, Gruner A, et al. Pharmacokinetics and pharmacodynamics of glucocorticoid suspensions after intra-articular administration. Clin Pharmacol Ther 1986; 39(3):313–317.
94. Lillich JD, Bertone AL, Schmall LM, et al. Plasma, urine, and synovial fluid disposition of methylprednisolone acetate and isoflupredone acetate after intra-articular administration in horses. Am J Vet Res 1996; 57(2):187–192.
95. Chunekamrai S, Krook L, Lust G, et al. Changes in articular cartilage after intra-articular injections of methylprednisolone acetate in horses. Am J Vet Res 1989; 50:1733–1741.
96. Trotter GW, McIlwraith CW, Yovich JV, et al. Effects of intra-articular administration of methylprednisolone acetate on normal equine articular cartilage. Am J Vet Res 1991; 52:83–87.
97. Frisbie DD, Kawcak CE, Baxter GM, et al. Effects of 6α-methylprednisolone acetate on an equine osteochondral fragment exercise model. Am J Vet Res 1998;59(12); 1619–1628.
98. Frisbie DD, Kawcak CE, Trotter GW, et al. Effects of triamcinolone acetonide on an in vivo equine osteochondral fragment exercise model. Equine Vet J 1997; 29(5):349–359.
99. Todhunter RJ, Fubini SL, Vernier-Singer M, et al. Acute synovitis and intra-articular methylprednisolone acetate in ponies. Osteoarthritis Cartilage 1998; 6:94–105.
100. MacLeod JN, Fubini SL, Gu DN, et al. Effect of synovitis and corticosteroids on transcription of cartilage matrix proteins. Am J Vet Res 1998; 59(8):1021–1026.
101. Robion FC, Doize B, Boure L, et al. Use of synovial fluid markers of cartilage synthesis and turnover to study effects of repeated intra-articular administartion of methylprednisolone acetate on articular cartilage in vivo. J Orthoped Res 2001; 19:250–258.
102. Murphy DJ, Todhunter RJ, Fubini SL, et al. The effects of methylprednisolone on normal and monocyte-conditioned medium-treated articular cartilage from dogs and horses. Vet Surg 2000; 29:546–557.
103. Caron JP, Tardif G, Martel-Pelletier J, et al. Modulation of matrix metalloprotease 13 (collagenase 3) gene expression in equine chondrocytes by interleukin 1 and corticosteoids. Am J Vet Res 1996; 57(11):1631–1634.
104. Pelletier JP, Mineau F, Soessner JFJ, et al. Intraarticular injections with methylprednisolone acetate reduce osteoarthritic lesions in parallel with chondrocyte stromelysin synthesis in experimental osteoarthritis. Arthritis Rheum 1994; 37:414–423.
105. Pelletier JP, Martel-Pelletier J. Protective effect of corticosteroids on cartilage lesions and osteophyte formation in the Pond-Nuki dog model of osteoarthritis. Arthritis Rheum 1989; 32:181–193.
106. Pelletier JP, DiBattista JA, Raynauld JP, et al. The in vivo effects of intraarticular corticosteroid injections on cartilage lesions, stromelysin, interleukin-1, and oncogene protein synthesis in experimental ostearthritis. Lab Invest 1995; 72:578–586.
107. Clegg PD, Jones MD, Carter SD. The effect of drugs commonly used in the treatment of equine articular disorders on the activity of equine matrix metalloproteinase-2 and 9. J Vet Pharmacol Ther 1998; 21:406–413.
108. Richardson DW, Dodge GR. Effects of tumour necrosis factor-alpha, interleukin-1-beta and dexamethasone on the matrix metabolism of culture equine chondrocytes. 42nd Annual Meeting of the Orthopaedic Research Society; 1996; 126.
109. Fubini SL, Todhunter RJ, Burton-Wurster N, et al. Corticosteroids alter the differentiated phenotype of articular chondrocytes. J Orthoped Res 2001; 19:688–695.
110. Todhunter RJ, Fubini SL, Wootton JA, et al. Effect of methylprednisolone acetate on proteoglycan and collagen metabolism on articular cartilage explants. J Rheumatol 1996; 23(7):1207–1213.
111. Jolly WT, Whittem T, Jolly AC, et al. The dose-related effects of phenylbutazone and a methylprednisolone acetate formulation (Depo-Medrol) on cultured explants of equine carpal articular cartilage. J Vet Pharmacol Ther 1995; 18(6): 429–437.
112. Foland JW, McIlwraith CW, Trotter GW, et al. Effect of betamethasone and exercise on equine carpal joints with osteochondral fragments. Vet Surg 1994; 23:369–376.
113. Kawcak CE, Norrdin RW, Frisbie DD, et al. Effects of osteochondral fragmentation and intra-articular triamcinolone acetonide treatment on subchondral bone in the equine carpus. Equine Vet J 1998; 30(1):66–71.
114. Oegema TRJ, Behrens F. Proteoglycan synthesis in normal and chronically hydrocortisone-suppressed rabbit articular cartilage explants. Arch Biochem Biophys 1981; 206:277.
115. Chen CL, Sailor JA, Collier J, et al. Synovial and serum levels of triamcinolone following intra-articular adminstration of triamcinolone in the horse. J Vet Pharmacol Ther 1992; 15:240–246.
116. Gibbs DA, Merrill EW, Smith KA. Rheology of hyaluronic acid. Biopolymers 1968; 6:777–791.
117. Hamerman D, Rojkind M, Sandson J. Protein bound to hyaluronate: chemical and immunological studies. FASEB J 1966; 25:1040–1045.
118. Radin EL, Paul IUL. A consolidated concept of joint lubrication. J Bone Joint Surg [Am] 1972; 54:607–616.
119. Swann DA, Radin EL, Nazimiec M, et al. Role of hyaluronic acid in joint lubrication. Ann Rheum Dis 1974; 33:318–326.
120. Freeman MAR, Kempson GE. Load carriage. In: Freeman MAR, ed. Adult articular cartilage. New York: Grune and Stratton; 1972; 228–246.
121. Cannon JH. Clinical evaluation of intra-articular sodium hyaluronate in the Thoroughbred horse. Equine Vet Sci 1985; 5:147–148.
122. Galley RH. The use of hyaluronic acid in the racehorse. Am Assoc Equine Pract 1986; 32:657–661.
123. Irwin DHG. Sodium hyaluronate in equine traumatic arthritis. J S Afr Vet Assoc 1980; 50:231–233.
124. Phillips MW. Intra-articular sodium hyaluronate in the horse. A clinical trial. Am Assoc Equine Pract 1980; 26:389–394.
125. Roneus B, Linblad A, Lindholm A, et al. Effects of intra-articular corticosteroid and sodium hyaluronate injections on synovial fluid production and synovial fluid content of sodium hyaluronate and proteoglycans in normal equine joints. Zentralbl Veterinarmed A 1993; 40:10–16.
126. Rose RJ. Intra-articular use of sodium hyaluronate for the treatment of osteoarthritis in the horse. NZ Vet J 1979; 27(1–2):5–8.
127. Ruth DT, Swites BJ. Comparison of the effectiveness of intra-articular hyaluronic acid and conventional therapy for the treatment of naturally occurring arthritic conditions in horses. Equine Pract 1985; 7:25–29.
128. Rydell NV, Butler J, Balazs EA. Hyaluronic acid in synovial fluid. VI. Effect of intra-articular injection of hyaluronic acid on the clinical symptoms of arthritis in track horses. Acta Vet Scand 1970; 11:139–155.

129. Swanstrom OG. Hyaluronate (hyaluronic acid) and its use. Am Assoc Equine Pract 1978; 24:345–348.
130. Vernon GT. Clinical successes and failures using new hyaluronic acid-Synacid. In: Proc Am Assoc Pract; 1983; 29:397–402.
131. Fraser JR, Kimpton WG, Pierscionek BK, et al. The kinetics of hyaluronan in normal and acutely inflamed synovial joints: observations with experimental arthritis in sheep. Semin Arthritis Rheum 1993; 22(6 suppl 1):9–17.
132. Gosh P. Osteoarthritis and hyaluronan – palliative or disease modifying treatment? Semin Arthritis Rheum 1993; 22:1–3.
133. Laurent UBG, Fraser JRE, Engstrom-Laurent A, et al. Catabolism of hyaluronan in the knee joint of the rabbit. Matrix 1992; 12:130–136.
134. Balazs EA, Darzynkiewiez A. The effect of hyaluronic acid on fibroblasts, mononuclear phagocytes and lymphocytes. In: Kulonen E, Pikkarainen JPK, eds. Biology of fibroblasts. London: Academic Press; 1973; 237.
135. Brandt KD. Modification of chemotaxis by synovial fluid hyaluronate. Arthritis Rheum 1970; 13:308.
136. Brandt KD. The effect of synovial fluid hyaluronate on the ingestion of monosodium urate crystals by leukocytes. Clin Chem Acta 1974; 55:307–315.
137. Forrester JB, Balazs EA. Inhibition of phagocytosis by high molecular weight hyaluronate. Immunology 1980; 40:435–446.
138. Grecomoro G, Martorana U, DiMarco C. Intra-articular treatment with sodium hyaluronate in gonarthrosis: a controlled clinical trial versus placebo. Pharmatherapeutica 1987; 5:137–141.
139. Hakansson L, Hallgren R, Benge P. Effect of hyaluronic acid on phagocytosis of opsonized latex particles. Scand J Immunol 1980; 11:649–653.
140. Partsch G, Scharzer C, Neumuller J, et al. Modulation of the migration and chemotaxis of PMN cells for hyaluronic acid. Z Rheumatol 1989; 48:123–128.
141. Pisko EJ, Turner RA, Soderstrom LP, et al. Inhibition of neutrophil phagocytosis and enzyme release by hyaluronic acid. Clin Exp Rheumatol 1983; 1:41–44.
142. Treadway WJ, Sederstrom LP, Turner RA, et al. The role of hyaluronic acid flux on modulation of neutrophil function. Arthritis Rheum 1981; 24(suppl 4):S94-S99.
143. Auer JA, Fackelman GE, Gingerich D, et al. Effect of hyaluronic acid in naturally occurring and experimental osteoarthritis. Am J Vet Res 1980; 41:568–574.
144. McIlwraith CW. Diseases of joints, tendons, ligaments, and related structures. In: Stashak TS, ed. Adam's Lameness. Philadelphia, PA: Lippincott Williams and Wilkins; 2002; 505–511.
145. Kikuchi T, Yamada H, Shimmei M. Effect of high molecular weight hyaluronan on cartilage degeneration in a rabbit model of osteoarthritis. J Osteoarthritis Cart 1996; 4:99–110.
146. Hilbert BJ, Rowley G, Antonas KN. Hyaluronic acid concentration in synovial fluid from normal and arthritic joints of horses. Aust Vet J 1984; 61:22–24.
147. Larsen NE, Lombard KM, Parent E, et al. Effect of hylan on cartilage and chondrocyte cultures. J Orthoped Res 1992; 10:23–32.
148. Shimazu A, Jikko A, Iwamato M, et al. Effects of hyaluronic acid on the release of proteoglycans from the cell matrix in rabbit chondrocyte cultures in the presence and absence of cytokines. Arthritis Rheum 1993; 36:247–253.
149. Wygren A, Falk J, Wik O. The healing of cartilage injuries under the influence of joint immobilization and repeated hyaluronic acid injections. An experimental study. Acta Orthop Scand 1978; 49:121–133.
150. Saari H, Kontinnen YT, Tulamo RM, et al. Concentration and degree of polymerization of nyaluronate in equine synovial fluid. Am J Vet Res 1989; 50:2060–2063.
151. Tulamo RM, Heiskanen T, Salonen M. Concentration and molecular weight distribution of hyaluronate in synovial fluid from clinically normal horses and horses with diseased joints. Am J Vet Res 1994; 55:710–715.
152. Hilbert BJ, Rowley G, Antonas KN, et al. Changes in the synovia after the intra-articular injection of sodium hyaluronate into normal horse joints and after arthrotomy and experimental cartilage damage. Aust Vet J 1985; 62: 182–184.
153. Gingerich DA, Auer JA, Fackelman GE. Force plate studies on the effect of exogenous hyaluronic acid on joint function in equine arthritis. J Vet Pharmacol Ther 1979; 2: 291–298.
154. Peloso JG, Stick JA, Caron JP, et al. Effects of hylan on amphotericin-induced carpal lameness in equids. Am J Vet Res 1993; 54:1527–1534.
155. Kawcak CE, Frisbie DD, Trotter GW, et al. Effects of intravenous adminstration of sodium hyaluronate on carpal joints in exercising horses after arthroscopic surgery and osteochondral fragmentation. Am J Vet Res 1997; 58: 1132–1140.
156. Churchill EA. Treating tendinitis with sodium hyaluronate. J Equine Sci 1985; 5:217–228.
157. Spurlock GH, Spurlock SL, Parker GA. Evaluation of hylartin-V therapy for induced tendinitis in the horse. J Equine Vet Sci 1989; 9:242–246.
158. Gaughan EM, Nixon AJ, Lennart PK, et al. Effects of sodium hyaluronate on tendon healing and adhesion formation in horses. Am J Vet Res 1991; 52:764–773.
159. Folland JW, Trotter GW, Powers BE, et al. Effect of sodium hyaluronate in collagenase-induced superficial digital flexor tendinitis in horses. Am J Vet Res 1992; 53:2371–2376.
160. Smith MM, Ghosh P. The synthesis of hyaluronic acid by human synovial fibroblasts is influenced by the extracellular environment. Rheumatol Int 1987; 7:113–122.
161. Phillips MW. Clinical trial comparison of intra-articular sodium hyaluronate products in the horse. Equine Vet Sci 1989; 9:39–40.
162. Gaustad G, Larsen S. Comparison of polysulfated glycosaminoglycan and sodium hyaluronate with placebo in treatment of traumatic arthritis in horses. Equine Vet J 1995; 27:356–362.
163. Aviad AD, Arthur RM, Brencick VA, et al. Synacid vs Hylartin-V in equine joint disease. Equine Vet Sci 1988; 8:112–116.
164. van Pelt RW. Monoarticular idiopathic septic arthritis in horses. J Am Vet Med Assoc 1971; 158:1658–1673.
165. Schmidt SR. Routine drug treatments of septic arthritis. Clin Rheum Dis 1984; 10 (2): 293–311.
166. Hackett RP. Intra-articular use of corticosteroids in the horse. J Am Vet Med Assoc 1982; 181:292–294.
167. Gustafson SB, McIlwraith CW, Jones RL, et al. Further investigations into the potentiation of infection by intra-articular injection of polysulfated glycosaminoglycan and the effect of filtration and intra-articular injection of amikacin. Am J Vet Res 1989; 50(12):2018–2022.
168. Gustafson SB, McIlwraith CW, Jones RL. Comparison of the effect of polysulfated glycosaminoglycan, corticosteroids, and sodium hyaluronate in the potentiation of a subinfective dose of *Staphylococcus aureus* in the midcarpal joint of horses. Am J Vet Res 1989; 50:2014–2017.
169. Arrioja A, ed. Compendium of veterinary products, 6th edn. Canada: North American Compendiums Ltd; 2001; 1665.

170. Arrioja A, ed. Compendium of veterinary products, 6th edn. Canada: North American Compendiums Ltd; 2001; 1346–1349.
171. Plumb DC. Hyaluronate sodium. In: Veterinary drug handbook, 3rd edn. Ames, IA: Iowa State University Press; 1999; 325–326.
172. Burba DJ, Collier MA, DeFault LE. In vivo kinetic study on uptake and distribution of intramuscular tritium-labeled polysulfated glycosaminoglycan in equine body fluid compartments and articular cartilage in an osteochondral defect model. J Equine Vet Sci 1993; 13:696–703.
173. Andrews JL, Sutherland J, Ghosh P. Distribution and binding of glycosaminoglycan polysulfate to intervertebral disc, knee joint articular cartilage and meniscus. Arzneimittelforschung 1985; 35(1):144–148.
174. Panse P, Zeiller P, Sensch KH. [Distribution and excretion of a glycosaminopolysulfate in the rabbit after parenteral application (author's transl)]. Arzneimittelforschung 1976; 26(11):2024–2029.
175. McIlwraith CW, Trotter GW. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 281–292.
176. Vacha J, Pesakova V, Krajickova J, et al. Effect of glycosaminoglycan polysulphate on the metabolism of cartilage ribonucleic acid. Arzneimittelforschung 1984; 34(5):607–609.
177. Adam M, Krabcova M, Musilova J, et al. Contribution to the mode of action of glycosaminoglycan-polysulphate (GAGPS) upon human osteoarthrotic cartilage. Biochemical study of the collagen and proteoglycan turnover. Arzneimittelforschung 1980; 30(10):1730–1732.
178. Hannan N, Ghosh P, Bellenger C, et al. Systemic administration of glycosaminoglycan polysulphate (arteparon) provides partial protection of articular cartilage from damage produced by meniscectomy in the canine. J Orthoped Res 1987; 5(1):47–59.
179. Verbruggen G, Veys EM. Influence of sulphated glycosaminoglycans upon proteoglycan metabolism of the synovial lining cells. Acta Rheumatol Belg 1977; 1(1–2): 75–92.
180. Glade MJ. Polysulfated glycosaminoglycan accelerates net synthesis of collagen and glycosaminoglycans by arthritic equine cartilage tissues and chondrocytes. Am J Vet Res 1990; 51(5):779–785.
181. Caron JP, Eberhart SW, Nachreiner R. Influence of polysulfated glycosaminoglycan on equine articular cartilage in explant culture. Am J Vet Res 1991;52(10): 1622–1625.
182. Caron JP, Toppin DS, Block JA. Effect of polysulfated glycosaminoglycan on osteoarthritic equine articular cartilage in explant culture. Am J Vet Res 1993; 54(7): 1116–1121.
183. McIlwraith CW. Intra-articular medication for traumatic joint problems: do we understand the choices? Comp Cont Educ Pract Vet 1989; 11:1287–1311.
184. Trotter GW, Yovich JV, McIlwraith CW, et al. Effects of intramuscular polysulfated glycosaminoglycan on chemical and physical defects in equine articular cartilage. Can J Vet Res 1989; 53(2):224–230.
185. Yovich JV, Trotter GW, McIlwraith CW, et al. Effects of polysulfated glycosaminoglycan on chemical and physical defects in equine articular cartilage. Am J Vet Res 1987; 48(9):1407–1414.
186. Todhunter RJ, Minor RR, Wootton JA, et al. Effects of exercise and polysulfated glycosaminoglycan on repair of articular cartilage defects in the equine carpus. J Orthoped Res 1993; 11(6):782–795.
187. Todhunter RJ, Freeman KP, Yeager AE, et al. Effects of exercise and polysulfated glycosaminoglycan on the development of osteoarthritis in equine carpal joints with osteochondral defects. Vet Surg 1993; 22(5):330–342.
188. Oryan A. Experimental tendon injury and repair [PhD thesis]. University of Bristol, UK; 1989.
189. Redding WR, Booth LC, Pool RR. Effects of polysulfated glycosaminoglycan on healing of collagenase-induced tendinitis of the equine superficial digital flexor tendon. Vet Comp Ortho Traumatol 1999; 12:48–56.
190. Walesby HA, Rosenbusch R, Booth LC, et al. Uptake and distribution of tritium-labeled polysulfated glycosaminoglycan in serum, urine, and superficial digital flexor tendon of rabbits after intramuscular administration. Am J Vet Res 2000; 61(1):20–23.
191. Nixon AJ. Intra-articular medication. In: Robinson NE, ed. Current therapy in equine medicine 3. Philadelphia, PA: Saunders; 1992; 127–131.
192. Rashmir-Raven AM, Coyne CP, Fenwick BW, et al. Inhibition of equine complement activity by polysulfated glycosaminoglycans. Am J Vet Res 1992; 53(1):87–90.
193. Arrioja A, ed. Compendium of veterinary products, 6th edn. Canada: North American Compendiums Ltd; 2001.
194. Hamm D, Goldman L, Jones EW. Polysulfated glycosaminoglycin: a new intra-articular treatment for equine lameness. Vet Med 1984; 6:811–816.
195. Plumb DC. Polysulfated glycosaminoglycan. In: Plumb DC, ed. Veterinary drug handbook, 3rd edn. Ames, IA: Iowa State University Press; 1999; 520–521.
196. Ghosh P, Smith M, Wells C. Second-line agents in osteoarthritis. In: Dixon JS, Furst DE, eds. Second-line agents in the treatment of rheumatic diseases. New York: Marcel Dekker; 1992; 363–427.
197. Ghosh P, Wells C, Smith M. Chondroprotection, myth or reality: an experimental approach. Semin Arthritis Rheum 1990; 19:3–9.
198. Avouac B. Slow acting drugs in osteoarthritis: a step towards disease modification. Rev Esp Rheumatol 1993; 20(suppl 1): 221–222.
199. Lequesne M, Brandt K, Bellamy N, et al. Guidelines for testing slow acting drugs in osteoarthritis. J Rheumatol 1994; 41(suppl):65–71; discussion 72–73.
200. Lualdi P. Bioavailability of oral chondroitin sulfate. Rheumatol Int 1993; 13(1):39–43.
201. Baici A, Wagenhauser FJ. Editorial comment. Rheumatol Int 1993; 13:41–43.
202. Palmieri L, Conte A, Giovannini L, et al. Metabolic fate of exogenous chondroitin sulfate in the experimental animal. Arzneimittelforschung 1990; 40(3):319–323.
203. Conte A, de Bernardi M, Palmieri L, et al. Metabolic fate of exogenous chondroitin sulfate in man. Arzneimittelforschung 1991; 41(7):768–772.
204. Ronca F, Palmieri L, Panicucci P, et al. Anti-inflammatory activity of chondroitin sulfate. Osteoarthritis Cartilage 1998; 6(suppl A):14–21.
205. Baici A, Horler D, Moser B, et al. Analysis of glycosaminoglycans in human serum after oral administration of chondroitin sulfate. Rheumatol Int 1992; 12(3):81–88.
206. Yamanashi S, Toyoda H, Furuya N, et al. [Metabolic study on chondroitin sulfates in rabbits.] Yakugaku Zasshi 1991; 111(1):73–76.
207. Salyers AA, O'Brien M. Cellular location of enzymes involved in chondroitin sulfate breakdown by Bacteroides thetaiotaomicron. J Bacteriol 1980; 143(2): 772–780.
208. Wright IM. Oral supplements in the treatment and prevention of joint diseases: a review of their potential application to the horse. Equine Vet Educ 2001; 13:135–139.

209. Morreale P, Manopulo R, Galati M, et al. Comparison of the anti-inflammatory efficacy of chondroitin sulfate and diclofenac sodium in patients with knee osteoarthritis. J Rheumatol 1996; 23(8):1385–1391.
210. Bourgeois P, Chales G, Dehais J, et al. Efficacy and tolerability of chondroitin sulfate 1200 mg/day vs chondroitin sulfate 3 × 400 mg/day vs placebo. Osteoarthritis Cartilage 1998; 6(suppl A):25–30.
211. Bucsi L, Poor G. Efficacy and tolerability of oral chondroitin sulfate as a symptomatic slow-acting drug for osteoarthritis (SYSADOA) in the treatment of knee osteoarthritis. Osteoarthritis Cartilage 1998; 6(suppl A):31–36.
212. Uebelhart D, Thonar EJ, Delmas PD, et al. Effects of oral chondroitin sulfate on the progression of knee osteoarthritis: a pilot study. Osteoarthritis Cartilage 1998; 6(suppl A):39–46.
213. Gibson RG, Gibson SL, Conway V, et al. Perna canaliculus in the treatment of arthritis. Practitioner 1980; 224(1347): 955–960.
214. Uebelhart D, Thonar EJ, Zhang J, et al. Protective effect of exogenous chondroitin 4,6-sulfate in the acute degradation of articular cartilage in the rabbit. Osteoarthritis Cartilage 1998; 6(suppl A):6–13.
215. Canapp SO Jr, McLaughlin RM Jr, Hoskinson JJ, et al. Scintigraphic evaluation of dogs with acute synovitis after treatment with glucosamine hydrochloride and chondroitin sulfate. Am J Vet Res 1999; 60(12):1552–1557.
216. White GW. Is oral supplementation of PSGAG a reliable method of therapy for equine joint disease? J Equine Vet Sci 1989; 9:232–233.
217. Muller-Fassbender H, Bach GL, Haase W, et al. Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee. Osteoarthritis Cartilage 1994; 2(1):61–69.
218. Noack W, Fischer M, Forster KK, et al. Glucosamine sulfate in osteoarthritis of the knee. Osteoarthritis Cartilage 1994; 2(1):51–59.
219. Hanson R. Oral glycosaminoglycans in treatment of degenerative joint disease in horses. Equine Pract 1996; 18:18–22.
220. White GW, Jones EW, Hamm J. The efficacy of orally administered sulfated glycosaminoglycan in chemically-induced equine synovitis and degenerative joint disease. J Equine Vet Sci 1994; 14:350–353.
221. Roden L. Effect of hexosamines on the synthesis of chondroitin sulphuric acid *in vitro*. Arkh Kemi 1956; 10:345–352.
222. Vidal y Plana RR, Karzel K. Glucosamine: its importance for the metabolism of articular cartilage. 2. Studies on articular cartilage. Fortschr Med 1980; 98(21):801–806.
223. Setnikar I, Cereda R, Pacini MA, et al. Antireactive properties of glucosamine sulfate. Arzneimittelforschung 1991; 41(2):157–161.
224. Setnikar I, Pacini MA, Revel L. Antiarthritic effects of glucosamine sulphate studies on animal models. Arzneim Forsch/Drug Res 1991; 41:542–545.
225. Fenton JI, Chelebek-Brown KA, Peters TL. Glucosamine inhibits interleukin-1β and lipopolysaccharide-induced cartilage degeneration *in vitro*. Vet Surg 1999; 28:388–392.
226. Fenton JI, Chlebek-Brown KA, Peters TL, et al. Glucosamine HCl reduces equine articular cartilage degradation in explant culture. Osteoarthritis Cartilage 2000; 8(4):258–265.
227. Bassleer C, Henrotin Y, Franchimont P. In-vitro evaluation of drugs proposed as chondroprotective agents. Int J Tissue React 1992; 14(5):231–241.
228. Bassleer C, Reginster JY, Franchimont P. Effects of glucosamine on differentiated human chondrocytes cultivated in clusters. Rev Esp Rheumatol 1993; 20(suppl 1): 96–101.
229. Setnikar I, Giachetti C, Zanolo G. Absorption, distribution and excretion of radioactivity after a single intravenous or oral administration of [14C] glucosamine to the rat. Pharmatherapeutica 1984; 3(8):538–550.
230. Setnikar I, Giacchetti C, Zanolo G. Pharmacokinetics of glucosamine in the dog and in man. Arzneimittelforschung 1986; 36(4):729–735.
231. Eichler J, Noh E. Therapy of deforming arthrosis through the action upon the cartilaginous metabolism. Orthop Prax 1970; 9:225–229.
232. Raiss R. [Effect of D-glucosamine sulfate on experimentally injured articular cartilage. Comparative morphometry of the ultrastructure of chondrocytes.] Fortschr Med 1985; 103(24):658–662.
233. Pujalte JM, Llavore EP, Ylescupidez FR. Double-blind clinical evaluation of oral glucosamine sulphate in the basic treatment of osteoarthrosis. Curr Med Res Opin 1980; 7(2):110–114.
234. Vaz AL. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in out-patients. Curr Med Res Opin 1982; 8:145–149.
235. Mund-Hoyn WD. Medical treatment of spinal arthrosis with glucosamine or phenylbutazone. A controlled study. Therapiewoche 1980; 30:5922–5928.
236. Giocovelli G, Rotavi LC. Clinical efficacy of glucosamine sulfate in osteoarthritis of the spine. Rev Esp Rheumatol 1993; 20(suppl 1):96–103.
237. Zupanets IA, Drogovoz SM, Bezdetko NV, et al. [The influence of glucosamine on the antiexudative effect of nonsteroidal anti-inflammatory agents.] Farmakol Toksikol 1991; 54(2):61–63.
238. Rovati LC, Setnikar I, Forster KK. Glucosamine sulfate in gonarthrosis: efficacy in placebo controlled studies. Rev Esp Rheumatol 1993; 20(suppl 1):72–78.
239. Reichelt A, Forster KK, Fischer M, et al. Efficacy and safety of intramuscular glucosamine sulfate in osteoarthritis of the knee. A randomised, placebo-controlled, double-blind study. Arzneimittelforschung 1994; 44(1):75–80.
240. Brayton CF. Dimethyl sulfoxide (DMSO): a review. Cornell Vet 1986; 76:61–90.
241. Koller LD. Clinical application of DMSO by veterinarians in Oregon and Washington. Vet Med Small Anim Clinic 1976; 71:591–638.
242. Wood DC, Wood J. Pharmacologic and biochemical considerations of dimethyl sulfoxide. Ann NY Acad Sci 1975; 243:7–28.
243. Fox RB, Fox WK. Dimethyl sulfoxide prevents hydroxyl radical-mediated depolymerization of hyaluronic acid. Ann NY Acad Sci 1983; 411:14–18.
244. Auer DE, Ng JC, Reilly JS, et al. Anti-inflammatory drugs inhibit degradation of equine synovial fluid induced by free radicals. Aust Vet J 1991; 68:403–405.
245. Auer DE, Ng JC, Seawright AA. Superoxide production by stimulated equine polymorphonuclear leukocytes – inhibition by anti-inflammatory drugs. J Vet Pharmacol Ther 1990; 13:59–66.
246. Plumb DC. Dimethyl sulfoxide. In: Plumb DC, ed. Veterinary drug handbook, 3rd edn. Ames, IA: Iowa State University Press; 1999.
247. Smith G, Bertone AL, Kaeding C, et al. Anti-inflammatory effects of topically applied dimethyl sulfoxide gel on endotoxin-induced synovitis in horses. Am J Vet Res 1998; 59(9):1149–1152.
248. Wooley RE, Gilbert JP, Shotts EB. Inhibitory effects of combinations of tetracycline, dimethyl sulfoxide and

EDTA-tromethamine on *Escherichia coli*. Am J Vet Res 1981; 42:2010–2013.
249. Gorog P, Kovacs IB. Antiarthritic and antithrombotic effects of topically applied dimethyl sulfoxide. Ann NY Acad Sci 1975; 243:91–103.
250. Smith G, Bertone AL, Kaeding C, et al. Anti-inflammatory effects of topically applied dimethyl sulfoxide gel on endotoxin induced synovitis in horses. Am J Vet Res 1998; 59:1149–1152.
251. More RC, Kabo JM, Dorey FJ, et al. The effects of dimethylsulfoxide on posttraumatic limb swelling and joint stiffness. A review and an experimental study in rabbits. Clin Orthop 1988; 233:304–309.
252. Auer DE, Ng JC, Reilly JS, et al. Anti-inflammatory drugs inhibit degradation of equine synovial fluid induced by free radicals. Aust Vet J 1991; 68(12):403–405.
253. Honnas CM, Welch RD, Ford TS, et al. Septic arthritis of the distal interphalangeal joint in 12 horses. Vet Surg 1992; 21(4):261–268.
254. Santos L, Tipping PG. Attenuation of adjuvant arthritis in rats by treatment with oxygen radical scavengers. Immunol Cell Biol 1994; 72:406–414.
255. Welch RD, DeBowes RM, Liepold HW. Evaluation of the effects of intra-articular injection of dimethylsulfoxide on normal equine articular tissues. Am J Vet Res 1989; 50:1180–1182.
256. Welch RD, Watkins JP, DeBowes RM, et al. Effects of intra-articular administration of dimethylsulfoxide on chemically induced synovitis in immature horses. Am J Vet Res 1991; 52:934–939.
257. Adair HS, Goble DO, Vanhooser S, et al. Evaluation of use of dimethyl sulfoxide for intra-articular lavage in clincally normal horses. Am J Vet Res 1991; 52(2):333–336.
258. Palmer JL, Bertone AL. Joint structure, biochemistry and biochemical disequilibrium in synovitis and equine joint disease. Equine Vet J 1994; 26:263–276.
259. Smith CL, MacDonald MH, Tesch AM, et al. In vitro evaluation of the effect of dimethyl sulfoxide on equine articular cartilage matrix metabolism. Vet Surg 2000; 29(4):347–357.
260. Rubin LF. Toxicologic update on dimethyl sulfoxide. Ann NY Acad Sci 1983; 411:6–10.
261. Little C, Ghosh P. Potential use of pentosan polysulfate for the treatment of equine joint disease. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia, PA: Saunders; 1996; 281–292.
262. Dencker L, Tengblad A, Odlind B. Preferential localization of 3H-pentosanpolysulfate to the urinary tract in rats. Acta Physiol Scand 1985; 124(suppl 542):351–359.
263. Odlind B, Dencker L, Tengblad A. Preferential localization of 3H-pentosanpolysulphate to the urinary tract in rats. Pharmacol Toxicol 1987; 61:162–166.
264. Andrews JL, Ghosh P, Lentini A, et al. The interaction of pentosan polysulfate (SP54) with human neutrophil elastase and connective tissue matrix components. Chem Biol Interact 1983; 47:157–173.
265. Ghosh P, Hutadilok N. Interactions of pentosan polysulphate with cartilage matrix proteins and synovial fibroblasts derived patients with osteoarthritis. J Osteoarthritis Cart 1995; 4:43–53.
266. Roberts BJ, Unsworth A, Main N. Modes of lubrication in human hip joints. Ann Rheum Dis 1982; 41:217–224.
267. Kruze D, Fehr K, Menninger H, et al. Effect of antirheumatic drugs on neutral protease from human leukocyte granules. Z Rheumatol 1976; 35:337–346.
268. Baici A, Salgam P, Fehr K, et al. Inhibition of human elastase from polymorphonuclear leukocytes by gold sodium thiomalate and pentosan polysulfate. Biochem Pharmacol 1981; 30:703–708.
269. Barg WF, Englert ME, Buermann CW, et al. Studies on the effect of pentosan polysulfate on proteoglycan degradation by leukocyte neutral proteases. Biochem Pharmacol 1979; 28:2639–2643.
270. Kruze D, Fehr K, Boni A. Effect of antirheumatic drugs on cathepsin B1 from bovine spleen. Z Rheumatol 1976; 35:95–102.
271. Steinmeyer J, Kalbhen DA. Influence of some natural and semisynthetic agents on elastase and cathepsin G from polymorphonuclear granulocytes. Arzneim Forsch/Drug Res 1991; 41:77–80.
272. Aydelotte MB, Kuettner KE. Differences between sub-populations of cultured bovine articular chondrocytes: 1. Morphology and cartilage matrix production. Connect Tissue Res 1988; 18:205–222.
273. Hutadilok N, Smith M, Cullis-Hill D, et al. Pentosan pentosulphate stimulates hyaluronate and DNA synthesis in synovial fibroblasts and partially reduces the suppressive effect of hydrocortisone on fibroblast metabolism. Curr Ther Res 1988; 44:845–860.
274. Ghosh P, Wells C, Smith M, et al. Chondroprotection, myth or reality: an experimental approach. Semin Arthritis Rheum 1990; 19(suppl 1):3–9.
275. Burkhardt D, Ghosh P. Laboratory evaluation of glycosaminoglycan polysulphate ester for chondroprotective activity. Curr Ther Res 1986; 40:1034–1053.
276. Saari H, Konttinen YT, Tulamo RM, et al. Concentration and degree of polymerization of hyaluronate in equine synovial fluid. Am J Vet Res 1989; 50:2060–2063.
277. Golding JC, Ghosh P. Drugs for osteoarthrosis: 1. The effects of pentosan polysulphate (SP54) on the degradation and loss of proteoglycans from articular cartilage in a model of osteoarthrosis induced in the rabbit knee joint by immobilization. Curr Ther Res 1983; 32:173–184.
278. Rogachefsky RA, Dean DD, Howell DS, et al. Treatment of canine osteoarthritis with insulin-like growth factor-1 and sodium pentosan polysulfate. J Osteoarthritis Cart 1993; 1:105–114.
279. Grumbles RM, Howell DS, Howard GA, et al. Cartilage metalloproteases in disuse atrophy. J Rheumatol 1995; 22(suppl 43):145–149.
280. Kongtawelert P, Brooks PM, Ghosh P. Pentosan polysulphate (Cartrophen) prevents the hydrocortisone induced loss of hyaluronic acid and proteoglycan from cartilage of rabbit joints as well as normalizes keratin sulphate levels in their serum. J Rheumatol 1989; 16:1454–1459.
281. Read R, Cullis-Hill D, Jones MP. Systematic use of pentosan polysulphate in the treatment of osteoarthritis. J Small Animal Pract 1996; 37:108–114.
282. Verbruggen G, Veys EM, Ghosh P. Pentosan polysulphate treatment in osteoarthritis, serological parameters which could correlate with clinical response. J Osteoarthritis Cart 1994; 2(suppl 1):60–65.
283. Verbruggen G, Veys EM, Ghosh P, et al. Pentosan polysulphate treatment in osteoarthritis, serological parameters which could correlate with clinical response. Clin Rheumatol 1996; 15:542.

CHAPTER 24

Neurologic causes of gait abnormalities in athletic horses

Bonnie R. Rush

Introduction

Performance horses often present for evaluation of neurologic gait deficits. Many owners interpret the abnormal gait as lameness, wherein the source of the gait abnormality is actually neurologic dysfunction. In some cases, neurologic gait deficits will be immediately obvious to the examining veterinarian and the owner learns to recognize the signs of spinal ataxia during the neurologic examination. In other cases, the source of the gait abnormality is obscure and may require extensive evaluation by an experienced clinician. Gait evaluation of horses with spinal ataxia may be confounded by an existing lameness that has been exacerbated by weakness or traumatic injury. A few neurologic diseases will present as a single limb lameness that fails to respond to regional anesthesia (i.e. equine protozoal myelitis). Systematic physical and neurologic examination will clarify a difficult gait analysis and determine whether the primary source of abnormal gait is lameness or neurologic dysfunction. Physical examination will identify concurrent problems related to neurologic disease such as traumatic injury to the musculoskeletal system, developmental orthopedic disease, focal muscle atrophy or multisystemic disease. Neurologic examination provides neuroanatomic lesion localization and allows the clinician to develop a list of differential diagnoses.

Head shaking is also common in performance horses and, in many cases, is neurogenic in origin. Head shaking was previously attributed to behavior and training, but is now recognized to result from numerous medical conditions. The most common cause of head shaking is trigeminal neuritis, which produces neuropathic pain upon exposure to natural sunlight. Head shaking is often performance limiting and can be career ending for individual horses.

Neurologic examination

- Neurologic examination should be performed in a systematic manner to avoid overlooking subtle abnormalities.
- Gait abnormalities are accentuated by manipulation such as inclines, circling and blindfolding.
- The goal of the neurologic examination is to determine grading of deficits, symmetry and neuroanatomic localization.
- Cranial nerve examination is normal with the majority of diseases producing spinal ataxia.

Gait evaluation

Neurologic gait deficits are graded on a scale of 0–5: grade 0 – normal, grade 1 – mild deficits detected by trained eye; grade 2 – deficits detected by most observers; grade 3 – prominent deficits detected by all observers; grade 4 – marked deficits (may fall during examination); grade 5 – recumbent.[1] Evaluation of gait for neurologic deficits is performed predominantly at the walk. Circling, head elevation and manipulation over obstacles accentuate neurologic gait abnormalities. Circles should begin large and slowly decrease in diameter until the horse is moving forward in a tight circle around the examiner. Symmetry and severity of weakness, ataxia and spasticity are evaluated during manipulation. Strength is assessed by the sway test, tail pull and manipulation on an inclined plane. Weakness is manifested by toe

dragging, muscle fasciculations, dipping of the trunk during weight bearing and inability to resist tail pull. Horses with ataxia will demonstrate delayed responses to proprioceptive positioning, stumbling, knuckling, circumduction (excessive flexion and abduction of the outside hindlimb during protraction), posting (pivoting on the inside hindlimb) and truncal sway. Spasticity (hypermetria) is characterized by excessive anterior phase of stride and failure to flex the hocks and carpi (tin soldier gait).

Observe the horse from the front, rear and side to assess muscle mass symmetry. Focal sweating or focal muscle mass loss indicates damage to focal gray matter in the spinal cord. Spontaneous movement, such as tremors, muscle fasciculations or myoclonia, indicates lower motor neuron dysfunction or primary muscle disease. The cervical vertebrae are palpated for pain and bony abnormalities. Gently pricking or pinching the neck, trunk and limbs in a caudal to cranial direction is performed to evaluate cutaneous sensation. Decreased cutaneous sensation will be observed caudal to a focal lesion in the spinal cord or nerve root. Hyperesthesia manifests as twitching, tensing of the abdomen, noxious behavior or self-mutilation and may indicate nerve root pain or neuritis.

Cranial nerve examination

A cranial nerve (CN) examination should be performed on horses with spinal ataxia to identify brain and brainstem dysfunction. Neurologic disorders that are most likely to result in cranial nerve abnormalities are equine protozoal myelitis, traumatic injury, cauda equina syndrome (polyneuritis equi) and viral encephalitides. Cervical stenotic myelopathy and equine degenerative myeloencephalopathy will not produce cranial nerve abnormalities.

The olfactory nerve (CN 1) is evaluated by determining the horse's interest in feed. The menace response is performed by stimulating the horse to blink by visual stimulation with your hand and assesses the optic nerve (CN 2, afferent) and the facial nerve (CN 7, efferent). The palpebral response is elicited by touching the patient's eyelid to stimulate blinking (Fig. 24.1), and this test evaluates the trigeminal nerve (CN 5, afferent) and the facial nerve (CN 7, efferent). The papillary light reflex produces bilateral miosis in response to a unilateral light source. The afferent response is induced by the optic nerve (CN 2), and the efferent response reflects activity of the oculomotor nerve (CN 3).

The eyes should be examined for evidence of strabismus (abnormal eye position) and nystagmus (rapid, rhythmic eye movement). Elevation of the head facilitates detection of strabismus in large animal patients. The oculomotor nerve (CN 3) controls the majority of extraocular muscles and dysfunction results in ventrolateral strabismus (in addition to failure of the papillary light response). Damage to the trochear nerve (CN 4) or trochlear nucleus paralyzes the dorsal oblique muscle of the globe, resulting in dorsal deviation of the medial angle of the iris. The abducens nerve (CN 6) controls the lateral rectus and retractor bulbi muscles and paralysis results in medial deviation of the globe and failure to retract the globe. The vestibulocochlear nerve (CN 8) provides upper motor neuron input to the extraocular muscles via the medial longitudinal fasciculus and vestibular dysfunction results in ipsilateral, ventrolateral strabismus (Fig. 24.2). The doll's eye response is performed by turning the patient's head in a horizontal plane to elicit physiologic nystagmus. Physiologic nystagmus requires normal f unction of the oculomotor, trochlear, abducens and vestibulocochlear nerves. Pathologic nystagmus is observed in horses with vestibulocochlear or cerebellar dysfunction without manipulation of the head. Peripheral vestibular damage (CN 8) produces horizontal nystagmus with the fast phase away from the lesion, whereas central damage (vestibular nuclei, cerebellum) produces horizontal, vertical or rotary nystagmus and the direction of nystagmus may change with head position.

Facial symmetry depends on function of the muscles of facial expression (facial nerve, CN 7) and the muscles of mas-

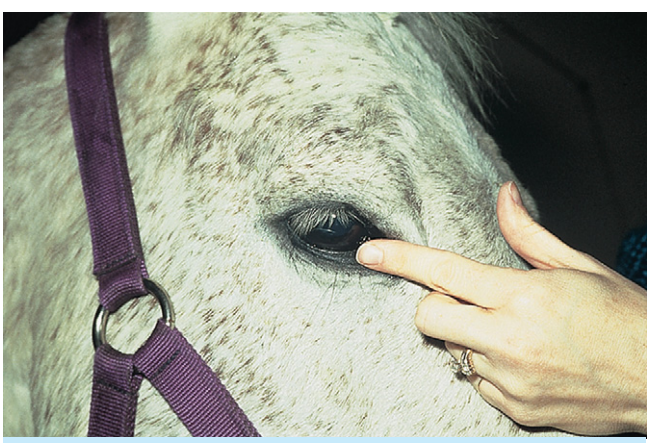

Fig. 24.1
Palpebral response elicited by touching the patient's eyelid to stimulate blinking (sensation – trigeminal nerve; motor response – facial nerve).

Fig. 24.2
Ventrolateral strabismus of the left eye in a horse with left vestibular dysfunction. Note the elevated head position to accentuate abnormal ocular position.

Fig. 24.3
Paralysis of the lips and nostrils in a horse with traumatic injury to the right buccal branch of the facial nerve (over the masseter muscle). The ipsilateral nostril is collapsed and the muzzle is pulled away from the lesion. The ear and eye are not affected by this peripheral lesion.

tication (trigeminal nerve, CN 5). Atrophy of the muscles of mastication (masseter and temporalis) is often accompanied by loss of facial sensation (failure to respond to digital pressure on the nasal septum). A dropped jaw is only observed in horses with bilateral trigeminal nerve damage. Damage to the facial nerve results in muzzle deviation away from the affected side, lack of palpebral response, ear droop, decreased nostril flare and buccal impaction of feed. Corneal ulceration is common due to inability to blink and decreased tear production due to damage to parasympathetic fibers to the lacrimal gland. Damage to the buccal branches of the facial nerve (over the masseter muscle) causes paralysis/paresis of the lips and nostrils only (Fig. 24.3). Tongue tone is controlled by the hypoglossal nerve (CN 12) and the gag reflex reflects function of the glossopharyngeal (CN 9) and vagus (CN 10) nerves.

Clinical signs of vestibular dysfunction (CN 8) include head tilt, nystagmus, falling, circling, reluctance to move and asymmetric ataxia with preservation of strength.[2] Horses prefer to lie on the side of the lesion and may lean on the wall towards the affected side when standing. When forced to move, the horse will take short, inco-ordinated steps in a circle toward the direction of the lesion. Extensor hypotonia ipsilateral to the lesion and hyper-reflexia of the extensor muscles of the contralateral side result in asymmetric ataxia. Nystagmus usually appears with the onset of other peripheral vestibular signs, but may last only 2–3 days due to central compensation. Other signs of vestibular disease may improve 2–3 weeks after onset due to visual and central compensation. Blindfolding a horse with compensated disease will result in ataxia and a head tilt (Romberg test).

Horner's syndrome results from damage to the sympathetic nerve and produces the classic clinical signs of miosis, ptosis, third eyelid prolapse and enophthalmos. Horner's syndrome in horses is unique in that they develop transient, ipsilateral sweating of head and neck (Fig. 24.4) and poor airflow through the ipsilateral nostril, in addition to the four classic signs.[3] The sympathetic nerve originates in the intermediate gray column from T1 to T3 and travels through the cranial mediastinum to the vagosympathetic trunk, to the cranial cervical ganglion caudomedial to tympanic bulla and guttural pouch, and travels with the ophthalmic branch of CN 5 to the periorbita. The most common sites of damage to the sympathetic nerve in horses are the jugular furrow (vagosympathetic trunk) and guttural pouch (internal carotid nerve). Lesions of the cervical intumescence and brachial plexus (avulsion) may produce Horner's syndrome in horses.

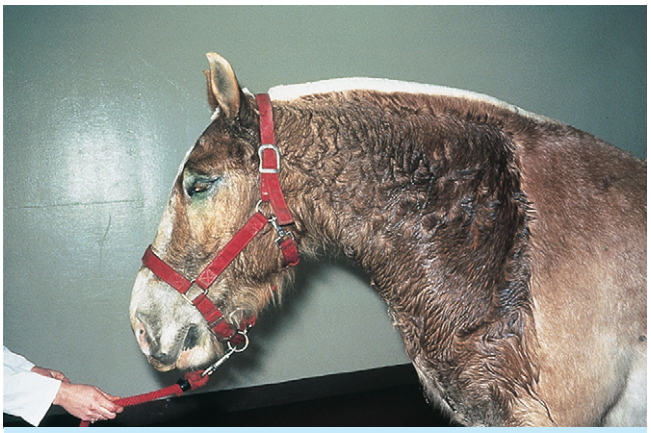

Fig. 24.4
Sweating of the head and neck in a horse with Horner's syndrome. Ipsilateral miosis, ptosis, enophthalmos and third eyelid prolapse are also present.

Differential diagnosis of spinal ataxia

- Cerebrospinal fluid (CSF) analysis and plain film radiography are often indicated for preliminary evaluation of horses with spinal ataxia.
- Cytologic evaluation of CSF obtained from the lumbosacral site most accurately reflects pathology of the spinal cord.
- The reference range for CSF white blood cell count is 0–6 cells/μL.
- The reference range of CSF total protein is 50–100 mg/dL.

There are numerous differential diagnoses for neurologic gait abnormalities in athletic horses, but the most common disorders in horses presenting for poor performance are cervical stenotic myelopathy (CSM), equine protozoal myeloencephalitis (EPM), spinal cord trauma and equine degenerative myeloencephalopathy (EDM). Plain film radiography, myelography and CSF analysis are indicated to evaluate horses with spinal ataxia. Horses with vertebral injuries usually demonstrate pain during manipulation of the neck and can be differentiated from CSM by plain film radiographic examination.

Abnormalities in CSF are rarely pathognomonic, but often are suggestive of the pathologic process. It is not unusual for horses with severe neurologic deficits to have normal CSF analysis due to the distance of the lesion from the sampling site, stage of the disease process or presence of non-exfoliative or extradural lesions.

Cerebrospinal fluid analysis

Cerebrospinal fluid flows in a cranial to caudal direction so cytologic evaluation of CSF obtained from the lumbosacral site more accurately reflects a pathologic process in the spinal cord.[4] Collection of CSF from the lumbosacral site is performed in standing, sedated horses and the conus medullaris can be penetrated without complication. Landmarks are the point of intersection of the dorsal midline and a line connecting the caudal border of the tuber coxae. A slight depression may be palpated caudal to L6, cranial to S2 and axial to the tuber sacrale. Upon penetration of the dura, some horses will react by flagging their tail, kicking or dropping in the hindlimbs. An 18 gauge, 15 cm needle with a stylet is recommended and CSF is collected passively or with gentle aspiration. Aggressive aspiration will result in blood contamination of the sample. Cerebrospinal fluid is submitted for analysis in a red top clot tube for cytologic analysis, immunoblot analysis and viral titers. If CSF fluid is bloody or discolored, the sample should be submitted in EDTA for cytologic evaluation.

Intracranial lesions are better represented in CSF samples obtained from the atlanto-occipital (AO) site. Atlanto-occipital collection of CSF requires general anesthesia and accidental penetration of the brainstem may result in death or neurologic dysfunction. The advantages of collection of CSF at the AO site include decreased risk of traumatic blood contamination of the sample and the ability to obtain CSF pressure with a water manometer.

Cerebrospinal fluid should appear clear, colorless and non-viscous and should not clot.[5] Cerebrospinal fluid can appear red from traumatic (iatrogenic) blood contamination or pathologic hemorrhage. Traumatic blood contamination is non-homogenous during collection and may clot. The CSF will appear clear following immediate centrifugation of a blood-contaminated sample. Pathologic hemorrhage appears homogenous during collection and the sample rarely clots. The supernatant is often xanthochromic following immediate centrifugation of the sample (see Fig. 24.13). Xanthochromia, or yellow discoloration of CSF, indicates the presence of bilirubin in the CSF due to peripheral hyperbilirubinemia or red blood cell lysis, within the central nervous system, secondary to hemorrhage or vasculitis. Turbidity of CSF can result from increased white blood cells, red blood cells, bacteria, fungi or epidural fat.

Cytologic examination should be performed within 30 minutes of sample collection. If expedient sample processing is not feasible, cells can be preserved by the addition of 40% ethanol to the sample at a 1:1 dilution. The range of total white blood cell count is 0–6 cell(s)/μL in normal horses. Differential cell count is determined from slides prepared by cytocentrifugation. Normal CSF consists of predominantly small lymphocytes and mononuclear cells. Neutrophils are not present in normal CSF and usually indicate an infectious disease process. Bacterial culture and Gram stain are recommended in cases with increased neutrophils in the CSF. Eosinophils in CSF samples may be associated with migrating parasites, fungal or protozoal infections. The reference range for protein content in equine CSF is 50–100 mg/dL. Increased protein in CSF can occur with blood contamination, hemorrhage, increased permeability of the blood–brain barrier, local immunoglobulin production or tissue degeneration.

Cervical stenotic myelopathy (Wobbler's syndrome, cervical vertebral malformation)

- Typical cases are characterized by symmetric ataxia with the hindlimbs more severely affected than the forelimbs.
- Plain film radiography provides an indication of the likelihood of spinal cord compression.
- Myelography determines the site(s) of spinal cord compression and characterizes the lesion as dynamic or static.
- CSM is likely a manifestation of developmental orthopedic disease and is primarily observed in young horses.
- Surgical intervention improves neurologic deficits by approximately two grades if performed within 1 month of onset of clinical signs.

Recognition

History and presenting complaint

Cervical stenotic myelopathy (CSM) is a common cause of symmetric spinal ataxia in horses from 6 months to 3 years of age.[6] In most instances, the rear limbs are more severely affected than the forelimbs by one neurologic grade. The clinical signs of spinal cord compression often progress for a brief period and then stabilize.

Physical examination

At rest, CSM-affected horses may have a basewide stance and demonstrate delayed responses to proprioceptive positioning. When prompted to back, horses may stand basewide, lean backward, drag their hindlimbs and/or step on their hindfoot with a forelimb. Moderate to severely affected horses will have lacerations on the heel bulbs (wobbler heels) and medial aspect of their forelimbs from over-reaching and interference. Horses with prolonged clinical signs of CSM will have hooves that are chipped, worn or squared at the toe. The muscula-

ture of the neck may appear disproportionately thin compared to the rest of the body and prominent articular processes of the fifth and sixth cervical vertebrae may be evident in some horses.[7]

Occasionally, forelimb ataxia may be more severe in horses with stenosis of the caudal cervical vertebrae (C6–C7) due to compression of the cervical intumescence. Alternatively, arthropathy of the caudal cervical vertebrae may produce cervical pain and forelimb lameness due to peripheral nerve compression, without producing clinical signs of spinal cord compression.[8] Affected horses typically travel with a short cranial phase of the stride and a low foot arc of their forelimb(s), and may stand or travel with their head and neck extended. Rarely, diskospondylosis of the cervical vertebrae will produce a short strided gait and cervical pain, with or without spinal ataxia. Horses with diskospondylosis or arthropathy of the caudal vertebrae may demonstrate increased rate and depth of respiration with cervical manipulation due to pain.

Owners often report a traumatic incident with the onset of clinical signs of CSM.[6] The traumatic incident may be the result of mild neurologic deficits with the injury exacerbating the clinical signs of spinal cord compression. Asymmetric ataxia and paresis may be occasionally observed in horses with dorsolateral compression of the spinal cord by proliferative, degenerative articular processes and periarticular soft tissue structures.[9] Infrequently, clinical signs of nerve root compression are seen such as cervical pain, atrophy of the cervical musculature, cutaneous hypalgesia and hyporeflexia of cervical reflexes adjacent to the site of spinal cord compression. These signs are more commonly observed in horses over 4 years of age with severe arthropathy of the caudal cervical vertebrae (C5–C7), and result from peripheral nerve compression by proliferative articular processes as the nerve root exits the vertebral canal through the intervertebral foramen.[7]

Special examination

Plain film radiography Equine protozoal myelitis and equine degenerative myeloencephalopathy are the most difficult diseases to differentiate from CSM. Cerebrospinal fluid analysis, radiographs of the cervical spine and myelography may be performed to differentiate these diseases. Cytologic analysis of cerebrospinal fluid is usually unremarkable in horses with CSM. In instances when cerebrospinal fluid analysis is abnormal, the alterations are consistent with acute spinal cord compression, such as mild xanthochromia or mild increases in protein concentrations.

Evaluation of standing cervical radiographs can determine the likelihood of CSM.[12] Radiographs of the cervical vertebrae can be obtained in standing, sedated horses. Three views, centered on C2, C4 and C6, are necessary in adult horses to obtain sufficient overlap for an adequate image of each cervical vertebra. A radiographic machine with a capacity of 1000 mA, 150 kV is required to obtain suitable radiographic quality. With the exception of ponies and neonatal horses, portable radiographic machines are inadequate for radiographic examination of the vertebral column. Radiographic cassette size for spinal studies is 35 × 43 cm and rare-earth intensifying screens, medium- to high-speed radiographic film, and aluminum interspaced focused grids are typically used. The standard focal spot to film distance for standing radiography and myelography is 100 cm. Long-scale (low mAs, high kVp) techniques may be used for survey radiographic examination to preserve resolution of soft tissues and vertebrae. Short-scale (high mAs, low kVp) techniques allow visualization of the contrast column and are used for myelographic examination.

Light sedation is sufficient for obtaining lateral projections of the cervical vertebrae in standing horses. Minimizing the distance of the neck to the cassette (minimize object–film distance) will diminish magnification artefact. In standing

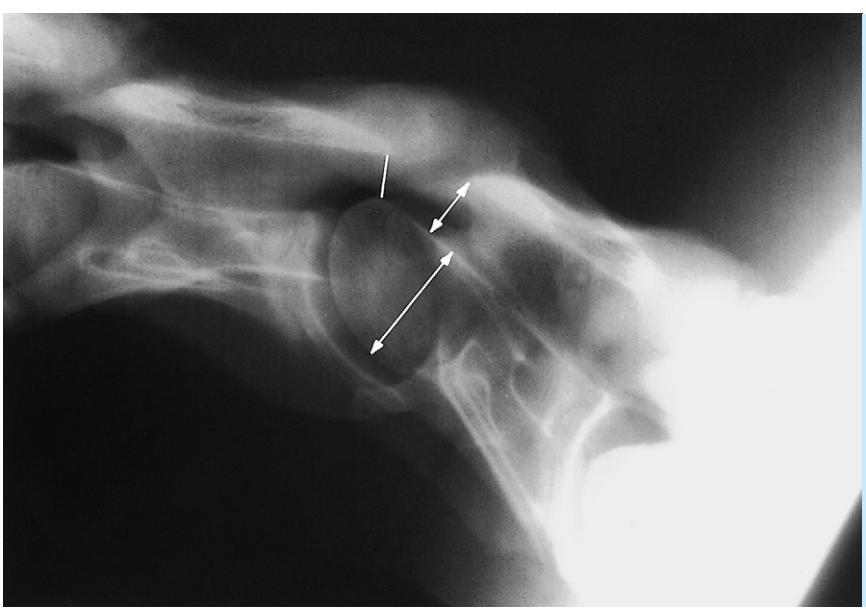

Fig. 24.5
Survey radiograph of the fifth and sixth cervical vertebrae in a horse with cervical stenotic myelopathy. The intervertebral canal diameter of the C5–C6 articulation is indicated by the solid line, and the intravertebral canal diameter of C6 is denoted by the double arrow. Sagittal ratio is calculated by dividing these measurements by the width of the vertebral body as shown on C6 (intravertebral sagittal ratio = 47%). Bony malformations include malalignment of the C5–C6 articulation, flare of caudal physis of C5 and caudal extension of the dorsal lamina of C5.

horses, only neutral views can be obtained. Precise positioning is imperative for interpretation of lateral radiographic projections of the cervical vertebrae. Rotation of the spine results in superimposition and distortion, which interfere with quantitative assessment of vertebral canal diameter.

Cervical radiographs are evaluated by subjective assessment of vertebral malformation and objective determination of vertebral canal diameter.[12] The five categories of bony malformation which are subjectively assessed in horses with CSM are degenerative joint disease of the articular processes, subluxation between adjacent vertebrae, flare of the caudal physis of the vertebral body, abnormal ossification patterns and caudal extension of the dorsal laminae (Figs 24.5–24.7). Although the presence of characteristic vertebral malformations supports the diagnosis of CSM, subjective evaluation of survey radiographs does not reliably discriminate between CSM-affected and unaffected horses.[10,13] Degenerative joint disease of the articular processes of the caudal cervical vertebrae is the most frequent and severe malformation observed in CSM-affected horses (Fig. 24.7). However, degenerative

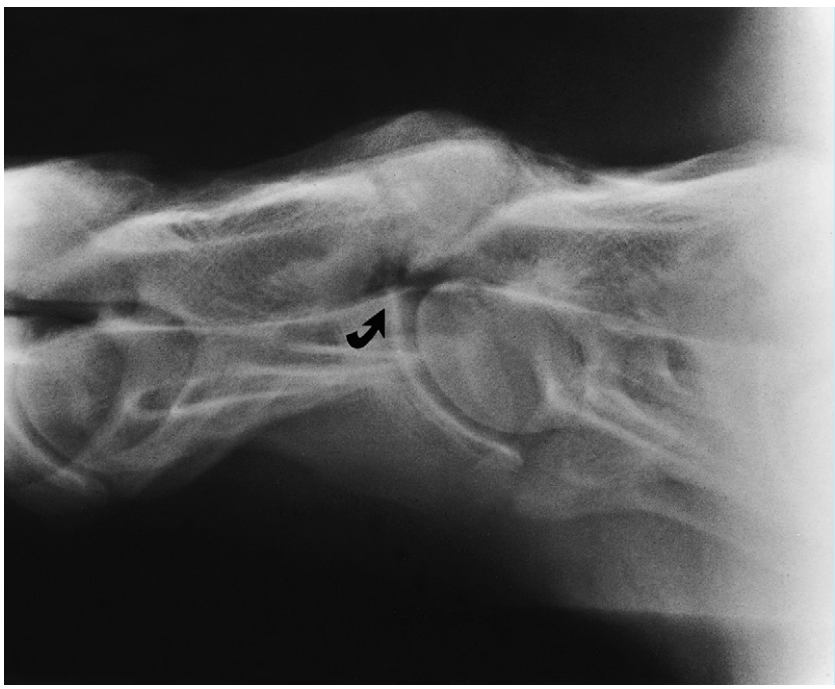

Fig. 24.6
Survey radiograph of the fifth and sixth cervical vertebrae. There is malalignment of the C5–C6 articulation, flare of caudal physis of C5 and mild degenerative joint disease on the articular processes of the C5–C6 articulation (arrow).

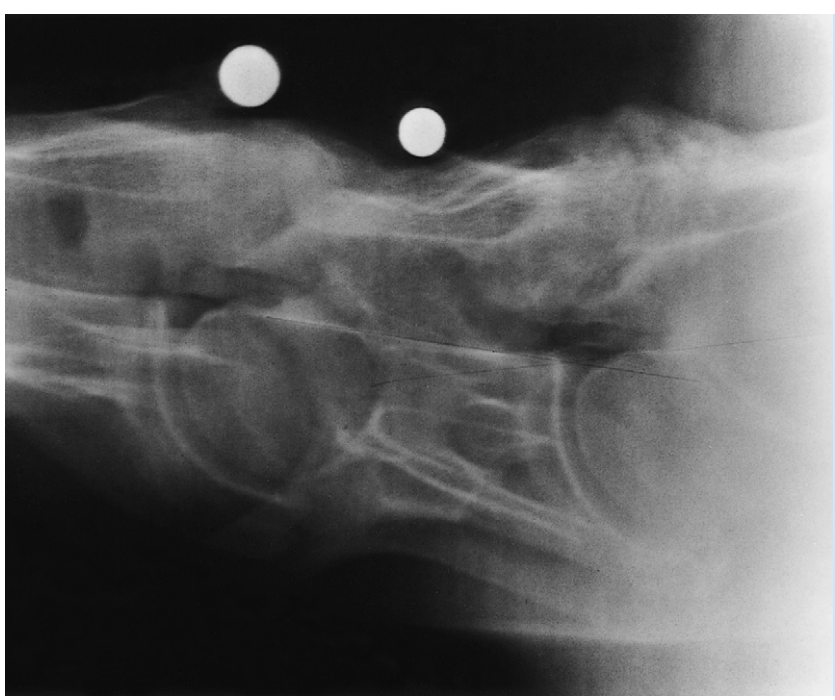

Fig. 24.7
Survey radiograph of the sixth and seventh cervical vertebrae demonstrating marked degenerative joint disease of the C6 (large dot) and C7 (small dot) articulation.

arthropathy occurs in 10–50% of non-ataxic horses and is the most frequent and severe vertebral malformation in horses without CSM.[12,13] Subjective evaluation of degenerative arthropathy of the articular processes without consideration of vertebral body diameter may lead to false-positive diagnosis of CSM.

The vertebral canal diameter is objectively assessed by determination of the sagittal ratio.[12] The sagittal ratio is obtained by dividing the minimum sagittal diameter of the vertebral canal by the width of the corresponding vertebral body (Fig. 24.5). The minimum sagittal diameter is measured from the dorsal aspect of the vertebral body to the ventral border of the dorsal laminae and the vertebral body width is measured perpendicular to the vertebral canal at the widest point of the cranial aspect of the vertebral body. The sagittal ratio eliminates error due to magnification because the vertebral canal and vertebral body are in the same anatomic plane. The sagittal ratio should exceed 52% from C4 to C6 and 56% at C7 in horses greater than 320 kg. The sensitivity and specificity of the sagittal ratio for identification of CSM-affected horses are approximately 89% for vertebral sites C4 through C7.

The semiquantitative scoring system developed by Mayhew should be used in foals less than 1 year of age to assess cervical radiographs for diagnosis of CSM.[14] The scoring system combines objective measurement of vertebral canal diameter and subjective evaluation of vertebral malformation. Stenosis of the vertebral canal is assessed by determination of the inter- and intravertebral minimum sagittal diameters which are corrected for radiographic magnification by dividing these values by the width of the vertebral body (Fig. 24.5). Foals that measure below the mean are allotted 5 points and foals that measure 2 SD below the mean or fall below the mean at multiple sites are allotted from 6 to 10 points. Cervical vertebral malformation is determined by subjective assessment of five categories: encroachment of the caudal epiphysis of the vertebral body dorsally into the vertebral canal, caudal extension of the dorsal lamina to the cranial physis of the next vertebra, angulation between adjacent vertebral bodies, abnormal ossification of the physis and degenerative joint disease of the articular processes. The maximal score allotted for each category of bony malformation is 5 points. A total score of 12 or higher (maximal total score 35) confirms the radiographic diagnosis of CSM. Stenosis of the vertebral canal and malalignment between adjacent vertebrae are the most discriminating parameters in this semiquantitative scoring system to differentiate CSM-affected from normal foals.

Survey radiographic examination of the cervical vertebrae determines the likelihood of spinal cord compression. Myelographic examination is required for the definitive diagnosis of CSM, identification of the location of affected vertebral sites and classification of spinal cord compressive lesions.[15] The clinician should use radiographic interpretation to classify the patient into one of the following categories:

1. Low sagittal ratio (< 48% at C4 through C6), moderate to severe bony malformation – perform myelographic examination to identify sites of spinal cord compression and classify lesions as static or dynamic
2. Marginal sagittal ratio (48% through 56%) mild to moderate bony malformation – perform myelographic examination to confirm or rule out CSM
3. High sagittal ratio (> 56%), minimal bony malformation – pursue other differential diagnoses.

Myelographic examination Myelography is performed under general anesthesia in lateral recumbency.[15] The landmarks for cisternal puncture at the AO site are the cranial border of the wings of the atlas, the caudal border of the occipital protuberance and the dorsal midline. The poll region is aseptically prepared and the head flexed at a 90° angle with the cervical vertebral column. The spinal needle (3.5 inch, 18 gauge with stylet) is introduced and directed towards the

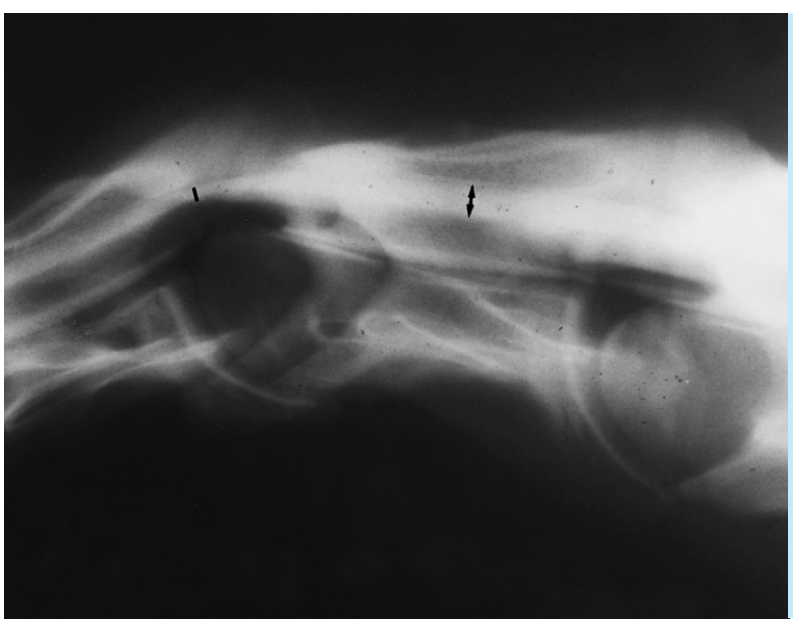

Fig. 24.8
Myelographic examination of C4 through C6 with the cervical spine in ventroflexion. Dynamic instability and spinal cord compression are present at C4–C5. The '50% rule' is determined by dividing the dorsal contrast column of the C4–C5 articulation (black line) to the midvertebral, dorsal contrast column caudal to the intervertebral space (double black arrow).

lower jaw. The spinal needle is advanced until the dura mater is penetrated, which often produces a 'popping' sensation. Clear cerebrospinal fluid should drip rapidly or flow from the hub with successful placement of the spinal needle. Twenty to 40 mL of contrast medium produces sufficient positive-contrast opacity to identify spinal cord compression in adult horses. The bevel of the spinal needle is directed caudally and contrast medium is injected at a constant rate over a 5-minute period. The head and neck are elevated under a wedged platform for 5 minutes at 30–45° to facilitate caudal flow of contrast medium. Iohexol (350 mg iodine/mL) is the most popular non-ionic, water-soluble contrast medium used for equine myelographic studies. This second-generation agent produces less neurotoxicity and meningeal irritation than metrizamide.

A complete myelographic examination should include neutral and stressed (flexed and extended) views of the cervical vertebrae.[15] Horses with obvious sites of spinal cord compression on neutral myelographic views, excessive flexion and extension of the neck should be avoided while obtaining dynamic views to prevent exacerbation of spinal cord injury. Spinal cord compression can be dynamic or static in horses with CSM.[6] Dynamic compression occurs due to vertebral instability and produces intermittent spinal cord compression during ventroflexion of the neck (Fig. 24.8); spinal cord compression is relieved when the neck is in the neutral position. Pathologic changes most commonly observed in horses with dynamic compression are instability between adjacent vertebrae, malformation of the caudal vertebral epiphysis (caudal epiphyseal flare) and malformation/malarticulation of the articular processes. Osteochondrosis of the articular processes is not always present at the site of spinal cord compression in horses with dynamic compression. The intervertebral sites most commonly affected by dynamic compression are C3–C4 and C4–C5. Static compression is defined as continuous spinal cord impingement, regardless of cervical position, and occurs predominantly in the caudal cervical region, C5–C6 and C6–C7 (Fig. 24.9). Static spinal cord compression is exacerbated by thickening of the dorsal lamina, hypertrophy of the ligamentum flavum and degenerative joint disease of the articular processes. Static and dynamic spinal cord compression are both associated with narrowing of the vertebral canal from C3 to C6, regardless of the site of spinal cord compression, indicating that generalized vertebral canal stenosis is an important factor in the pathophysiology of CSM.[12]

The ventral contrast column is often obliterated at the intervertebral space in normal myelographic studies, particularly when the neck is in the flexed position. A decrease of 50% or greater of the dorsal and ventral columns or less than 2 mm dorsal contrast column (or smaller) have been used previously as diagnostic criteria for CSM but have recently been discredited due to frequent false-positive diagnosis. Some investigators prefer to use a 20% reduction in the dural diameter compared to an adjacent midbody site to diagnose spinal cord compression. The decrease in the sagittal diameter of the contrast column is determined by comparing the value at the intervertebral space to a midvertebral site, cranial or caudal to the suspected intervertebral space.

Horses should be monitored for 24 hours after the myelographic procedure for depression, fever, seizure and worsening in neurologic status.[15] Worsening of neurologic status after myelography may result from spinal cord trauma during hyperflexion, iatrogenic puncture of the spinal cord or chemical meningitis. Administration of phenylbutazone (4.4 mg/kg, p.o., q.o.d.) from 1 day before to 1 day after myelographic examination will attenuate fever and depression associated with chemical meningitis.

Treatment and prognosis

Medical therapy

Conservative management of CSM-affected horses consists of anti-inflammatory therapy (glucocorticoids, dimethylsulfoxide, non-steroidal anti-inflammatory drugs) and exer-

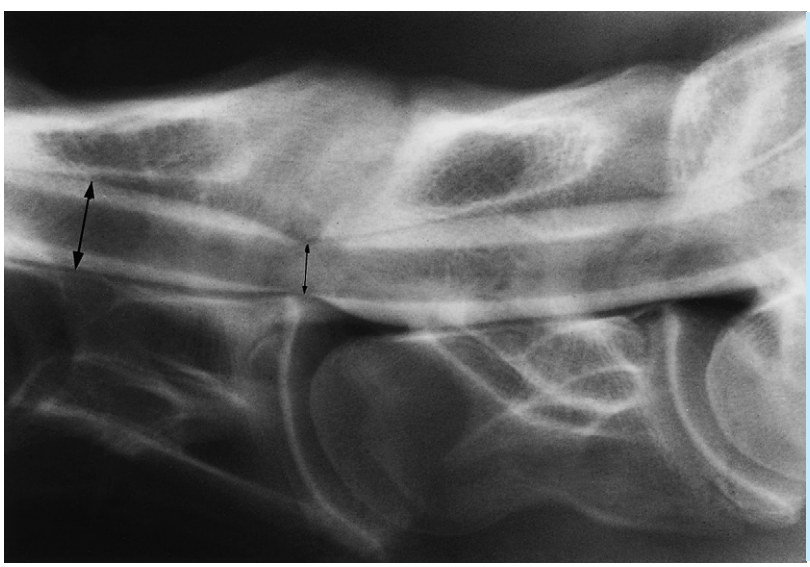

Fig. 24.9
Myelographic examination of C6–C7 with the cervical spine in neutral position. Static spinal cord compression is demonstrated by obliteration of the dorsal and ventral contrast columns. Percent reduction in dural diameter is determined by comparing the intervertebral space (small black arrow) to the midvertebral site cranial to the intervertebral space (large black arrow). Twenty percent or greater is diagnostic of compression (40% reduction in this case).

cise restriction. Anti-inflammatory therapy alone may decrease edema associated with spinal cord compression but full recovery without dietary or surgical intervention is unlikely. The most successful conservative treatment option for CSM-affected foals (< 1 year) is the 'paced diet' program[16] which is designed to correct endocrine imbalance associated with a high carbohydrate diet. This dietary program is restricted in energy and protein (65–75% NRC recommendations), but maintains balanced vitamin and mineral intake (minimum 100% NRC recommendations). Vitamins A and E are provided at three times NRC recommendations and selenium is supplemented to 0.3 ppm. Roughage is provided by pasture or low-quality (6–9% crude protein) grass hay. Stall confinement is recommended to minimize repetitive spinal cord compression from dynamic instability.

Horses with cervical pain and forelimb lameness due to cervical vertebral arthropathy may benefit from intra-articular administration of corticosteroids and/or chondroprotective agents.[17] Arthrocentesis of the cervical vertebral articulations (facets) is performed with ultrasound guidance using a 6″, 18 gauge spinal needle in the standing, sedated or recumbent horse. The cranial facet of the caudal vertebrae will appear superficial to the caudal facet of the cranial vertebrae. The articular space is accessed at the cranioventral opening of the articular facet, which is angled approximately 60° from the ultrasound beam. The needle should be introduced 5 cm cranial to the facet and inserted at a 30° angle to the skin surface. Joint penetration should be confirmed by aspiration of synovial fluid. If the neck is extended, the transverse process of the cranial vertebrae may obscure the path to the articulation. Intra-articular triamcinolone (6 mg/joint) or methylprednisolone (100 mg/joint) have produced a positive clinical response in approximately 50% of horses with arthrosis of the articular processes. The goal of intra-articular anti-inflammatory therapy should be to improve cervical mobility, reduce cervical pain and/or eliminate forelimb lameness. It is unlikely that intra-articular therapy will significantly improve clinical signs of spinal ataxia.

Surgical intervention

Surgical intervention is the most widely reported treatment for CSM.[18–20] The goals of surgical intervention are to stabilize the cervical vertebrae and decompress the spinal cord. Cervical vertebral interbody fusion (ventral stabilization) provides intervertebral stability for horses with dynamic spinal cord compression. Affected cervical vertebrae are fused in the extended position to provide immediate relief of spinal cord compression and prevent repetitive spinal cord trauma.

Dorsal laminectomy (subtotal Funkquist type-B) is performed to decompress static lesions by removing portions of the dorsal lamina, ligamentum flavum and joint capsule at the compressed site.[20] This procedure provides immediate decompression of the spinal cord but fatal postoperative complications may occur.[18] Ventral stabilization in horses with static compression induces remodeling of the articular processes and soft tissue structures, resulting in delayed decompression of the spinal cord over a period of weeks to months. Decompression is immediate with dorsal laminectomy but because of its relative safety, ventral stabilization is the technique of choice for dynamic and static compressive lesions for many equine surgeons.

Ventral stabilization improves the neurologic status of horses with CSM by one to two neurologic grades, with 12–62% of horses returning to athletic function. Dorsal laminectomy results in improvement in neurologic status in 40–75% of horses with static compression. The most important patient factor for determination of postoperative prognosis is duration of clinical signs prior to surgical intervention. Horses with clinical signs less than 1 month prior to surgery are more likely to return to athletic function than are horses with clinical signs of greater than 3 months' duration.[18] Subtotal laminectomy and ventral stabilization for static compression of the caudal cervical vertebrae are associated with fatal postoperative complications including vertebral body fracture, spinal cord edema and implant failure.

Postoperatively, horses should be maintained with strict stall rest for 3 weeks and fed from a hay net to minimize motion at the surgery site. The duration of convalescence and rehabilitation following cervical vertebral interbody fusion is approximately 6–12 months. An individualized exercise program, determined by projected use and neurologic status of the horse, should be designed for promotion of muscular strength. Extended exercise at slow speed, including ponying and lunging on inclines, is recommended during rehabilitation. Neurologic examination should be performed to determine ability to return to athletic function following surgery. It is unlikely that significant improvement in neurologic status will occur beyond the 1 year postoperative time period.

Etiology

Cervical stenotic myelopathy appears to be a manifestation of developmental orthopedic disease. Developmental orthopedic disease of the appendicular skeleton, such as physitis, joint effusion, osteochondrosis and flexural limb deformities, occurs more frequently in young horses with CSM.[11] A direct cause-and-effect relationship between osteochondrosis and CSM has not been identified; however, the association between the frequency of occurrence of osteochondrosis and CSM indicates that the pathophysiology of these two conditions is similar. It is unlikely that CSM is heritable by simple Mendelian dominant/recessive patterns. The mode of inheritance more likely involves multiple alleles and variable penetrance which determine genetic predisposition to CSM. A high plane of nutrition, micronutrient imbalance, rapid growth, trauma and abnormal biomechanical forces are environmental factors that appear to contribute to the development of CSM in genetically predisposed individuals.

Epidemiology

Cervical stenotic myelopathy typically produces spinal ataxia in young horses from 6 months to 3 years of age. Cervical

stenotic myelopathy has been reported in most light and draft breeds. Thoroughbreds are particularly predisposed, wherein the prevalence is approximately 2% of the population. Approximately 10–50% of Thoroughbreds have characteristic developmental malformations of the cervical vertebrae without spinal cord compression.[10] Male horses are more frequently affected than females. The majority of CSM-affected horses are less than 3 years of age at presentation, although middle-aged horses are occasionally diagnosed with acute-onset CSM.[6]

Equine protozoal myeloencephalitis

- EPM may manifest a variety of neurologic deficits including single limb dysfunction, spinal ataxia or cranial nerve abnormalities.
- The definitive host of EPM is the opposum, and numerous small mammals can serve as intermediate hosts.
- Diagnosis is primarily based on neurologic examination, history and disease progression; immunoblot analysis of CSF provides supportive evidence of EPM.
- Ponazuril is the first FDA-approved drug labeled for treatment of EPM.

Recognition

Presenting complaint

Clinical EPM is often reported in well-maintained, young (3–6 years) performance horses.[22] The onset of clinical signs can vary from acute to insidious and distribution of neurologic deficits may be focal or multifocal. Horses may progress from normal to recumbent over a period of hours. Conversely, an owner of an EPM-affected horse may describe an obscure lameness of weeks' to months' duration.

Physical examination

The clinical signs are dependent on the location of the organism within the central nervous system. The spinal cord is most frequently affected (85%) and the most recognizable manifestation of EPM is asymmetric spinal ataxia with focal muscle mass loss or focal sweating. Asymmetric gluteal muscle atrophy is particularly common (Fig. 24.10). Horses may present with a single limb lameness, which does not originate from a musculoskeletal disorder. Symmetric spinal ataxia without muscle mass loss is also frequently observed. Horses with EPM rarely demonstrate pain or response to analgesic medication. Administration of analgesic medication may help distinguish traumatic injury from EPM. Horses with damage to the brainstem and cerebral cortex by EPM are less frequently observed (15%), and clinical signs of parasites within these regions of the central nervous system reflect the neuroanatomic localization of the organisms, including cranial nerve deficits, proprioceptive deficits, weakness, altered mentation and/or seizures. Dysphagia, vestibular dysfunction, facial nerve paralysis and atrophy of the masseter and temporalis muscles and tongue are frequently reported clinical signs in horses with EPM of the brainstem. Vital parameters are typically unremarkable in affected horses.

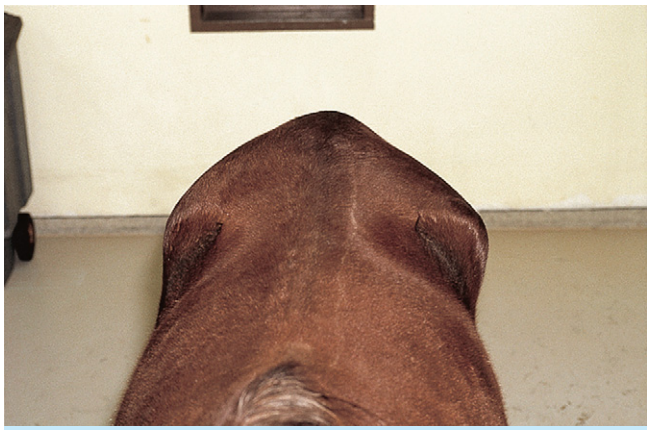

Fig. 24.10
Asymmetric gluteal muscle atrophy in a horse with equine protozoal myelitis.

Diagnosis

In most instances, CSM is the most difficult disease to differentiate from EPM. Asymmetric ataxia, focal sweating and focal muscle mass loss should direct diagnostic efforts towards EPM. However, symmetric spinal ataxia does not preclude a diagnosis of EPM. Horses with symmetric ataxia due to EPM are differentiated from CSM on the basis of standing radiographic evaluation, CSF immunoblot analysis for *Sarcocystis neurona*, and myelographic evaluation. Horses with EPM of the brain and brainstem may be difficult to distinguish from those with viral encephalitis (Eastern equine encephalitis, Western equine encephalitis, West Nile virus and rabies). Viral encephalitides may be differentiated from EPM by viral serology, CSF cytology and antibody detection and clinical course of disease.

Hematologic and biochemical analysis are unremarkable in horses with EPM. Cytologic analysis of CSF may reveal mild, non-specific inflammation characterized by mononuclear pleocytosis and mild protein elevation. However, CSF analysis is often unremarkable in horses with EPM. Immunoblot analysis (Western blot analysis) identifies antibody against the organism in serum and CSF. Positive immunoblot analysis of serum samples cannot be used to definitely diagnose EPM because it simply indicates exposure to the organism and not necessarily the presence of disease (poor positive predictive value). A negative immunoblot analysis test of serum from a horse with neurologic disease does indicate that the diagnosis of EPM is unlikely (high negative predictive value).[26]

Positive immunoblot analysis of cerebrospinal fluid may indicate intrathecal production of antibody to the organism. The sensitivity and specificity of immunoblot analysis for diagnosis of EPM are approximately 90%.[22] The most

common cause of false-positive diagnosis is iatrogenic hemorrhage during CSF tap. However, damage to the blood–brain barrier due to a pathologic process (i.e. trauma, vasculitis) may also result in false-positive test results from CSF of seropositive horses. It is important to recognize that immunoblot analysis of CSF is frequently false positive in CSM-affected horses if they live in a geographic area with a high EPM seroprevalence. Therefore, differentiation of CSM and EPM should not be determined on the basis of immunoblot analysis alone.

Treatment and prognosis

Prompt initiation of antiprotozoal treatment is warranted in suspect cases of EPM, often prior to obtaining results of immunoblot analysis on CSF. Ponazuril (Marquis®, Bayer Animal Health) is the first FDA-approved drug for treatment of EPM. It is a coccidiacidal drug, belonging to the triazine family, and is a primary metabolite of toltrazuril.[27] Ponazuril is readily absorbed from the gastrointestinal tract and penetrates the CSF to attain therapeutic drug concentrations. Serum concentrations are approximately 25 times CSF concentrations. The label treatment regimen is 5 mg/kg orally, once a day for 28 days. If a horse does not improve on this dose within 2 weeks of initiation of therapy, 10 mg/kg per day can be prescribed for an additional 28 days. Some horses relapse after a 28-day course of therapy indicating a longer period of drug administration may be warranted.[27] Sixty percent of horses with EPM improve one neurologic grade during the 28-day treatment period with 5 mg/kg, and approximately 65% of horses improve one neurologic grade with 10 mg/kg.[28] During the safety phase of the approval process, the following adverse effects were recorded in horses receiving either 1×, 2× or 6× the recommended dosage: blisters on the nose and mouth, hives, loose stools, mild colic, sporadic inappetance and edema of the lamina propria of the uterine epithelium.[29] Ponazuril has not been approved for use during pregnancy or lactation and has not been evaluated for drug interactions.

Traditional therapy consists of a combination of sulfa antimicrobials and pyrimethamine (1.0 mg/kg s.i.d.).[30] Sulfadiazine (20 mg/kg s.i.d.) appears to be superior to sulfamethoxazole for treatment of EPM, on the basis of volume of distribution, protein binding, longer $t_{1/2}$, lower MIC for *Toxoplasma* and higher mean plasma concentrations. Potential adverse effects associated with administration of pyrimethamine and sulfa antimicrobials include anemia, leukopenia, abortion, antibiotic-induced colitis and treatment crisis. Hay and grain inhibit intestinal absorption so EPM therapy should be administered on an empty stomach. Sulfadiazine and pyrimethamine inhibit protozoal replication but are not cidal, which relies on an immunologic response to destroy the organism.[22] The recommended treatment period is 90–120 days, and the prognosis for return to normal neurologic function is approximately 60%. Poor prognostic indicators include recumbency, focal muscle mass loss and prolonged duration of clinical signs prior to administration of antimicrobial therapy. The decision to discontinue therapy is determined by significant improvement in clinical signs of EPM. Premature discontinuation of therapy may result in relapse of neurologic signs. The neurologic signs of relapse are similar to the first episode, and the incidence of relapse is approximately 10–15%.

Immunostimulant therapy has been suggested as ancillary therapy for EPM, although efficacy of these products has not been rigorously tested in horses with clinical signs of disease. Corticosteroids should be avoided in horses suspected to have EPM due to the immunosuppressive effects. *Sarcocystis neurona* organisms are more likely to be observed at necropsy examination of the central nervous system of horses receiving corticosteroids for treatment of EPM. However, administration of a single dose may be beneficial in a recumbent horse with EPM.

Epidemiology

Equine protozoal myeloencephalitis is the most common cause of neurologic disease in horses in most regions of North America. Protozoal myeloencephalitis has been recognized in horses since the 1970s but it was not until 1991 that the primary parasite responsible for EPM was cultured from a horse and given the name *Sarcocystis neurona*. Opossums are the definitive host of *S. neurona* and several small mammals (skunk, armadillo, domestic cat, raccoon) are capable of serving as intermediate hosts to complete the lifecycle.[21] The role of each of these potential intermediate hosts in the natural lifecycle of *S. neurona* is not clear. Transmission of the parasite from the above-mentioned intermediate hosts to the definitive host is probably accomplished by ingestion of dead intermediate hosts by the opossum, rather than the typical prey-predator lifecycle observed with most *Sarcocystis* spp.

Horses appear to be dead-end, aberrant hosts (not capable of transmitting infection from horse to horse).[22] The sporocyst in opossum feces appears to be the infectious form of the organism for horses. The route of migration of the parasite from the time of ingestion of sporocysts to parasitism of the central nervous system is unknown. Control of the disease should be centered on limiting exposure of horses to opossum feces; approximately 20% of opossums excrete infectious sporocysts in the wild.[23] Disposal of skunk, raccoon, armadillo or cat carcasses from equine premises will prevent opossums from eating carrion, which may remove the primary source of infection for the definitive host. The most important form of contaminated equine feeds (i.e. hay, pasture, grain, water) is currently unknown.

Recent studies estimate 44–55% of horses in North America have been exposed to *S. neurona*, based on seroconversion.[24] Variability in seroprevalence across the United States appears dependent on environmental factors such as number of freezing days (decreased incidence) and relative humidity (increased incidence). Despite the high exposure rate, clinical disease remains infrequent (approximately 2%) in horses exposed to the parasite. Evidence suggests that some horses may clear the organism from the central nervous

system routinely, which may explain the relatively high number of normal horses with CSF antibodies to *S. neurona* compared to the prevalence of clinical disease. Individual risk factors for development of clinical disease are suspected to be stress, corticosteroid administration, general anesthesia, strenuous exercise, long-distance transport and natural individual susceptibility. Most commonly, a single horse on a farm will develop clinical signs of disease. Epizootics with > 50% clinical attack rates have been reported on farms with large resident opossum populations with access to the feed sources.[25]

Vertebral trauma

- The most common sites of vertebral injury in horses vary with the age.
- Diagnosis of vertebral fracture is determined by plain film radiography or nuclear scintigraphy.
- Medical therapy is indicated in ambulatory patients with stable fractures.
- Surgical therapy is indicated in unstable fractures of the cervical or sacral vertebrae.

Cervical fractures

Traumatic spinal cord injury is a common etiology of spinal ataxia in performance horses, and can be difficult to diagnose. The most common site of traumatic spinal cord injury is dependent on age of the horse.[31] Cervical fractures are more common in foals and result from hyperextension, hyperflexion and luxation. Adult horses are more likely than foals to develop fractures of the caudal thoracic and lumbar spine. Regardless of the site of the fracture, the prognosis is dependent on the severity of the initial injury.

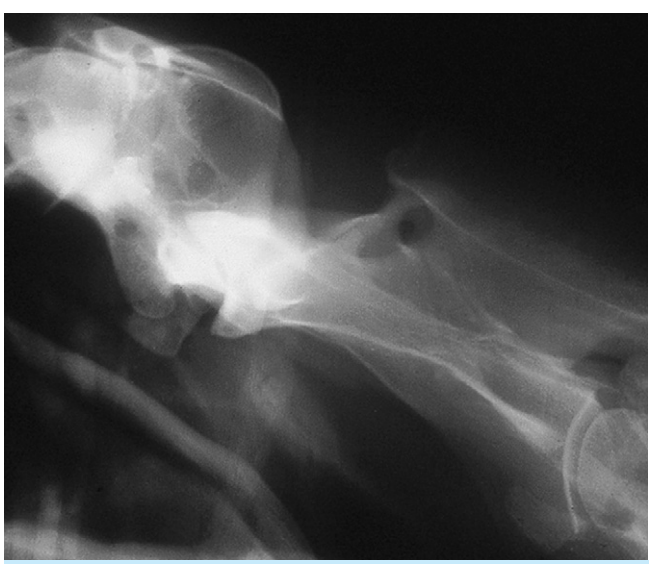

Fig. 24.11
Cervical radiograph from a weanling that reared over backward and impacted on the pole. One wing of atlas (C1) is displaced ventrally. The odontoid process (dens) of the axis (C2) is fractured and the entire axis is displaced ventrally. The foal demonstrates grade 2 symmetric ataxia and a mechanical head tilt.

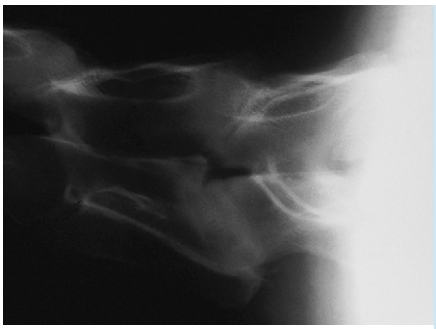

Fig. 24.12
Cervical radiograph of C4 through C7 from an adult horse after a head-on collision with a tree. A vertebral body compression fracture is present at C6. The horse was recumbent.

The most common cervical vertebral fracture in foals is axial dens fracture and atlantoaxial subluxation (Fig. 24.11).[32] Atlantoaxial subluxation may result from resisting head restraint (hyperextension) or somersault (hyperflexion) injuries in young horses. Foals with atlantoaxial subluxation will have a stiff, splinted neck and, in some instances, audible crepitation with manipulation of the head. Neurologic gait deficits range from none to marked tetraparesis and ataxia. Foals may have a head tilt, without other signs of vestibular dysfunction, due to mechanical malalignment of the C1–C2 articulation. Radiograph views of the cervical spine reveal widening of the cranial physis of the axis. In foals with neurologic gait deficits, cranioventral luxation of axis usually occurs with increased distance between the spine of the atlas and axis and between the floor of the atlas and the axial dens.

In adult horses, compression fractures of the vertebral body and articular facet fractures are the most common fractures of the cervical vertebrae and occur with head-on collision and falling, rolling injuries in horses (especially jumping and steeplechasing), respectively (Fig. 24.12).[31] Cervical vertebral fractures are associated with pain, resistance to manipulation and splinting of the neck. Focal sweating, loss of cutaneous sensation and torticollis may be observed if exiting nerve roots are damaged by the fracture. The severity of neurologic gait deficits will range from none to tetraplegia dependent on the degree of vertebral luxation and spinal cord injury.

Thoracic fractures

Thoracic fractures are more common in adult horses than foals and result from falling over a jump or flipping over backwards.[31] The first three thoracic vertebrae are most likely to fracture, followed by T12. Fracture of the thoracolumbar junction is observed in horses that fall and roll down an embankment. Clinical signs in horses with T12 or thoracolumbar fractures include paraparesis and tracking or drifting of the hindlinbs to one side. Dorsal spinous process fractures of T4 to T8 occur in horses that flip over backwards. These fractures are not usually associated with fracture of

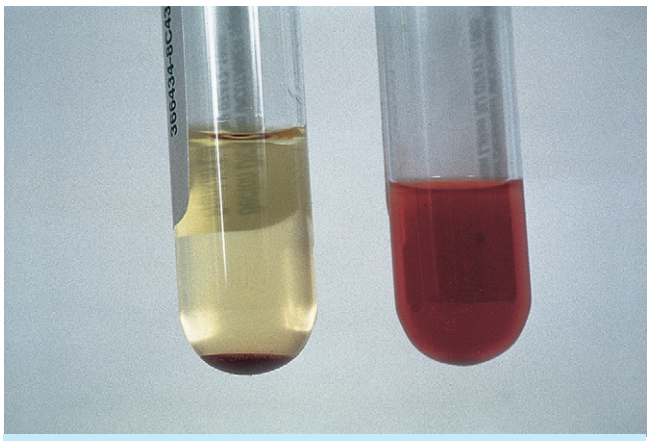

Fig. 24.13
Cerebrospinal fluid from a horse with head trauma. CSF appears hemorrhagic prior to centrifugation (right) and xanthochromic (supernatant) with a red cell pellet after centrifugation (left).

the vertebral bodies, although neurologic gait deficits may result from contusion of the spinal cord. Sacral fractures occur with dog-sitting incidents and may result in loss of tail function, urinary incontinence, loss of anal tone and fecal retention.

Diagnosis of vertebral fractures can be difficult. Despite the presence of a fracture, overlapping structures and surrounding muscle mass render radiographic projections of the vertebrae difficult to interpret.[33] Vertebral fracture should be investigated in horses that have a history of a traumatic event, pain on palpation, clinical signs of tetra- or paraparesis and/or hyperesthesia or loss of cutaneous sensation. Plain film radiography may identify cervical, sacral and thoracic fractures. Fractures of the lumbar vertebrae are not amenable to radiographic examination due to the soft tissue mass surrounding the vertebral bodies in this region.[31] Nuclear scintigraphy may enable the clinician to identify non-displaced cervical fractures and fractures of the lumbar spine which are inaccessible to radiographic examination. Cerebrospinal fluid is often hemorraghic in horses with CNS trauma. The supernatant will appear xanthochromic after centrifugation if the hemorrhage is pathologic in origin (as opposed to iatrogenic) (Fig. 24.13).

Treatment and prognosis

Medical therapy

Conservative management, consisting of stall rest and anti-inflammatory therapy, may be rewarding in horses that are ambulatory after vertebral fracture.[33] The therapeutic approach for foals with atlantoaxial subluxation is dependent upon the severity of neurologic deficits and the degree of malalignment and instability of the vertebrae. Stall rest and conservative anti-inflammatory therapy may be successful in foals with relatively stable, non-displaced fractures.

Early medical therapy (less than 8 hours after injury) to prevent edema formation consistently produces a more favorable outcome than does late intervention.[33] Glucocorticoids (dexamethasone 0.1–0.2 mg/kg, i.v., q 8–12 h) minimize cerebral edema and secondary injury by prevention of membrane lipoperoxidation and inhibition of arachidonic acid metabolites. Dimethyl sulfoxide (1 g/kg, i.v., s.i.d. to b.i.d.) may prevent or reduce cerebral edema. Rapid administration of the 10% DMSO solution may result in intravascular hemolysis and hemoglobinuria. Mannitol (0.25–1 g/kg, i.v. over 20 minutes as a 20% solution, b.i.d. to t.i.d.) reduces existing CNS edema via hyperosmolar dehydration and may reduce CSF pressure within 30 minutes of administration. Non-steroidal anti-inflammatory drugs have limited ability to reduce CNS edema and inflammation but analgesic properties may relieve malaise and reduce depression. Liberal administration of anti-inflammatory drugs may permit excessive movement by the horse and loss of muscular splinting of the fracture, which may promote displacement of fracture fragments.

Surgical intervention

Surgical intervention is recommended for foals with unstable cervical fractures and severe neurologic gait deficits.[32] Surgical approaches for correction of atlantoaxial subluxation in foals includes compression plating, Steinmann pin fixation, dorsal laminectomy of the caudal atlas and ventral cervical fusion.[31] Surgical stabilization of vertebral fractures is rarely attempted in adult horses. Successful lag screw fixation of vertebral body fracture and dorsal decompression of a transverse, ventrally displaced sacral fracture have been reported.[34] Surgical intervention has not been reported in horses with thoracic or lumbar vertebral fractures. Dorsal spinous process fractures may require surgical removal if sequestration of bone fragments occurs.

Exuberant callus formation may impinge on the spinal cord and produce neurologic gait deficits months after the injury. Therefore, the ultimate usefulness of a horse with traumatic spinal cord damage may not be determined for a prolonged period of time after injury. Nonetheless, response to therapy within the first few days is a good prognostic indicator.

Equine degenerative myeloencephalopathy

- EDM produces symmetric spinal ataxia in young (6 mo to 2 yr) horses.
- There is no ante-mortem diagnostic test so EDM is a diagnosis of exclusion.
- Vitamin E supplementation may prevent or stabilize disease in predisposed individuals.
- Predisposing factors include heredity and environmental factors that reduce or inhibit dietary vitamin E.

Recognition

Neurologic examination

Horses with EDM demonstrate symmetric ataxia, spasticity and weakness.[35] Hypermetria and weakness are particularly prominent. During neurologic examination, affected horses demonstrate circumduction, posting, abnormal proprioceptive positioning and abnormal sway test. The severity of forelimb ataxia may equal that of the hind limbs.[40] Most horses with EDM have difficulty backing and may dog-sit or fall when forced to back. Horses with chronic disease may develop signs of lower motor neuron dysfunction such as decreased cutaneous truncal, cervical, cervicofacial and laryngeal adductory slap reflexes.[40] The typical clinical course of EDM is characterized by insidious progression of neurologic gait deficits, followed by stabilization of clinical signs. Clinical signs do not progress after maturity and affected horses rarely develop quadriparesis or tetraplegia.

Diagnosis

Equine degenerative myeloencephalopathy is a diagnosis of exclusion.[41] There is no ante-mortem diagnostic test so lumbosacral CSF analysis, cervical radiographs and/or myelography are performed to eliminate other potential causes of spinal ataxia in young horses.[36] The results of these tests are unremarkable in horses with EDM. Plasma α-tocopherol concentration may be low (< 1.0 μg/mL) or normal (1.5–3.0 μg/mL) in horses with EDM depending on the stage of the disease process. A single sample reflects the current status of the horse and cannot detect a deficiency that may have existed prior to or during the degenerative process.[41] Therefore, plasma α-tocopherol provides supportive evidence, but cannot be used to diagnose or rule out EDM. The clinician may suspect EDM based on neurologic signs (hyporeflexia, forelimbs and hindlimbs equally affected, weakness and hypermetria) and familial history. Foals of dams that have previously produced an EDM-affected foal are 25 times more likely to develop EDM.[37] Nonetheless, the definitive diagnosis is determined by necropsy examination.

There are no gross lesions of EDM. The caudal medulla oblongata and midthoracic spinal cord demonstrate the most severe histopathologic lesions of EDM.[40] Findings include neuroaxonal dystrophy of brainstem nuclei (nucleus cuneatus, nucleus gracilis and the lateral cuneate nucleus) and throughout the spinal cord.[40] The most prominent gray matter lesions in the spinal cord are in the nucleus of the spinocerebellar tracts of the thoracic spinal cord. The most prominent white matter lesions are spheroid formation (swollen dystrophic axons – Fig. 24.14) and lipofuscin accumulation in the dorsal and ventral spinocerebellar tract in the lateral funiculus and ventromedial funiculus of the cervicothoracic spinal cord. The lipofuscin pigment is believed to represent malonaldehyde, the end-product of lipid peroxidation of degenerating spinal cord.[40]

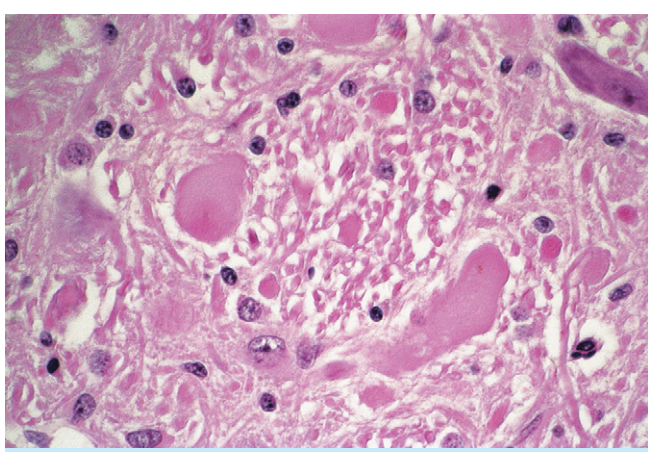

Fig. 24.14
Photomicrograph from the brainstem of a 6-month-old colt with equine degenerative myeloencephalopathy. Spheroids, representing swollen dystrophic axons, are characteristic of EDM. H&E ×100.

Treatment and prevention

Dietary vitamin E supplementation may be used to prevent or treat EDM. The current recommendation for treatment of horses with clinical signs of disease is 6000 IU of d,l-α-tocopherol acetate (with 60 mL corn oil) daily through the third year of life. This dose has been reported to improve the neurologic status of affected horses.[41] For prevention of EDM in genetically predisposed horses, α-tocopherol acetate is supplemented in the diet at 1000–2000 IU/day during pregnancy and through the first year of life. Horses with access to pasture or properly cured hay ingest adequate amounts of vitamin E and do not require supplementation. Supplementation is recommended for all horses eating hay that has been improperly cured or stored for an extended period of time. Combination vitamin E/selenium products can produce selenium toxicity at doses required to achieve the recommended level of vitamin E supplementation.[41]

Epidemiology and pathophysiology

Equine degenerative myeloencephalopathy is a diffuse degenerative disease of young horses affecting the brainstem and spinal cord. Ataxia typically develops between 3 and 12 months of age.[35] Equine degenerative myeloencephalopathy has been reported in most light breeds of horses and appears familial in Standardbreds, Appaloosas, Paso Finos and zebras.[36] There is no gender predilection. Equine degenerative myeloencephalopathy has been reported most frequently from the north-eastern United States, wherein up to 45% of ataxic horses have a histopathologic diagnosis of EDM. Predisposing factors for development of EDM include use of insecticides, exposure to wood preservatives and turnout in dirt lots. Access to green pasture appears protective.[37]

Vitamin E is suspected to play a pivotal role in the pathophysiology of EDM. The histopathologic lesions of EDM are similar to experimentally induced vitamin E deficiency in other

species. Low plasma α-tocopherol concentrations are observed in clinical cases of EDM and prophylactic administration of vitamin E to genetically predisposed foals and pregnant mares decreases the incidence of EDM.[38] Low plasma α-tocopherol concentration from 6 weeks to 10 months of age appears to be a critical factor in the development of EDM in hereditarily predisposed foals. Low α-tocopherol values do not reflect a primary defect of gastrointestinal absorption in this population of foals, but may reflect inappropriate assimilation of vitamin E.[39]

Head shaking

- Head shaking is seasonal and may be triggered by exposure to sunlight.
- Affected horses are suspected to experience neuropathic pain in the form of a burning sensation around their muzzle.
- Response to medical therapy is variable and may be transient.
- Surgical therapy should be considered a salvage procedure and should only be performed in horses demonstrating a consistent response to diagnostic nerve blocks.

Recognition

Presenting complaint

Horses with head shaking disorder toss their heads in the absence of obvious external stimuli. Some horses will head shake with such violence that they are dangerous to the handler or rider. Photo-induced horses attempt to avoid direct sunlight by seeking shade or hiding their heads in unusual places. Clinical signs are often seasonal, abating during winter months and returning in spring. The condition affects adult horses, and geldings and Thoroughbreds appear to be over-represented.[45] The behavior is exhibited at rest and during exercise. Violent head shaking at the beginning of exercise is common and can render the horse unusable for riding. A change in environment may result in some horses failing to exhibit the behavior on the day of examination so the owner should obtain a videotape of the head shaking behavior prior to their appointment.

Physical examination

Head shakers demonstrate sudden, violent jerking movements of the head in the absence of obvious external stimuli.[44] Quick vertical flips or jerking movements (as if stung by a bee on the end of the nose) are characteristic, but some horses may intersperse horizontal and rotary activity.[42] Affected horses often snort, sneeze and rub their nose. Horses that demonstrate head shaking behavior due to other etiologies usually perform intentional, head tossing behavior, rather than rapid, bee-sting vertical flips characteristic of photic head shaking.

Diagnosis

There are numerous differential diagnoses for head shaking in horses. Next to trigeminal neuritis, otitis, dental disease, TMJ osteitis and foreign body may be the most common causes of head shaking. Ophthalmologic, otic, oral and endoscopic examination of the upper respiratory tract (including guttural pouches) and radiographic examination of the skull may be performed in horses demonstrating head shaking behavior to rule out these differential diagnoses. Findings are unremarkable in horses with photic head shaking. To determine if the behavior is induced by natural light, the horse should be placed under the following conditions: direct sunlight, blindfolded, night-time outdoors, dark lenses in direct sunlight. If sunlight has been identified as the stimulus for infraorbital pain, reduced sunlight exposure by providing shelter or a mask is indicated.[42]

Treatment and prognosis

Medical therapy

The response of photic head shakers to medical therapy is variable. Favorable, transient and non-response to therapy are commonly reported outcomes of medical management. Cyproheptidine (0.3–0.6 mg/kg, p.o., b.i.d.) is an antihistamine, serotonin antagonist with anticholinergic effects. The mechanism of action for treatment of photic head shaking is unknown.[44] A 7-day course of cyproheptidine is recommended to determine response to therapy and horses that respond should be treated during the season in which they exhibit head shaking behavior. Approximately two-thirds of photic head shakers will respond to cyproheptidine.[45] Clinical signs typically recur 24 hours after discontinuation of cyproheptidine. Transient lethargy, depression, colic or anorexia may be observed in some horses with cyproheptidine administration. Carbamazepine (3–4 mg/kg, p.o., t.i.d. to q.i.d.) is the drug of choice for treatment of trigeminal neuritis in humans. This drug may be administered alone or in combination with cyproheptidine to horses that fail to respond to cyproheptidine alone.[46] The response to carbamazepine is approximately 80% of cases. Melatonin (12 mg p.o. between 1700 and 1800 h) has been reported to diminish clinical signs in some head shaking horses. Transient relief may be obtained with topical EMLA cream (lidocaine 2.5% and pilocarpine 2.5%) applied to the muzzle. Cover the topical cream with plastic wrap (make holes for nostrils) and leave on for 45 minutes. Administration of topical therapy prior to exercise may facilitate riding, training and showing of affected horses. The ideal combination of drug therapy is tailored to the individual horse, based on trial and error response to therapy. Corticosteroids, NSAIDs and antihistamines are ineffective in the treatment of photic head shaking.

Surgical intervention

Surgical intervention should be considered for horses that cannot be controlled with medical therapy. Bilateral infra-

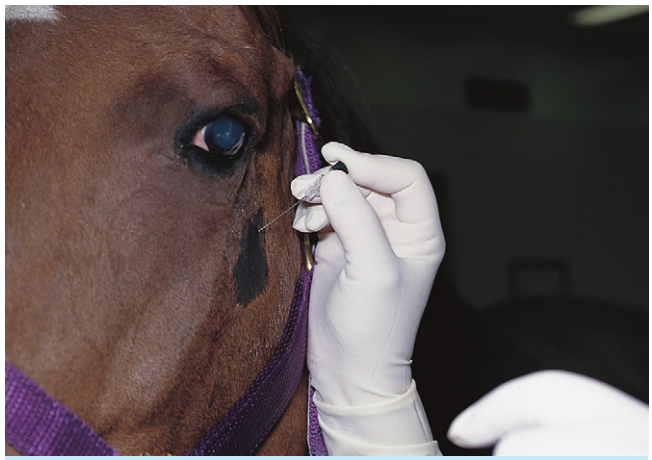

Fig. 24.15
The bilateral posterior ethmoidal nerve block is performed for diagnostic purposes in horses with head shaking. A 7 cm, 18 gauge spinal needle is inserted below the zygomatic arch and directed rostral ventral towards the upper sixth cheek tooth (approximately 5 cm). Local anesthetic is infused at the level of the maxillary foramen.

orbital neurectomy is a salvage procedure for refractory cases. Surgical candidates must demonstrate a consistently positive response to serial infraorbital nerve blocks.[44] Bilateral infraorbital nerve block is performed by infusion of mepivicaine (10 mL) over and within the infraorbital canal. Approximately 30–40% of photic head shakers improve after bilateral infraorbial neurectomy, and successful outcome may be improved by careful case selection (i.e. consistent response to infraorbital nerve block). Postoperative complications may include nasal pruritus (common, temporary), reinnervation and neuroma formation.

An alternative procedure to infraorbital neurectomy is bilateral sclerosis of the posterior ethmoidal branch of the trigeminal nerve.[46] Prior to considering the procedure, horses should respond favorably to bilateral posterior ethmoidal nerve block. This block is performed using a 7 cm, 18 gauge spinal needle inserted below the zygomatic arch and directed rostral ventral towards the upper sixth cheek tooth (approximately 5 cm) (Fig. 24.15). Five milliliters of mepivacaine is infused at the level of the maxillary foramen. Bilateral sclerosis of the posterior ethmoidal branch of the trigeminal nerve is achieved by perineural injection (5 mL) of 10% phenol in almond oil.[46] This procedure is performed under anesthesia, by inserting a 20 cm stiletted needle up the infraorbital nerve to the level of the maxillary foramen. Proper positioning of the needle at the maxillary foramen is confirmed by fluoroscopy. Approximately 65% of horses demonstrate a 90–100% improvement after bilateral sclerosis of the posterior ethmoidal branch of the trigeminal nerve.

Pathophysiology

Prior to the 1990s, the cause of head shaking was rarely identified and the condition was largely unresponsive to therapy. In 1995, Madigan and co-workers presented a series of photic head shaking horses in which head shaking was triggered by natural sunlight and darkness provided relief from the condition.[42] Photic head shaking horses are suspected to experience a burning sensation or tingling of the muzzle (neuropathic pain) in response to bright sunlight. The mechanism of photic head shaking may be similar to photic sneezing in humans, in which exposure to bright light triggers sneezing episodes. Photic sneezing in humans is a heritable, non-allergic disorder. Photic head shaking may represent a form of referred pain in which stimulation of one of the cranial nerves enhances irritability of the other, in this instance optic-trigeminal summation. This may be associated with convergence between optic and trigeminal tracts in the brainstem. Some clinicians suspect trigeminal ganglioneuritis, due to latent equine herpesvirus infection, may contribute to irritability of the infraorbital nerve. Bright sunlight is the most common trigger for neuropathic head shakers but other stimuli, including specific feeds (gustatory head shaking), may also serve as a trigger for infraorbital nerve irritability.[43] In some horses, the triggering stimulus is not identified but their head shaking behavior appears characteristic for neuropathic pain and they respond to medical therapy. Many other disorders besides neuropathic pain may induce head shaking behavior in horses. A thorough diagnostic evaluation is indicated to eliminate other etiologies of head shaking behavior.

References

1. Reed SM. The neurologic examination of the horse for purchase. Vet Clin North Am Equine Pract 1992; 8(2):377–386.
2. Rush BR. Vestibular disease: otitis media/interna. Standards Care Equine Diagn Treatment 2001; 1(1):5–7.
3. Bacon CL, Davidson HJ, Yvorchuk K, et al. Bilateral Horner's syndrome secondary to metastatic squamous cell carcinoma in a horse. Equine Vet J 1996; 28(6):500–503.
4. Johnson PJ, Constantinescu GM. Collection of cerebrospinal fluid in horses. Equine Vet Educ 2000; February:13–20.
5. Johnson PJ, Constantinescu GM. Analysis of cerebrospinal fluid in horses. Equine Vet Educ 2000; February:21–26.
6. Wagner PC, Grant BD, Reed SM. Cervical vertebral malformations. Vet Clin North Am Equine Pract 1987; 3:385–396.
7. Rush BR, Holbrook T, Reed SM. Contrast-enhanced computed tomography in six horses with cervical vertebral myelopathy. Equine Vet J 1992; 24:297–202.
8. Ricardi G, Dyson S. Forelimb lameness associated with radiographic abnormalities of the cervical vertebrae. Equine Vet J 1993; 24:197–202.
9. Powers BE, Stashak TS, Nixon AJ. Pathology of the vertebral column of horses with cervical static stenosis. Vet Pathol 1986; 23:392–399.
10. Papageorges M, Gavin P, Sande R. Radiographic and myelographic examination of the cervical vertebral column in 306 ataxic horses. Vet Radiol 1987; 28:53–59.
11. Stewart R, Reed SM, Weisbrode S. The frequency and severity of osteochondrosis in cervical stenotic myelopathy in horses. Am J Vet Res 1991; 52:873–879.

12. Rush BR, Reed SM, Biller DS. Assessment of vertebral canal diameter and bony malformations of the cervical part of the spine in horses with cervical stenotic myelopathy. Am J Vet Res 1994; 55:5–13.
13. Whitwell KE, Dyson S. Interpreting radiographs. 8: Equine cervical vertebrae. Equine Vet J 1987; 19:8–14.
14. Mayhew IG, Donawick WJ, Green SL. Diagnosis and prediction of cervical vertebral malformation in Thoroughbred foals based on semi-quantitative radiographic indicators. Equine Vet J 1993; 25:435–440.
15. Neuwirth L. Equine myelography. Compend Cont Ed Pract Vet 1992; 14:72–79.
16. Donawick WJ, Mayhew IG, Galligan DT. Recognition and non-surgical management of cervical vertebral malformation in foals. Proceedings of the 20th Annual Surgical Forum 1992; 103–105.
17. Grisel RG, Grant BD, Rantanen NW. Arthrocentesis of the equine cervical facets. Amer Assoc Equine Pract 1996; 42:197–198.
18. Rush BR, Reed SM, Robertson JT. Surgical treatment of cervical stenotic myelopathy in horses: 73 cases (1983–1992). J Am Vet Med Assoc 1993; 203:108–112.
19. Wagner PC, Grant BD, Gallina AM. Ataxia and paresis in horses. Part III. Surgical treatment of cervical spinal cord compression. Compend Cont Ed Pract Vet 1981; 3:192–202.
20. Nixon AJ, Stashak TS, Ingram J. Dorsal laminectomy in the horse. III. Results in horses with cervical vertebral malformation. Vet Surg 1983; 12:184–188.
21. Dubey JP, Saville WJ, Lindsay DS, et al. Completion of the life-cycle of *Sarcocystis neurona*. J Parasitol 2000; 86:1276–1280.
22. Dubey JP, Lindsay DS, Saville WJ, et al. A review of Sarcocystis neurona and equine protozoal myeloencephalitis (EPM). Vet Parasitol 2001; 95:89–131.
23. Dubey JP. Prevalence of Sarcocystis species sporocysts in wild caught opossums (Didelphis virginiana). J Parasitol 2000; 86:705–710.
24. MacKay R. Serum antibodies to *Sarcocystis neurona* – half the horses in the United States have them! J Am Vet Med Assoc 1997; 210:482–483.
25. Fenger CK, Granstrom DE, Langemeier JL, et al. Epizootic of equine protozoal myeloencephalitis on a farm. J Am Vet Med Assoc 1997; 210:923–927.
26. Cohen ND, MacKay R. Interpreting immunoblot testing of cerebrospinal fluid for equine protozoal myeloencephalitis. Compend Cont Ed Pract Vet 1997; 19:1176–1181.
27. Lech PJ. Ponazuril. Compend Cont Ed Pract Vet 2002; 24:484–488.
28. Furr M, Kennedy T, MacKay R. Efficacy of ponazuril 15% oral paste as a treatment for equine protozoal myeloencephalitis. Vet Ther 2001; 2(3):232–237.
29. Kennedy T, Campbell J, Selzer V. Safety of ponazuril 15% oral paste in horses. Vet Ther 2001; 2(3):223–231.
30. MacKay R. Equine protozoal myeloencephalitis. Vet Clin North Am Equine Pract 1997; 13:79–96.
31. Wagner PC. Surgical treatment of traumatic disease of the spinal column. In: Auer JA, ed. Equine surgery. Philadelphia, PA: Saunders; 1992; 1093–1098.
32. Nixon AJ, Stashak TS. Laminectomy for relief of atlantoaxial subluxation in four horses. J Am Vet Med Assoc 1988; 193(6):677–682.
33. Rush BR. Central nervous system trauma. In: Robinson NE, ed. Current therapy in equine medicine. Philadephia, PA: Saunders; 1997; 301–305.
34. Collatos C, Allen D, Chambers J, et al. Surgical treatment of sacral fracture in a horse. J Am Vet Med Assoc 1991; 198(877):880.
35. Toenniessen JG, Morin DE. Degenerative myelopathy: a comparative review. Compend Cont Ed Pract Vet 1995; 17(2):271–283.
36. Miller MM, Collatos C. Equine degenerative myeloencephalopathy. Vet Clin North Am Equine Pract 1997; 13(1):43–52.
37. Dill SG, Correa MT, Erb HN, et al. Factors associated with the development of equine degenerative myeloencephalopathy. Am J Vet Res 1990; 51(8):1300–1305.
38. Mayhew IG, Brown CM, Stowe HD, et al. Equine degenerative myeloencephalopathy: a vitamin E deficiency that may be familial. J Vet Intern Med 1987; 1:45–50.
39. Blythe LL, Craig AM, Lassen ED, et al. Serially determined plasma alpha-tocopherol concentrations and results of the oral vitamin E absorption test in clinically normal horses and in horses with degenerative myeloencephalopathy. Am J Vet Res 1991; 52(6):908–911.
40. Blythe LL, Craig AM. Equine degenerative myeloencephalopathy. Part I. Clinical signs and pathogenesis. Compend Cont Ed Pract Vet 1992; 14(9):1215–1221.
41. Blythe LL, Craig AM. Equine degenerative myeloencephalopathy. Part II. Diagnosis and treatment. Compend Cont Ed Pract Vet 1992; 14(12):1633–1637.
42. Madigan JE, Kortz G, Murphy C, et al. Photic head shaking in horses: 7 cases. Equine Vet J 1995; 27(4):305–311.
43. Rush BR. Photic head shaking. Standards Care Equine Diagn Treatment 2001; 1(1):1–4.
44. Wilkins PA. Cyproheptidine: medical treatment of photic headshakers. Compend Cont Ed Pract Vet 1997; 19(1):98–111.
45. Madigan JE, Bell SA. Owner survey of head shaking in horses. J Am Vet Med Assoc 2001; 219(3):334–337.
46. Newton SA, Knottenbelt DC, Eldridge PR. Head shaking in horses: possible aetiopathogenesis suggested by results of diagnostic tests and several treatment regimens used in 20 cases. Equine Vet J 2000; 32(3):208–216.

CHAPTER 25

Physical treatment of the equine athlete

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Introduction

Physical treatment is the application of non-pharmacologic techniques and methodologies for the treatment of musculoskeletal disorders. Thermal, sound and light treatments, manual techniques and controlled exercise will be described in this chapter.

Accurate localization and diagnosis of the injury or lameness must precede the choice of appropriate physical treatment methods. Treatments should be chosen based on the goals of the therapy program and the circumstances of treatment, such as a hospital setting or a competition, the availability of trained people to apply treatments, and available technology.

Physical treatment of horses is often a major adjunct to surgical or medical therapy. It may also be the primary therapy where a horse is competing under Federation Equestre Internationale (FEI) or other competition regulations that prohibit use of medications. Some of these treatment techniques have undergone scientific scrutiny, while others have not. It therefore behoves the attending veterinarian to carefully review available current literature before using some of these methods.

Table 25.1 Aspects of thermal therapy

Therapy type	Indications	Methods of application	Responses to treatment
Cold	Acute injury (first 24–48 hours) Pain reduction	Ice water immersion Ice surface application Cold packs	Restricts blood flow Reduces metabolism Reduces activity of inflammatory enzymes Reduces pain
Heat	Chronic injury (after 72 hours) Enhance tissue stretching Enhance healing response	Warm water from hose Hot packs Leg sweat Therapeutic ultrasound	Increases blood flow Increases metabolism Increases activity of tissue enzymes Relaxes muscle spasm Reduces pain Increased tissue extensibility

Thermal therapy

Physiological effects of heat application

One of the most accessible and time-tested methods of physical treatment is thermal therapy. The major physiological benefits of heat therapy are increased local circulation, decreased pain, reduction of muscle spasm resulting in muscle relaxation, and increased tissue extensibility.[1–3]

The primary effect of local heat application is stimulation of local circulation by dilation of blood vessels. Increased local blood flow helps mobilize tissue metabolites, increases tissue oxygenation and raises the metabolic rate of cells and enzyme systems. As a rule, an increase in tissue temperature of 10°C increases the metabolic rate 2–3 times.[1] These factors are especially beneficial for wound healing or other soft tissue injuries.

Increased local blood flow may be initiated by three mechanisms. The axonal reflex is a direct response of the blood vessels to local increases in tissue temperature. Local

inflammatory mediators such as histamine, prostaglandins (such as PGE_2 and prostacyclin) and bradykinin may also initiate vasodilation and increase capillary permeability. Local spinal reflexes are stimulated by afferent impulses from the thermoreceptors at the site of heating and result in decreased postganglionic sympathetic adrenergic nerve activity, which decreases smooth muscle tone of vessels, allowing them to dilate.[1]

Edema reduction is a common reason for heat application in horses. Increased blood flow and vascular permeability may promote resorption of edema. However, vasodilation of a dependent limb, such as in a standing horse or human, may actually lead to edema in the limb(s) by the same mechanisms that cause edema, specifically increased blood flow and vascular permeability. Application of heat at one location may also cause reflex vasodilation at a distant site. For example, when heat is applied to the lower back of humans, the vessels of the distal limb dilate in response.

Heat application is also recognized to decrease pain. Stimulation of heat receptors may result in closing of the neural gate, which blocks afferent stimuli from peripheral pain receptors. Heat may also act as a counterstimulus to pain, making the afferent impulses of pain less noticeable.[1–3]

Muscle spasms are decreased following heat application. Increased muscle temperature results in decreased firing of muscle spindles, which helps to break the cycle of pain–spasm–pain. The same sort of cycle may be partially responsible for flexural contractures in foals with physitis. The flexor muscles are the largest group of forelimb muscles in the foal. Severe physeal pain results in reflex increased muscle spindle firing and muscle spasm leads to flexural contracture.

Soft tissues may be stretched most effectively when they are heated. Heat decreases tissue viscosity and increases tissue elasticity. Low-load, prolonged stretching of tissues heated to 40–45°C (104–113°F) results in increased extensibility of tendon, joint capsule and muscle.[1–3]

Indications for heat therapy

Heat is best applied after the acute inflammation has subsided, usually no sooner than 48–72 hours after an injury. It is also useful for reducing muscle spasm and pain due to musculoskeletal injuries. Heat therapy can be used to increase joint and tendon mobility, particularly by heating before active stretching. Heat application may be beneficial for accelerating the healing response of localized soft tissue injuries.

Heat: methods of application

Superficial heat may be applied with hot packs, hydrotherapy, paraffin baths or moist air. These methods provide heat penetration to approximately 1 cm from the skin surface.[1–3] This is often sufficient for many distal limb injuries because of the lack of an insulating fatty subcutaneous tissue layer in horses. Deep heat may be applied using therapeutic ultrasound.

The most profound physiological effects of heat occur when tissue temperatures are raised to 40–45°C (104–113°F).[1,3,4] Tissue temperatures above 45°C may result in pain and irreversible tissue damage.[4] Skin and subcutaneous tissue temperature increases approximately 5°C after 6 minutes of treatment and maintains that temperature for up to 30 minutes.[5] For deeper tissues, 15–30 minutes heating is required to elevate tissue temperature into the therapeutic range.[1,3]

Direct contact of the skin to temperatures over 45°C (115°F) may cause thermal injury and tissue damage. Heat sources warmer than 45°C must be wrapped in several layers of moist towels before application.[4] Superficial heat using hydrocollator packs, which are heated to 71–79°C, or rechargeable hot packs is usually applied for 15–20 minutes, but timing depends on the warmth of the heat source.

Warm water is probably the most accessible method of heat therapy. Methods of application may be from a hose or with wet towels, or water immersion in a bucket, therapy tub or turbulator boot. A rule of thumb is that water as hot as one's hand can comfortably endure is about 38–41°C (101–105°F). Tissue heated by water at this temperature may only reach the lowest tissue therapeutic range. To make warm hydrotherapy most effective, a thermometer should be used to determine water temperature. Horses will commonly experience pain with water 45°C and higher.

In a study of hot water hose therapy applied to the metacarpal region in a horse, it was found that water as warm as a human could comfortably endure resulted in skin surface temperatures on the horse of 39.5–41°C.[5] Temperature of subcutaneous and deep tissues stabilized at 39–40°C approximately 9 minutes after therapy was started. Tissue temperatures returned to baseline approximately 15 minutes after therapy ceased.[5] Heating the equine digit by standing in a 47°C water bath for 30 minutes resulted in significant increases in soft tissue perfusion and laminar temperatures.[6] Vascular perfusion increased, but not significantly.[6]

Commercial hot packs provide marginally effective treatment temperatures, yet they are very simple to use. The packs consist of a chemical that rapidly changes from a gel to a crystalline structure in an exothermic reaction. The packs attain temperatures of about 54°C (130°F) within minutes of activation. Heat is maintained for 20–30 minutes. The packs are either single use and disposable or rechargeable in a microwave by immersion in near-boiling water. Hot packs of this type are available from Tempra Technology, Bradenton, Florida, USA (single-use disposable) or Cyan Massage Products, Edmonton, Alberta, Canada (rechargeable).

Hydrocollator packs are commonly used in human physical therapy practices. Heat is retained by blocks of silica gel encased in a flexible canvas cover. Hydrocollator packs are heated to 71–79°C (160–174°F).[4] They are somewhat heavy for use in standing horses, but the weight helps maintain good contact with the treatment area. Moist towels should be wrapped around the packs to prevent thermal injury.

Therapeutic ultrasound (US) may be used for superficial or deep heating of tissues. In horses, treatment is usually conducted at 1.5 W/cm^2 for 10 minutes. Ultrasound selectively heats tissue with high protein and/or collagen content.[4] Tendon, muscle, fibrous connective tissue and bone may be effectively heated to 45°C, while adipose tissue is relatively

transparent to the effects of therapeutic US. The greatest heating occurs at tissue interfaces, similar to the sharp image delineations between tissue interfaces of skin, tendon and fluid seen with diagnostic US. Ultrasound effectively heats tissues to a depth of more than 7 cm (3″). In dog thigh muscles, US treatment at 1.5 W/cm^2 resulted in temperature increases of 4.6°C, 3.6°C and 2.4°C at 1 cm, 2 cm, and 3 cm depths, respectively.[7] An additional benefit of US is the deep massage of tissues because the sound waves compress and expand tissues and tissue fluids.[7] Fibrous connective tissue scars may be loosened and reabsorbed to a certain degree with therapeutic US. Treatment is usually performed once or twice daily for 10–14 days. Ultrasound coupling gel must be used to provide good contact between the US transducer and the skin.

Physiological effects of cold application

The major physiological benefits of cold therapy are decreased local circulation, decreased pain and decreased tissue extensibility.[1–3,8,9] The viscoelastic properties of soft tissues are reduced with cold therapy, which may be an undesirable effect.[1–3]

The primary effect of local cold application is to constrict blood vessels. Local reflexes and central nervous system responses mediate vasoconstriction. Reduced blood flow may help reduce edema, hemorrhage and extravasation of inflammatory cells. Just 10 minutes of ice pack application to the stifle of dogs resulted in a 56% decrease in local tissue blood flow.[8] Reduced tissue metabolism may inhibit the effect of inflammatory mediators and enzyme systems. Because of these effects, cold therapy is often indicated within the first 48 hours of injury.

Cyclical rebound vasodilation is another response of cold therapy.[10] Following a minimum of 15 minutes of cold therapy that results in tissue temperatures of 10–15°C, cycles of vasoconstriction and vasodilation occur. An example of this effect is the warm, tingling sensation in one's fingers after long-term exposure to cold.

Pain is reduced by mechanisms similar to that described for heat therapy. Small myelinated nerve fibers are more sensitive to cold therapy and reduce conduction earlier than similar sized unmyelinated fibers. Application of an ice pack for 20 minutes over the ulnar nerve in cats reduced nerve conduction velocity by 29%.[9]

Indications for cold therapy

Cold therapy is indicated in acute musculoskeletal injuries and is particularly effective during the first 24–48 hours after injury.[11] Distal limb injuries are the most easily and effectively treated.

Cold: methods of application

Cold may be applied by ice water immersion, ice packs or cold packs and Freon or ice water-charged circulating bandages or boots.

Therapeutic effects of cold occur at tissue temperatures between 15° and 19°C (59–66°F).[1–3] Tissue temperatures of 10°C and less may cause cold thermal damage. Average time of cold application is 15–20 minutes. Treatments should be repeated every 2–4 hours during the first 24–48 hours of injury if the goal is to reduce tissue inflammation and edema.

Cold therapy is effective to a depth of 1–4 cm from the skin surface, depending on the amount of adipose tissue and the local blood supply.[1–3] Cold treatment is rapid and effective in the distal limbs of horses because they lack an adipose layer and target tissues such as tendons, ligaments and joint capsules are close to the skin surface.

Direct contact of ice water with the skin is the most effective method of cold therapy. In human physical therapy, ice baths are maintained at temperatures of 13–18°C (55–64°F).[1] In a study of ice water immersion therapy applied to the metacarpal region of a horse, skin surface temperatures stabilized at 9–10°C approximately 10 minutes after therapy was started.[5] Temperature stabilized at 17–19°C in subcutaneous tissue and at 20–24°C between the deep and superficial flexor tendons approximately 10 minutes after therapy was started. Tissue temperatures had not returned to baseline by 10 minutes after therapy was stopped.[5] Ice water immersion of the equine digit for 30 minutes resulted in significant decreases in soft tissue perfusion and laminar temperatures.[6]

Cold packs saved from shipments of pharmaceutical supplies are easily adapted for therapeutic use. They may be applied directly to the treatment site or wrapped in a wet or dry towel and held in place with a bandage. The cold packs maintain their cold temperatures well and are easily reused. One disadvantage is that these types of cold packs do not conform well to the limbs. Even a small air gap between the pack and the skin often results in subtherapeutic tissue temperatures. The cold packs may be thawed, shaped to the anticipated site using a form such as a cardboard tube or plastic pipe, and refrozen. Commercial products such as cold leg wraps have the same gel substance as cold packs. The gel is formed as a tape that may be wrapped on a limb and held in place with a wet bandage. Cold packs may be applied for greater than 30 minutes, but the intensity of cold is less than that of ice. Cold packs developed primarily for equine use are also available in sizes that conform specifically to the cannon bone, carpus or tarsus (Dura*Kold Corporation, Oklahoma City, OK, USA).

Manipulative therapy

Stretching and massage are physical methods of treatment that may be applied without the need for sophisticated equipment. Stretching is useful for maintaining or increasing the range of motion of an injured joint and for increasing a horse's flexibility and elasticity to improve performance. Stretching is especially beneficial following joint injury or surgery. This technique should not be used on limbs that may have acute tendon or ligament injuries.

Evaluating the flexibility of a horse's joints, including joints of the neck, is often carried out during a lameness or

neurologic examination. Being familiar with the normal ranges of motion of these structures is necessary to determine if there is a restriction in the range of motion. Comparisons can be made to the contralateral joint or structure if there is uncertainty.

Limb mobility is usually easy to evaluate during flexion tests for lameness. Head and neck flexibility may be evaluated with gentle manipulation using the halter or by encouraging the horse to reach for a carrot. Evaluation of back and trunk mobility is described in Chapter 21.

Stretching exercises should begin 24 hours after joint surgery or after a joint injury, providing that the injury has been accurately diagnosed. Flex and extend the joint to the point of mild discomfort and hold at that point for 10–15 seconds. Repeat the sequence up to 12 times twice daily.

Massage may be used to warm muscles prior to exercise and for soothing tired muscles after exercise. Experience with human athletes has shown that pre- and postexercise massage makes athletes more comfortable and helps decrease stiffness following competition.[12]

There are variations in massage therapy techniques that focus on specific mechanisms of action. Trigger point massage focuses on relaxing tight bands of muscle or fascia that are sensitive to manipulation, thereby reducing sensitivity of the affected areas. This type of massage has been found to reduce heart rate and blood pressure and to significantly relax human patients.[13] The technique also aims to decrease the sensitivity of active myofascial zones that may cause discomfort in a distant area.[14] Acupressure massage results in stimulation of regions that are connected to Chinese meridians similar to acupuncture points.[15]

Massage therapy should be considered palliative. Few of the claimed advantages of the techniques have been scientifically evaluated.[16] Using a trained therapist with a close professional relationship with the attending veterinarian is imperative for safe and effective treatment.

Exercise

Controlled exercise regimens may be used during the rehabilitation period after injury or surgery. Controlled exercise protocols have been established for rehabilitation of tendon and ligament injuries (see Chapter 20). Gradually increasing the time and intensity level of exercise is beneficial for healing of soft tissues and bone as both become stronger with use, particularly in growing horses.[17–19] Harness race horses may enter a controlled exercise program by designating the number of jogging miles at a given pace for each exercise session.

Swimming or underwater treadmill exercise is another method of providing controlled exercise with the advantage of minimal concussion. These methods spare the musculoskeletal system, but enhance cardiorespiratory fitness. Swimming should not replace conditioning for fitness under normal weight-bearing conditions. Swimming is also an excellent method for increasing joint mobility after injury or surgery. Horses do not use the same muscle groups during swimming that are used during weight-bearing exercise and may cause hyperextension of the back muscles.[14,20] Because of this, swimming should be combined with regular ring or track work to condition the muscles, bones and joints that are used for normal weight-bearing activities.

Treadmills, although not often readily available, are a good intermediate step between exercise with minimal concussion and the horse's regular exercise. Most treadmills have a rubber running surface that reduces concussion during weight-bearing exercise. Speed and inclination of the treadmill can be adjusted to the level of exercise intensity that is appropriate for the horse.

Control of the exercise program may be useful during and after rehabilitation is complete.[21] Treadmill exercise was used in one study to establish a base level of fitness, then regular track workouts were gradually added.[21] Regular exercise over the track eventually made up 50–70% of the total work for each horse. Horses trained in this fashion had fewer training and racing injuries and better race times than conventionally trained horses.[21]

Ultimately horses must train under the same conditions they will encounter in competition. This means that riding or driving with a gradual increase in duration and intensity of exercise will be needed. The key to retraining a horse is to realize that cardiovascular fitness declines significantly after 4–6 weeks of rest[22] and that bone strength decreases significantly within 12 weeks of rest.[23] Retraining will result in noticeable improvement of cardiac measurements within 6 weeks, increased bone mineral density within $16\frac{1}{2}$ weeks and tendon dimensions within 16 weeks.[18,24,25] Published studies on bone and tendon response to exercise do not identify the earliest time that significant strength returns to these tissues after reintroduction of exercise. Three to 4 months may be the minimum time required to re-establish musculoskeletal tissue strength following 2 or more months of complete rest.

Light therapy

Light of any type emits energy, as evidenced by the heat given off by a light bulb. Specialized sources of light energy have been used to enhance tissue healing, reduce swelling and increase local circulation.[26–29] Light therapy has also been used to produce analgesia and to stimulate acupuncture points.[26] Many of these effects have been verified in laboratory animal-based research, but other studies have failed to measure effects of this modality.[27–29] Light therapy is not universally accepted in mainstream veterinary medicine.

Laser is an acronym for Light Amplification by Stimulated Emission of Radiation. Lasers produce coherent, monochromatic light. Indications for laser therapy in equine practice include tendinitis, desmitis, soft tissue bruising, wounds, myofascial injuries and burns. Helium-neon, gallium-arsenide and gallium-aluminum-arsenide are common sources of laser light used for treatment purposes in equine

practice.[26] Monochromatic infrared light sources have also been used to enhance wound healing in humans and horses.[30] Laser energy at a dose of 2–8 J/cm^2 is recommended for treatment of soft tissue injuries and 0.5–1 J/cm^2 is recommended for acupuncture point stimulation.[26,31] Treatment protocols are different for each device and manufacturers' instructions should be carefully followed.

No deleterious effects of light therapy have been reported. Lasers have the potential to cause eye injury so operators need to wear eye protection when using certain laser devices that emit a concentrated, high-power beam.

Extracorporeal shockwave therapy

A new application of sound wave energy is currently undergoing critical evaluation in clinical and scientific settings. Extracorporeal shockwave therapy (ESWT) consists of short-duration (5 μs), high-pressure shockwaves (up to 80 MPa) that stimulate tissue. Originally these devices were used for non-invasive lithotripsy of cystic and renal calculi in humans.[32]

Focused and non-focused ESWT devices are currently marketed for use in horses. Reports of positive treatment effects have been made for both types of devices.[32–34] Each treatment usually consists of 2000 pulses. The intensity of shockwave therapy is set in a range of 0.9–1.8 mJ/mm^2 or according to the atmospheric pressure at the output probe (2.5–4 bar), depending on the manufacturer's recommendations.[32,34] Horses must be sedated and often need to have regional anesthesia proximal to the site of application. Each treatment lasts 10–15 minutes and is repeated at 1–4-week intervals. Treatment protocols require 1–4 separate treatments depending on the nature of the injury and response to initial therapy.

As the shockwaves pass through tissue interfaces, compression and shear loads occur within the tissues, resulting in stimulation of healing of bone and soft tissue injuries. Bone healing and remodeling have been enhanced and an analgesic effect has been noted for 2–4 days following treatment.[32,35,36] Use of ESWT to treat arthritis of equine distal tarsal joints (bone spavin) resulted in improvement of lameness grade in 59 of 74 horses treated.[33] Chronic suspensory desmitis was successfully treated in 24 of 30 horses after three ESWT treatments.[34]

Extracorporeal shockwave therapy is indicated for treatment of tendinitis and insertional desmopathies. Injuries of the origin or insertion of the suspensory ligament, dorsal cortical stress fractures, incomplete fractures of the proximal sesamoid bone(s), arthritis and navicular disease have been successfully treated with ESWT.[32–34] Continuing clinical experience and research using this therapeutic modality will ultimately identify effective applications in the near future.

References

1. Michlovitz SL, ed. Thermal agents in rehabilitation, 3rd edn. Philadelphia, PA: FA Davis; 1996.
2. Prentice WF. Therapeutic modalities in sports medicine. St Louis, MO: Mosby; 1994.
3. Lehmann JF. Therapeutic heat and cold, 3rd edn. Baltimore, MD: Williams and Wilkins; 1982.
4. Hayes KW. Conductive heat. In: Hayes KW ed. Manual for physical agents. East Norwalk, CT: Appleton and Lange; 1993; 9–15.
5. Kaneps AJ. Tissue response to hot and cold therapy in the metacarpal region of a horse. Proc Am Assoc Eq Pract 2000; 46:208–213.
6. Worster AA, Gaughan EM, Hoskinson J. Effects of external thermal manipulation on laminar temperature and perfusion of the equine digit. Proc Am Assoc Eq Pract 2001; 47:329–333.
7. Levine D, Millis DL. Effects of 3.3 MHz ultrasound on caudal thigh muscle temperature in dogs. Vet Surg 2001; 30:170–174.
8. Cobbold AF, Lewis OJ. Blood flow to the knee joint of the dog: effect of heating, cooling and adrenaline. J Physiol 162; 289:1962.
9. Douglas WW, Malcom JL. The effect of localized cooling on conduction in cat nerves. J Physiol 1955; 130:53.
10. Lewis T. Observations upon the reactions of the vessels of the human skin to cold. Heart 1930; 15:177.
11. Hocutt JE, Jaffe R, Rylander CR, Beebe JK. Cryotherapy in ankle sprains. Am J Sports Med 1982; 10:316–319.
12. Cafarelli E, Flint F. The role of massage in preparation for and recovery from exercise. Sports Med 1992; 14:1–9.
13. Delaney JP, Leong KS, Watkins A, Brodie D. The short-term effects of myofascial trigger point massage therapy on cardiac autonomic tone in healthy subjects. J Adv Nurs 2002; 37(4):364–371.
14. Porter M. The new equine sports therapy. Lexington, KY: The Blood-Horse; 1998.
15. Gach MR. Acupressure's potent points. New York, NY: Bantam; 1990.
16. Ramey DW, Tiidus PM. Massage therapy in horses: assessing its effectiveness from empirical data in humans and animals. Compend Cont Educ Pract Vet 2002; 24(5):418–423.
17. van Weeren PR. Exercise at young age may influence the final quality of equine musculoskeletal system. Proc Annu Conv Am Assoc Equine Pract 2000; 46:29–35.
18. Gillis CL, Meagher DM, Pool RR, et al. Ultrasonographically detected changes in equine superficial digital flexor tendons during the first months of race training. Am J Vet Res 1993; 54(11):1797–1802.
19. Reilly GC, Currey JD, Goodship AE. Exercise of young thoroughbred horses increases impact strength of the third metacarpal bone. J Orthop Res 1997; 15(6):862–868.
20. Harman JC. Holistic approach to equine practice. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine. St Louis, MO: Mosby; 1998; 601–630.
21. Kobluk CN, Geor RJ, King VL, et al. Case control study of racing thoroughbreds conditioned on a high speed treadmill. J Equine Vet Sci 1996; 16(11):511–513.
22. Kriz NG, Rose RJ. Effect of detraining on cardiac dimensions and indices of cardiac function in horses. Proc Annu Conv Am Assoc Equine Pract 1996; 42:96–97.
23. Porr CA, Kronfeld DS, Lawrence LA, et al. Deconditioning reduces mineral content of the third metacarpal bone in horses. J Anim Sci 1998; 76(7):1875–1879.

24. Shapiro LM, Smith RG. Effect of training on left ventricular structure and function. An echocardiographic study. Br Heart J 1983; 50(6):534–539.
25. Firth EC, Goodship AE, Delahunt J, et al. Osteoinductive response in the dorsal aspect of the carpus of young thoroughbreds in training occurs within months. Equine Vet J 1999; 30(suppl):552–554.
26. Pöntinen PJ. Low-energy photon therapy. In: Schoen AM, Wynn SG, eds. Complementary and alternative veterinary medicine. St Louis, MO: Mosby; 1998; 247–274.
27. Kaneps AJ, Hultrgren BD, Riebold TW, et al. Laser therapy in the horse: histopathologic response. Am J Vet Res 1984; 45(3):581–582.
28. Ramey DW, Basford JR. Laser therapy in horses. Compend Cont Educ Pract Vet 2000; 22(3):263–272.
29. Peterson SL, Botes C, Olivier A, et al. The effect of low level laser therapy (LLLT) on wound healing in horses. Equine Vet J 1999; 31(3):228–231.
30. Horwitz LR, Burke TJ, Carnegie D. Augmentation of wound healing using monochromatic infrared energy. Adv Wound Care 1999; 12:35–40.
31. American Veterinary Laser. Laser therapy of small animals, exotics and horses. Farmington Hills, MI: American Veterinary Laser; 1999.
32. McClure S, Van Sickle D, White R. Extracorporeal shock wave therapy: what is it? What does it do to equine bone? Proc Annu Conv Am Assoc Equine Pract 2000; 46:197–199.
33. McCarroll GD, McClure S. Extracorporeal shock wave therapy for treatment of osteoarthritis of the tarsometatarsal and distal intertarsal joints of the horse. Proc Annu Conv Am Assoc Equine Pract 2000; 46:200–202.
34. Boenig KJ, Löffeld S, Weitkamp K, et al. Radial extracorporeal shock wave therapy for chronic insertion desmopathy of the proximal suspensory ligament. Proc Annu Conv Am Assoc Equine Pract 2000; 46:203–207.
35. Valchanov VD, Michalov P. High energy shock waves in the treatment of delayed and nonunion of fractures. Int Orthop 1991; 15:181–184.
36. Johannes EJ, Kaulesar Sukul DM, Matura E. High-energy shock waves for treatment of nonunions: an experiment in dogs. J Surg Res 1994; 57:246–252.

CHAPTER 26

Upper airway function of normal horses during exercise

Susan J. Holcombe and Norm G. Ducharme

The horse is a magnificent athlete that can run in excess of 30 miles per hour. In order to accommodate the tremendous oxygen demand of skeletal muscles during such intense exercise, the horse increases its minute ventilation nearly 50-fold. High airflow rates required to meet this ventilatory demand are created principally by diaphragmatic contraction, which produces driving pressures within the upper airway exceeding -30 cmH_2O. Because the horse is an obligate nasal breather and rarely breathes orally, the horse's upper airway must quickly prepare for these large changes in airflow and pressures by dilating and becoming more rigid (less compliant). Such accommodation is achieved by synchronous and coordinated contraction of upper airway muscles and constriction of capacitance vessels within the mucosa of the upper airway.[1,2] These remarkable and somewhat unique

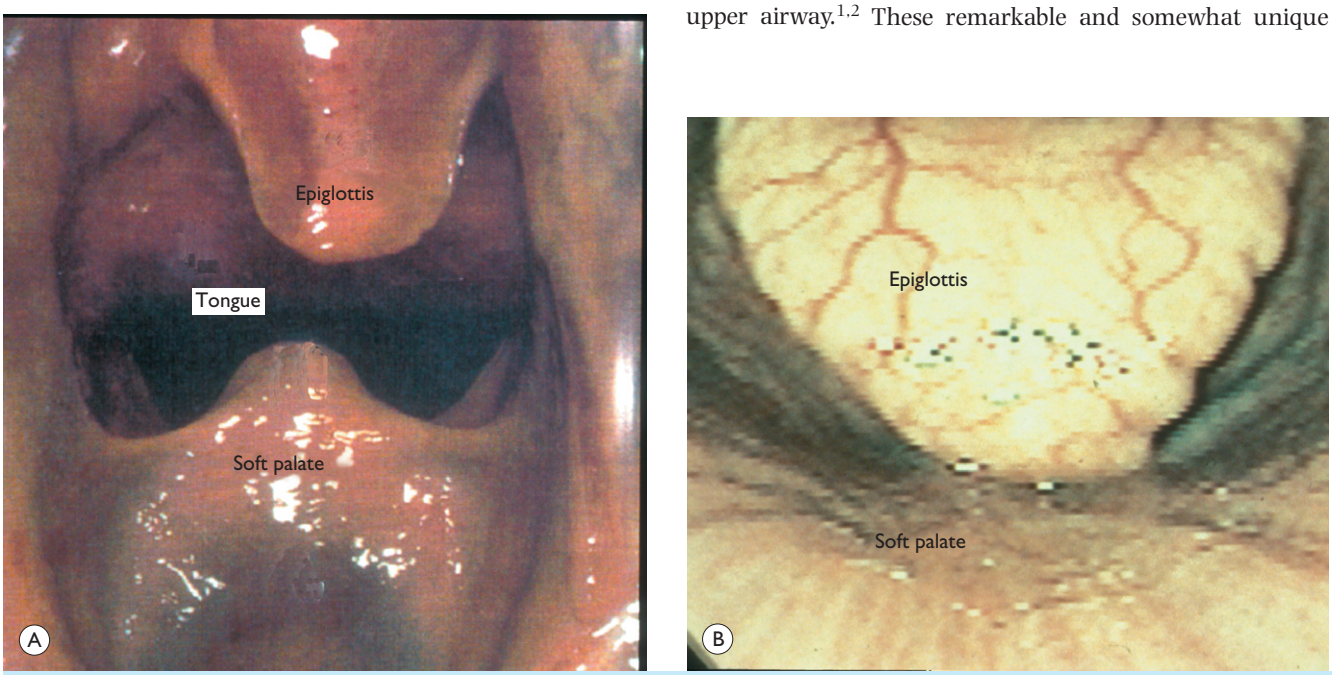


Fig. 26.1
(A) Endoscopic image of a human oropharynx and nasopharynx. Notice the space between the epiglottis and the soft palate, which forms the communication between the oropharynx and nasopharynx in people. (B) Endoscopic image of the equine epiglottic and soft palate apposition. There is no communication between the oropharynx and nasopharynx in the horse due to the tight apposition of the soft palate and epiglottis.

adaptations of the equine upper airway to exercise are the subject of this chapter.

Obligate nasal breathing

Teleologically, obligate nasal breathing is thought to be advantageous to a fight or flight creature, because obligate nasal breathers can graze and masticate while moving air through the nasal passages, maintaining olfaction and the ability to sense predators.[3] To accomplish this, the soft palate is tightly apposed to the base of the larynx, such that there is no communication between the oropharynx and the nasopharynx, as exists in people (Fig. 26.1A,B). In people, the 'switch point' from nasal to oronasal breathing during exercise is determined by the flow resistance in the nasal airway and the turbulence of the airflow.[4] Estimated airflow rate associated with the switch from nasal to oronasal breathing is variable and reported to be between 22 and 44 L/min.[4–6] Horses maintain nasal breathing, normally, throughout exercise and rely on capacitance vessel constriction and contraction of upper airway dilating muscles to minimize airflow resistance.[1] Exactly at what level of exercise intensity these factors occur in exercising horses is not known.

Basic upper airway mechanics

The upper airway begins at the nares and includes the nasal passages, the nasopharynx, and oropharynx, guttural pouches, larynx, and trachea. Some segments of the upper airway, such as the larynx, are supported by cartilage, and some portions such as the nasal passages, are supported by bone. The pharyngeal region is formed principally by skeletal muscle and relies on the contraction of these muscles and muscles of the hyoid apparatus and tongue for stability.

At rest, the average 450 kg horse breathes 12 times per minute with a tidal volume of 5 liters and peak inspiratory flow of 5.09 ± 0.34 L/s, making its resting minute ventilation approximately 60 L/min.[7] During intense exercise, respiratory frequency increases to 120 breaths per minute, peak inspiratory airflow increases to 75 ± 9.35 L/s, tidal volume increases to 12–15 Ls, and minute ventilation increases to approximately 1400–1800 L/min.[7] All the upper airway segments are exposed to varying degrees of negative pressure as the diaphragm contracts during inhalation, creating negative driving pressure for airflow to the lungs. These pressures range from –1.9 ± 0.2 cmH_2O during normal tidal breathing to –38.6 ± 3.9 cmH_2O while running at speeds that result in maximal heart rate (HR_{max}).[8] The ratio of the peak pressure that occurs to produce a given peak airflow is the airway impedance and impedance is a measure of how the airflow is opposed by the airway.[9] The determinants of airway impedance include resistance, which is dependent on the airway geometry, and the elastance and inertance of the tissues.[9] The most important component of airway impedance is resistance, which is principally determined by the radius of curvature of the airway or its diameter. Resistance is defined by the formula $R = (8\eta l)/\pi r^4$, where η is the viscosity of the air, l is the length of the airway, and r is the radius.[10] The viscosity of air does not change and the length of the airway changes minimally with head and neck flexion and extension. The diameter of the airway, however, does change during inhalation and exhalation. In the resting horse, two-thirds of the total resistance to airflow resides in the upper airway.[1] As the horse inhales, the largest pressure changes occur at the nares and larynx due to narrowing in these areas.[1] During exercise, upper airway resistance increases to 80% of total airway resistance, because the tissues of the upper airway tend to collapse dynamically as airway pressures become more negative.[1] Positive pressure tends to dilate the upper airway during exhalation and therefore upper airway resistance to airflow during exhalation is only 50% of total expiratory airway resistance.[1] Static or dynamic obstructive airway disease can result in large changes in airway resistance. For example, if the diameter of the airway decreases by 20% due to a small amount of granulation tissue on the left arytenoid cartilage, airway resistance would double. Therefore, throughout the respiratory cycle, the horse relies on neuromuscular mechanisms to dilate and stabilize the airway during intense exercise to expand and stabilize the airway in order to accommodate such high flow rates and pressure changes while minimizing resistance to airflow.

Head position

The position of the horse's head and neck does affect upper airway flow mechanics in exercising horses.[11] Measurements of airway mechanics made in six horses with the head and neck in neutral, extended, and flexed positions confirmed that head and neck position significantly increases inspiratory impedance.[11] The induced obstruction is typical of a dynamic upper airway obstruction because inspiratory values but not expiratory values are altered. Head and neck flexion may cause the airway to be more compliant, because tissues, such as the pharyngeal walls and soft palate, bulge into the airway, or because the nasopharynx shortens with this maneuver. Horses with most types of obstructive upper airway dysfunction show more severe signs of respiratory distress and exercise intolerance while exercising with the head and neck flexed rather than in a neutral or extended position. Posture or head position alters upper airway muscle activity such that head flexion, or cervical spine flexion increases genioglossus nerve activity in other species.[12,13] Therefore, altered upper airway muscle activity may result from postural changes in head and neck position in exercising horses and these changes may be due to stimulation of local upper airway receptors that sense changes in tissue tension, pressure, and airflow.

Neuromuscular control of upper airway function

During intense exercise multiple stimuli trigger contraction of upper airway dilating muscles, including chemical stimuli such as hypercapnia and hypoxia, limb movement, central locomotor-linked cortical influences, receptors located in the lower airways, and upper airway sensory receptors.[14–21]

The laryngeal mucosa has an abundant supply of sensory receptors that control a complex pattern of respiratory reflexes that influence the patency of the upper airway and the pattern of breathing.[22] These receptors are mechanoreceptors or temperature sensing receptors and include pressure, flow, and drive receptors that line the mucous membranes and deeper tissues of the nose, nasopharynx, and larynx.[22] They receive afferent innervation from branches of the trigeminal, glossopharyngeal, and vagus nerves.[23,24] Receptors in the nasopharynx are innervated by branches of the glossopharyngeal and trigeminal nerves.[22] These receptors are principally tactile receptors and stimulate the gag response, important in airway protection.

Especially relevant to dilation and stability of the upper airway during exercise are the pressure receptors. Pressure receptors account for 60% of the sensory receptors within the laryngeal mucosa in horses, which is similar to other species.[22,25] These receptors are innervated by the superior laryngeal branches of the vagus nerve.[23] They are stimulated during upper airway obstruction, when large collapsing pressures are produced in the upper airway, and they provide afferent information to the central nervous system, signaling contraction of upper airway muscles to resist dynamic collapse in the upper airway. For example, studies in dogs, cats, rabbits, monkeys, and people have shown that reflex augmentation of muscle contraction by application of negative pressure in the upper airway occurs in the genioglossus and other tongue muscles, muscles of the hyoid apparatus, and the soft palate.[16,18–21,26,27] In horses, negative pressure stimulates increased electromyographic activity in the cricoarytenoideus dorsalis muscle, the primary laryngeal abductor.[25] During incremental exercise testing the palatinus, palatopharygeus, hyoepiglotticus, sternohyoideus and sternothyroideus, geniohyoideus, and genioglossus muscles all had increasing levels of electromyographic activity as treadmill speed increased, and upper airway pressures became more negative.[28–30]

In species other than horses, it has been noted that the time of application of negative pressure during the breathing cycle is an important variable in determining the magnitude of the response of upper airway muscles. Specifically, upper airway motor neurons are more responsive during early inspiration to pressure changes in the airway than during later stages of inspiration.[27] The onset of inspiratory upper airway muscle activity often precedes that of the diaphragm, and is modulated by chemical drive, and mechanical afferent input from the upper airways that is, primarily, vagally mediated.[31] Many of the upper airway muscles are maximally active during early to mid inspiration, with a subsequent decrement in activity during the remainder of inspiration. Inspiratory activation of upper airway muscles prior to the diaphragm will dilate or stiffen the upper airway, promoting upper airway patency, prior to the onset of inspiratory airflow and hence produce an early inspiratory stabilization of upper airways.[31] The degree of negative pressure established in the upper airway will increase the amount of muscular preactivation.[21]

Topical anesthesia of the luminal surface of the larynx or bilateral superior laryngeal nerve sectioning markedly reduces the response to changes in upper airway pressure and upper airway muscle activity in laboratory species and people.[24,32] In horses, topical anesthesia of the laryngeal

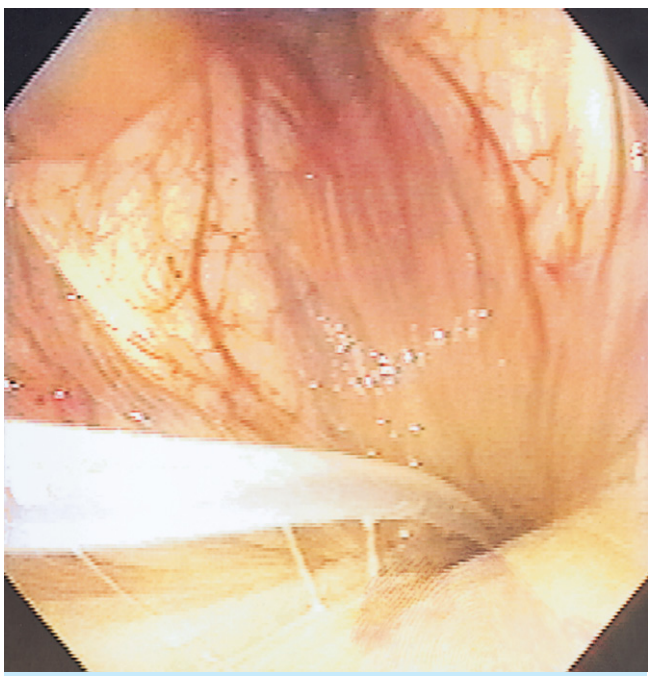


Fig. 26.2
Endoscopic image of the nasopharynx while the nares are occluded following topical anesthesia of the laryngeal mucosa. Notice how the nasopharynx collapses, almost forming a sphincter.

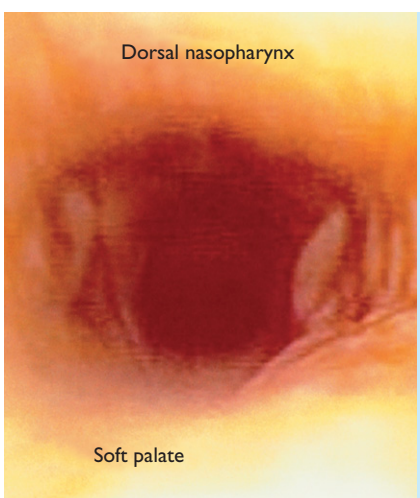


Fig. 26.3
Endoscopic image of the nasopharynx during treadmill exercise (10 m/s) following topic anesthesia of the laryngeal mucosa. Notice how the nasopharynx is collapsing, obstructing the view of the corniculate processes of the arytenoids and the epiglottis.

mucosa results in increased inspiratory upper airway and nasopharyngeal impedances, and decreased respiratory frequency and minute ventilation.[33] The dynamic upper airway obstruction was caused by nasopharyngeal collapse due to decreased skeletal muscle support. Following topical anesthesia of the laryngeal mucosa, horses exhibit dorsal displacement of the soft palate and nasopharyngeal collapse during endoscopic examination at rest (Fig. 26.2) and varying degrees of nasopharyngeal collapse during incremental treadmill exercise (Fig. 26.3).[33] These results suggest that local sensory receptors in the upper airway of horses, as has been shown in laboratory species, contribute to upper airway patency and that disrupting the sensory component of the local reflex that controls contraction of upper airway muscles can cause dynamic upper respiratory obstruction in horses.

Nasal occlusion

Because negative pressure induces contraction of upper airway muscles, a nasal occlusion test was developed in horses in order to mimic pressure changes that might occur during intense exercise to challenge the upper airway with more negative pressures during resting videoendoscopic examination. Peak tracheal inspiratory pressure during nasal occlusion (-24.9 ± 3 cmH_2O) is not significantly different from peak inspiratory pressure while horses exercise at HR_{max} (-25.6 ± 2.7 cmH_2O), and peak pharyngeal inspiratory pressure is significantly more negative (-28.9 ± 4.9 cmH_2O) during nasal occlusion than while horses exercise at HR_{max} (-17.5 ± 2.1 cmH_2O).[34] These data indicate that nasal occlusion in standing horses results in pharyngeal and tracheal inspiratory pressures that equal or exceed those that are generated during exercise at HR_{max}, making it a potentially useful test for evaluating the activity of laryngeal and pharyngeal muscle function. However, anecdotally, horses that exhibit varying degrees of nasopharyngeal collapse at rest frequently have normal airway function during treadmill exercise. As well, horses that readily displace their soft palates at rest frequently displace during treadmill exercise, but the correlation between displacement at rest and during treadmill exercise is not a strong one.

Other sensory receptors within the upper airway include flow and drive receptors. Drive receptors represent 20% of laryngeal sensory receptors in horses.[22,25] These receptors respond to changes in airway deformation, such as collapse, muscle contraction and movement of the laryngeal cartilages.[22] Flow receptors are temperature-sensing receptors.[22] These receptors sense cool air temperatures, which occur as airflow increases. The majority of these receptors are responsive during inspiration, but some (approximately 20%) respond during exhalation, and a small population of the airway sensory receptors is active during both inspiration and expiration.[22]

In addition to afferent sensory receptor stimulation in the upper airway, chemical stimuli such as hypercapnia and hypoxia also increase the activity of upper airway dilator muscles.[16,17] Horses exercising at HR_{max} become hypercarbic ($Paco_2$ of 50.2 mmHg) and hypoxemic (Pao_2 of 56.1 mmHg).[35] Hypoxia and hypercarbia stimulate inspiratory and expiratory motor neuron activity.[36,37] The neural mechanism by which central and peripheral chemoreceptors affect cranial motor neuron activity and signaling upper airway dilating muscles, and the role of vagal afferents in these responses are unknown.

Measurement techniques for upper airway mechanics in exercising horses

Evaluating upper airway function in exercising horses requires a combination of qualitative and quantitative measurement techniques. Videoendoscopic evaluation of the upper airway in exercising horses has proven invaluable in assessing both normal and abnormal airway function. Sometimes combined with visual observations of airway function, upper airway mechanics measurements are made by measuring airway pressures and airflows. Using the data, calculations can be made to determine respiratory frequency, tidal volume, minute ventilation, and impedance. Tidal breathing flow volume loops can be constructed if airflow is quantitatively measured and appropriate computer software is available.[38] As well, pressure volume curves can be constructed if both airway pressure and tidal volume are measured, permitting work of breathing to be calculated.[10] Muscle activity can be assessed by measuring the electromyographic activity of muscles.[16–19] Finally, because many upper airway abnormalities cause the horse to produce unique respiratory related sounds during exercise, sound analysis can be used to evaluate upper airway function and dysfunction.[39]

The goal when measuring tracheal pressures in exercising horses is to obtain accurate measurements in a minimally invasive manner. Error in measurements can occur due to the high tracheal airflow velocities in running horses and the presence of the measurement apparatus.[40] Trancutaneous placement of tracheal catheters minimizes airflow obstruction and provides excellent measurement of tracheal static pressure.[41,42] However, percutanous tracheal catheterization, especially repeated catheterization, causes tissue trauma that may be unacceptable. Therefore, nasotracheal catheters are frequently used for measuring tracheal static pressures.[40] These catheters are constructed using polyethylene tubing with a series of side ports created for pressure measurement.[40] The catheter is then connected to a differential pressure transducer (Model DP/45, Validyne, Northridge, CA) and recordings can be made on chart recorders or computers capable of recording respiratory function measurements.

Airflow can be measured qualitatively or quantitatively. Qualitative measurement can be performed using temperature sensors.[43] Temperature sensors, such as thermisters can be placed at the nostril or within the trachea. Respiratory rate and respiratory:stride coupling can be assessed, but quantitation of the airflow is not possible. Facemask systems are used to quan-

titate airflow measurements.[43,44] The facemask must cover the horse's nose and mouth, be airtight, and allow for unimpeded nostril dilation. In addition, the mask should be light enough and comfortable for the horse to wear while running. Pneumotachographs are instruments used to measure instantaneous rate of volume flow of respired gas.[43,44] Briefly, the pneumotachograph is attached to the end of the facemask and as the horse breathes through the pneumotachograph, it creates a resistance to airflow. The pneumotachograph is calibrated prior to the experiment using a rotameter such that a given pressure, measured using a pressure transducer, is proportional to the airflow. Therefore, the difference in pressure measured across the pneumotachograph is proportional to the airflow rate. A pneumotachograph facemask system imposes added resistance to airflow, and may alter upper airway pressures, respiratory frequency, ventilation, and respiratory pattern in exercising horses.[45,46] Alternatively, quantitative airflow measurements can be made by ultrasonic flow determination, using ultrasonic pneumotachometers.[43] These flow meters impose low resistance and have a high frequency response, but are prone to baseline drift.[43]

Pressure and airflow can be recorded on chart recorders or computers, allowing calculation of various indices that describe the patterns of the airflow. Peak inspiratory and expiratory pressures and flows are determined by measuring from baseline to the peak of the curve. Impedance (Z) is calculated by dividing peak pressure by peak flow. Tidal volume (V_T) can be determined by measuring the area under the airflow curve during exhalation. Respiratory frequency (f_R) is determined by counting the number of breaths per minute. Minute ventilation ($\dot{V}_E$) is the product of respiratory frequency and tidal volume. Respiratory timing can also be determined by measuring the inspiratory time (T_I) and expiratory time (T_E) for each breath.[10]

Tidal breathing flow volume loops can be constructed by plotting airflow and tidal volume. Indices used to describe the loop and the pattern of breathing include peak inspiratory and expiratory flow, and inspiratory and expiratory flows at various tidal volumes, including 50, 25, and 12.5% of tidal volume.[38] Tidal breathing flow volume loop analysis is a very sensitive method for detecting airway obstruction in exercising horses because airflows are so high.[38] Pressure volume curves can also be constructing by plotting pressure and volume. Work of breathing can then be calculated by determining the area under the pressure volume curve.[10]

Sound analysis or spectrum analysis of respiratory sounds has been used to help identify the source of specific airway obstructive diseases and to evaluate the effect of various surgical procedures on airway noise. Respiratory sounds can be recorded using a dynamic, unidirectional microphone positioned in front of the horse's nose.[39] Recordings can be made while the horse exercises freely or on a treadmill. The respiratory sounds are then analyzed using a computer-based spectrum analysis program (Spectrogram version 6.0 (shareware), available at: http://www.monumental.com/rshorne/gram.html). Spectrograms of horses with laryngeal hemiplegia and dorsal displacement of the soft palate have been described.[39]

Electromyographic measurements of muscles can be made using unipolar or bipolar fine wire or surface electrodes, if the muscle is superficial. Electromyography provides information about the timing of muscle activity and relative increases and decreases in electrical activity, but does not provide information about muscle lengthening or shortening.[47] Sonomicrometry can be used to assess muscle lengthening and shortening.[48]

Muscular anatomy and function of the upper airway

The nose

The horse's nose includes the paired external nares, the nasal cavities, and the paranasal sinuses. The nostril has two compartments: a dorsal blind sac called the nasal diverticulum and the ventral part, which is the true nostril.[49] The alar fold divides the nostril into the dorsal and ventral parts. The nasal cavity is divided in half by the nasal septum and vomer bone. Each nasal cavity has a dorsal and ventral nasal concha, which divide the cavity into dorsal, ventral, middle, and common meatus (Fig. 26.4).[49] The ethmoid turbinates project from the ethmoid bone in the caudal part of the nasal cavity (Fig. 26.5). The nasal valve is the narrowest point in the nasal cavity and, thus, is a major contributor to nasal resistance.[1] This region is caudal to each nostril and immediately rostral to the nasoincisive notch within the dorsal meatus. It is bound medially by the nasal septum, ventrally by the concha, and dorsolaterally by the skin and dorsal conchal fold (Fig. 26.6).[49] Expansion of the nasal valve during exercise occurs by constriction of capacitance vessels and contraction of

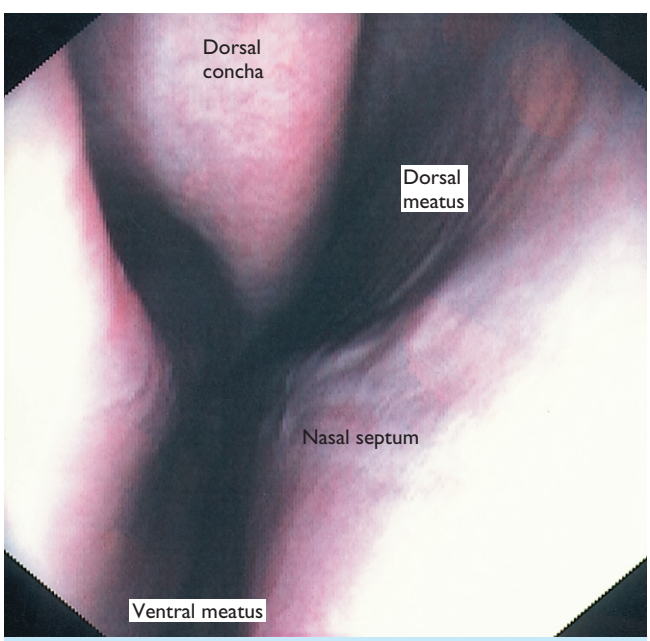


Fig. 26.4
Endoscopic image of the concha and turbinates within the nasal passage.

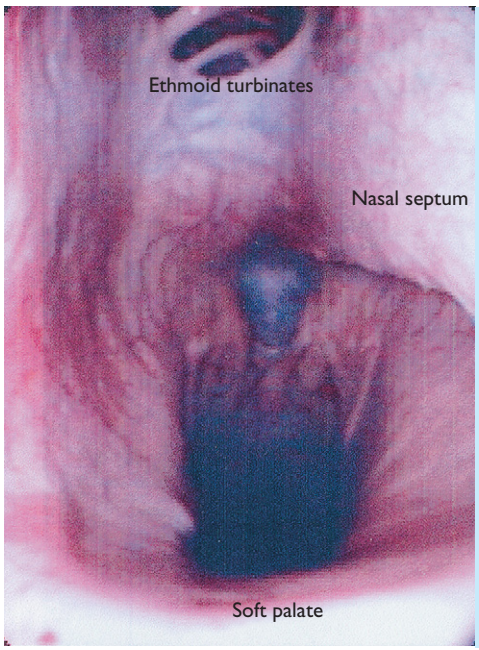


Fig. 26.5 Endoscopic image of the ethmoid turbinates and nasopharynx.

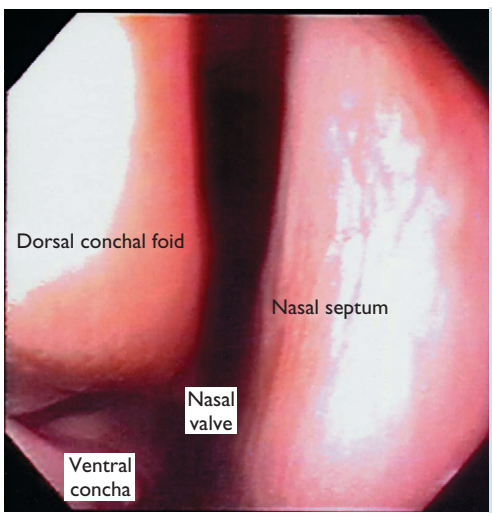


Fig. 26.6 Endoscopic image of the nasal valve region.

muscles that pull the skin taut at the dorsal aspect of the notch. The respiratory portion of the nasal cavity has a vascular submucosa, which contains a rich vascular plexus. This plexus is concentrated on the ventral portion of the nasal septum and ventral meatus and is important for warming and humidifying air. The capacitance blood vessels in the airways, especially those lining the nasal mucosa, are innervated by sympathetic, parasympathetic, and peptidergic systems that regulate blood flow.[50] This extensive vasculature is responsible for warming and humidifying inspired air. When these vessels are dilated, the sinuses and nasal passages become engorged with blood, resulting in airway narrowing and increased airway resistance. Such nasal congestion is a cause of airway obstruction and poor performance in horses with Horner's syndrome. During exercise, sympathetic stimulation causes vasoconstriction, increasing airway dimensions and decreasing resistance to airflow.[50]

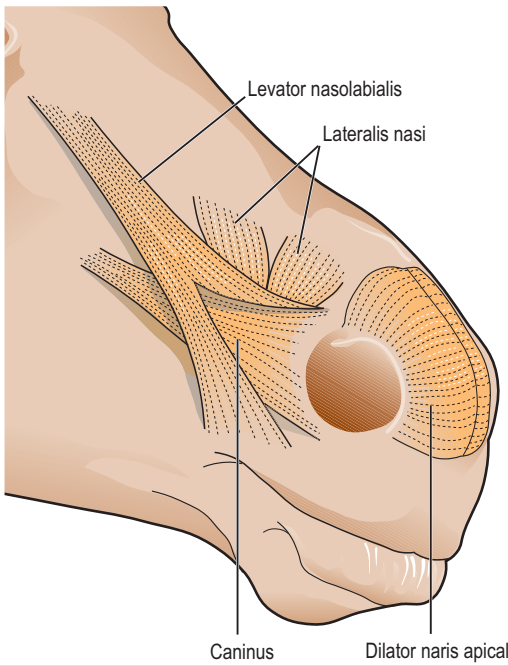


Fig. 26.7 Illustration of the dilating muscles of the nares.

In obligate nasal breathers such as the horse, increasing nasal patency during exercise is critical to minimizing work of breathing. At rest, the horse's nostril is shaped like a comma, but as the horse increases its respiratory effort the nostril dilates and becomes circular in shape. Horses can actually decrease their nasal resistance during exercise by increasing nasal volume and flaring their nostrils. Nostril dilation is accomplished by the contraction of four different muscles (Fig. 26.7).[49] Contraction of the lateralis nasi dilates the nostril, rotates the conchal cartilages laterally, and expands the nasal vestibule, which forms the floor of the nasal valve.[49] Other muscles involved in dilatation of the nostrils include the caninus, dilator naris apicales, and levator nasolabialis. Contraction of the caninus or dilator naris lateralis muscle helps expand the lateral aspect of the nostrils.[49] Dilator naris apicales is an unpaired muscle that lies between the nostrils and aids in dilatation of the nostrils.[49] Levator nasolabialis dilates the nostrils and also elevates the maxillary lip and commissures.[49] Horses with dysfunction, weakness, or lack of contraction of one or more of these muscles will likely have dynamic nasal obstruction that may limit performance.

The nasopharynx

The nasopharynx is a musculomembranous unit that functions during breathing, deglutition, and vocalization and connects the nasal cavity to the larynx. It is attached to the pterygoid, palatine, and hyoid bone, and to the arytenoid, cricoid, and thyroid cartilages by nasopharyngeal muscles that cause pharyngeal dilation and constriction.[51] The nasopharynx is not directly supported by cartilage or bone, yet contraction of these pharyngeal muscles allows the nasopharynx to withstand large

changes in intraluminal pressures that occur during tidal breathing at rest and during exercise. Such activation of these muscle groups is synchronous with breathing and this synchronization is coordinated by multiple stimuli.[17,27] These same muscles are also important during deglutition. This dichotomy of action, contracting the pharyngeal walls during swallowing and dilating the airway during breathing, seems contradictory. But these muscles are uniquely situated to perform both activities, because the pharynx is a conduit for both food and air. Muscles responsible for altering the size and configuration of the nasopharynx include the muscles that alter the shape and position of the tongue, the muscles that control the position of the hyoid apparatus, a constrictor group of muscles located in the dorsal pharynx, and a group of muscles that regulate the position of the soft palate.

Soft palate

The soft palate completely divides the pharynx into nasal and oral compartments in the horse. Because the horse is an obligate nasal breather, it is critically important that the soft palate remains ventral to the epiglottis, except during swallowing, to allow unimpeded nasal breathing. The soft palate extends caudally from the hard palate to the base of the larynx and consists of the oral mucous membrane, which contains ductile openings of the palatine glands, the palatine glands, the palatine aponeurosis, palatinus and palatopharyngeus muscles, and the nasopharyngeal mucous membrane.[51] The caudal free margin of the soft palate continues dorsally, on either side of the larynx, forming the lateral pillars of the soft palate. These pillars unite dorsally, forming the posterior pillar of the soft palate or the palatopharyngeal arch.

The position of the soft palate is determined by the coordinated activity of groups of antagonistic muscles which include the levator veli palatini, tensor veli palatini, palatinus, and palatopharyngeus muscles (Fig. 26.8).[52,53] The *levator veli palatini* muscle attaches to the petrous part of the temporal bone and the lateral lamina of the guttural pouch. It travels along the lateral wall of the nasopharynx and terminates within the soft palate. A branch of the pharyngeal branch of the vagus nerve innervates this muscle.[51] It acts to elevate the soft palate during swallowing and vocalization. The action of the levator veli palatini muscle can be seen during endoscopic examination of the upper airway when the gag reflex is stimulated (Fig. 26.9). A 'sling' forms within the nasopharynx as the nasopharynx contracts into a sphincter.

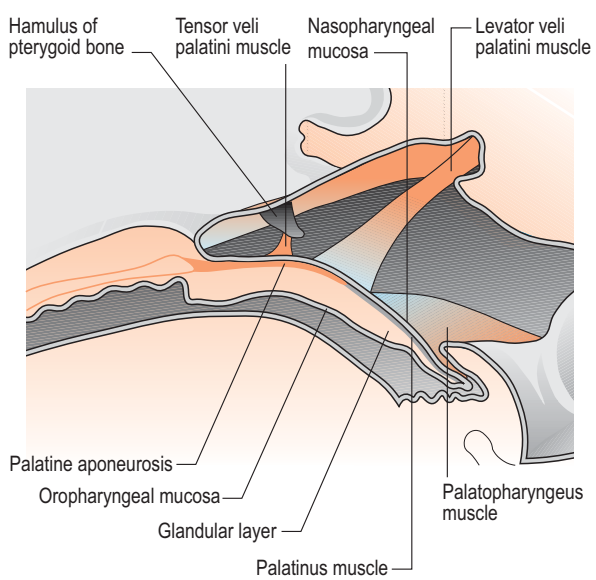


Fig. 26.8
Illustration of the muscles of the soft palate.

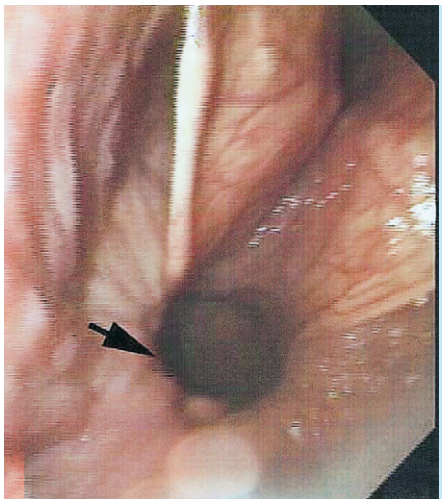


Fig. 26.9
Endoscopic image of the nasopharynx during a 'gag' reflex. Notice the 'sling' formed by partial contraction of the levator veli palatini muscles (arrow).

The *tensor veli palatini* is a flat, fusiform muscle that, like the levator, attaches to the petrous part of the temporal bone, the pterygoid bones, and the lateral lamina of the guttural pouch.[51] Its tendon is reflected around the hamulus of the pterygoid bone, where it is lubricated by a bursa. The tendon then ramifies in the palatine aponeurosis.[51] It receives motor innervation from the mandibular branch of the trigeminal nerve. Contraction of this muscle tenses the palatine aponeurosis and, therefore, the rostral portion of the soft palate, and depresses this portion of the soft palate toward the tongue.[51–53] Contraction of the tensor veli palatini muscle also aids in opening the pharyngeal opening of the guttural pouch.[54] Bilateral transection of the tendon of the tensor veli palatini muscle in horses causes instability of the rostral portion of the soft palate resulting in inspiratory obstruction during intense exercise (Fig. 26.10A–C).[55] The rostral portion of the soft palate is more compliant and its action dependent on airway pressures, such that during inspiration the rostral portion of the soft palate billows dorsally in the airway and during expiration it is depressed toward the tongue by the positive pressure within the airway.[55]

The *palatinus* muscle (uvula retractor muscle) consists of two fusiform muscles that lie on either side of midline of the soft palate, beneath the nasopharyngeal mucosa, extending caudally from the hard palate.[51] The muscles attach to the caudal aspect of the palatine aponeurosis and terminate near the caudal free margin of the soft palate. A small muscle bundle arising from the lateral aspect of each muscle continues a short distance caudodorsally into the palatopharyngeal arch.[51] It receives motor innervation from a branch of the

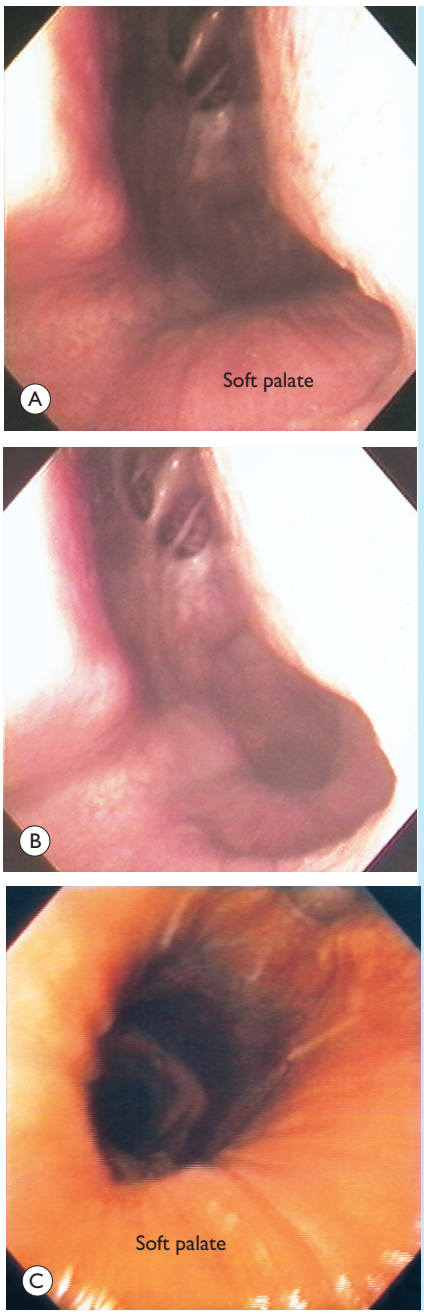


Fig. 26.10
(A) Endoscopic image of the nasopharynx during inhalation while the nares are occluded following bilateral tensor veli palatini tenectomy. Notice how the rostral portion of the soft palate billows dorsally into the airway.
(B) Endoscopic image of the nasopharynx during exhalation while the nares are occluded following bilateral tensor veli palatini tenectomy. Notice how the rostral portion of the soft palate billows dorsally into the airway.
(C) Endoscopic image of the nasopharynx during treadmill exercise following bilateral tensor veli palatini tenectomy. Notice how the rostral portion of the soft palate collapses dorsally into the airway.

pharyngeal branch of the vagus nerve.[51] Contraction of the palatinus muscle shortens the soft palate.[51–53]

The *palatopharyngeus* muscle originates from the palatine aponeurosis and the lateral border of the palatinus muscle.[51] It travels caudally along the lateral wall of the nasopharynx to the pharyngeal raphe, forming part of the superior constrictor muscle group. A branch of the pharyngeal branch of the vagus nerve innervates it.[51] Contraction of this muscle shortens the soft palate and draws the larynx and esophagus toward the root of the tongue.

Contraction of both the palatinus and palatopharyngeus muscles shortens the soft palate and depresses the caudal portion toward the tongue.[52,53,56] Both the palatinus and palatopharyngeus muscles receive efferent motor innervation from the pharyngeal branch of the vagus nerve.[51] This nerve branches from the parent vagus nerve at the level of the cranial cervical ganglion and courses cranioventrally along the medial wall of the guttural pouch to the dorsal wall of the pharynx where it ramifies in the pharyngeal plexus. Bilateral local anesthesia of the pharyngeal branches of the vagus nerve induced persistent dorsal displacement of the soft palate and dysphasia in horses.[57] Horses can become dysphasic, with or without persistent soft palate dysfunction, following guttural pouch lavage with caustic solutions, guttural pouch empyema, trauma, or mycosis.[58,59] Based on this information, there was convincing evidence to suggest that dysfunction of the neuromuscular group, including the pharyngeal branch of the vagus nerve, palatinus and palatopharyngeus muscles, might be involved in the pathogenesis of intermittent dorsal displacement of the soft palate in exercising horses.

Electromyographic measurements of the palatinus and palatopharyngeus muscles in normal horses exercising on a treadmill showed that these muscles are active, synchronous with respiration, and their activity increases as exercise intensity and inspiratory pressures increase (Fig. 26.11).[60] Phasic expiratory activity of the palatinus muscles increases 310 ± 67%, whereas phasic expiratory activity of the palatopharyngeus muscles increases 120 ± 30% as the treadmill speed increases from 6 m/s to 13 m/s (or until exhaustion).[60] Palatinus muscle EMG activity is diminished in horses with dorsal displacement of the soft palate and does not significantly increase as treadmill speed increases.[60]

The palatinus muscle is composed of principally type IIA fast twitch fibers (5–25% type I and 75–95% type IIA) with darkly staining mitochondria, which suggests that these fibers have increased endurance relative to most skeletal muscle fast-twitch fibers.[61] The palatopharyngeus muscles are also principally composed of type IIA fibers (10–25% type I and 75–90% type IIA fibers).[61] Pathologic abnormalities are

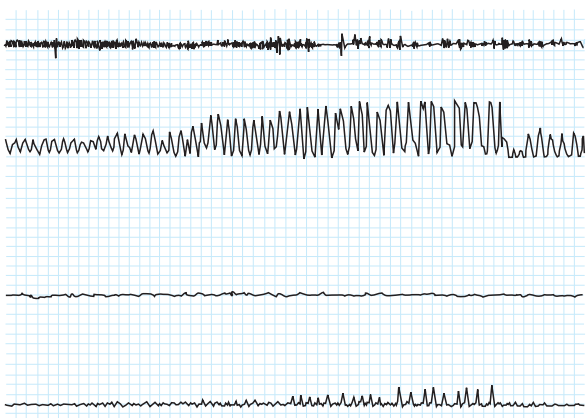


Fig. 26.11
Raw and moving time average electromyographic activity tracings of the palatinus and palatopharyngeus muscles during treadmill exercise and during recovery.

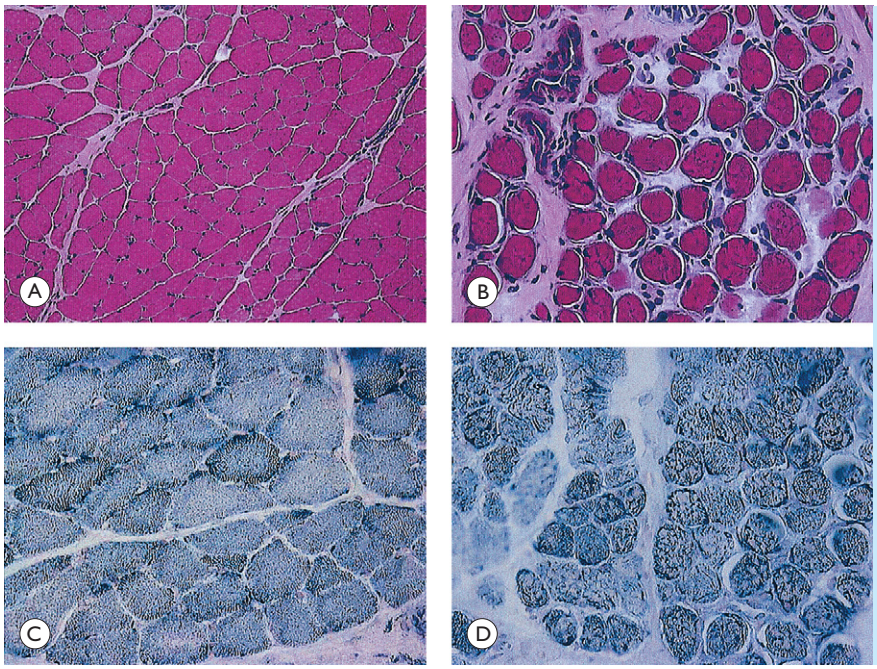


Fig. 26.12
(A) H&E stained section of the palatinus muscle from a normal horse. (B). H&E stained section of the palatinus muscle from a horse with intermittent dorsal displacement of the soft palate. Notice the increased amount of connective tissue (light pink) and tissue degeneration. (C). NADH stained section of the palatinus muscle from a normal horse. (D). NADH stained section of the palatinus muscle from a horse with intermittent dorsal displacement of the soft palate. Notice the moth-eaten fibers and areas of increased amounts of connective tissue.

also observed in the palatinus muscle of horses with intermittent dorsal displacement of the soft palate (DDSP). These abnormalities are consistent with chronic denervation and include fiber type grouping, mild atrophy, moth-eaten fibers and target fibers (Fig. 26.12A–D).[61]

Muscles of the hyoid apparatus

The hyoid apparatus in horses consists of an assembly of bony rods, some of which articulate together.[62] Several muscles are attached to this apparatus, and the contraction of theses muscles alters the shape and position of the apparatus, which in turn, changes the position and shape of the larynx and nasopharynx.[63,64] The hyoid apparatus consists of the paired stylohyoid, epihyoid, ceratohyoid, thyrohyoid bones, and the central basihyoid bone (Fig. 26.13). The stylohyoid bone articulates with the petrous part of the temporal bone, allowing the stylohyoid bones to move cranial to caudal, in a pendulous manner. The ceratohyoid bone attaches to the distal end of the stylohyoid bone (by way of the epihyoid bone), and movement at this articulation lengthens the stylohyoid–ceratohyoid unit (Fig. 26.14). The base or root of the tongue is attached to the lingual process of the basihyoid bone. The tongue is located on the floor of the mouth between the rami of the mandible. The base of the tongue is attached to the hyoid apparatus, soft palate, and pharynx.[51] Folds of mucous membrane pass dorsally on either side of the base of the tongue to form the palatoglossal arches, which attach the tongue to the soft palate.[51] The genioglossus, hyoglossus, and styloglossus muscles are extrinsic muscles of the tongue that, in part, control the position and function of the tongue and provide attachments to the hyoid apparatus.[51]

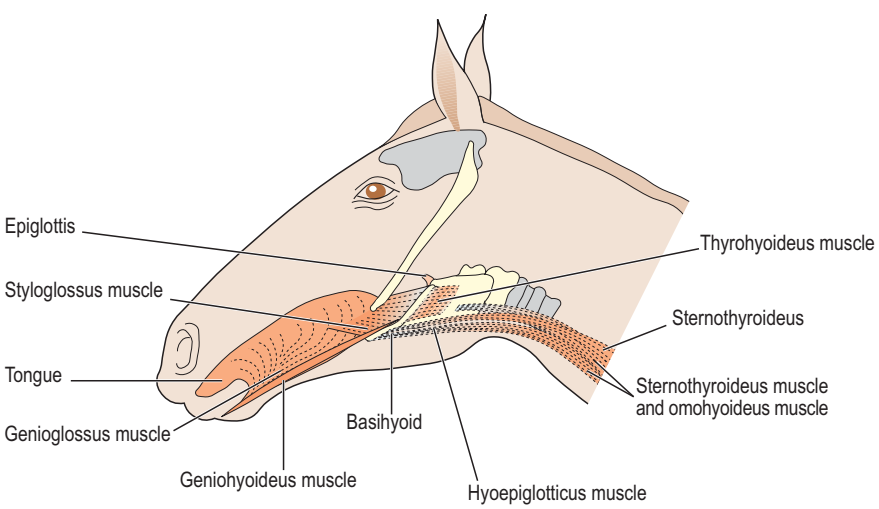


Fig. 26.13
Illustration of some of the muscles that control nasopharyngeal function.

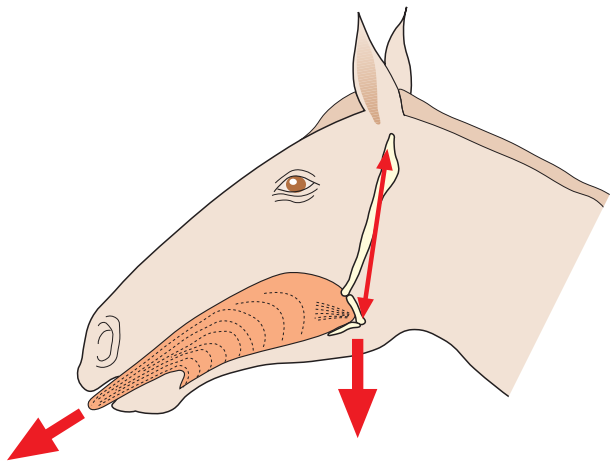
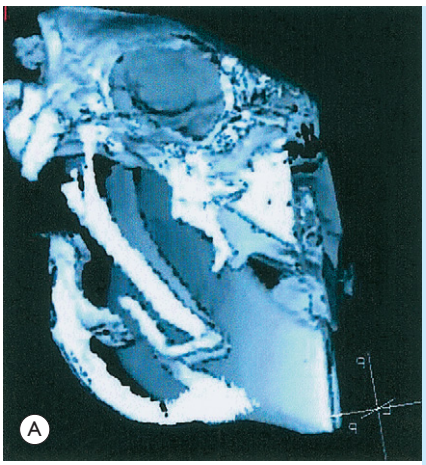


Fig. 26.14
Illustration showing the effect of various muscles on hyoid length and position.



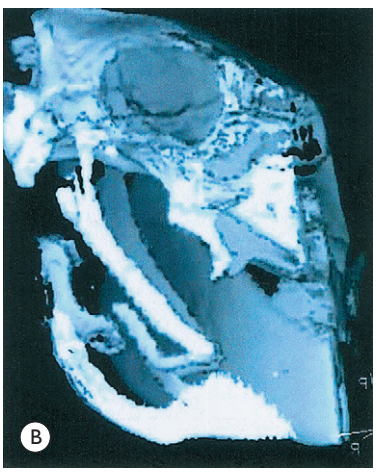


Fig. 26.15
(A) Computed tomographic image of the hyoid apparatus of a horse with its tongue tied out of its mouth under general anesthesia. (B) Computed tomographic image of the hyoid apparatus of a horse under general anesthesia with the tongue in a neutral position.

The genioglossus is a fan-shaped muscle that lies within and parallel to the median plane of the tongue.[51] The genioglossus muscle originates from the medial surface of the mandible, just caudal to the symphysis, and is innervated by the medial branch of the hypoglossal nerve.[51] A large tendon runs throughout the muscle. Muscle fibers radiate rostrally toward the tip of the tongue, dorsally, and distally toward the root of the tongue. The hyoglossus is a flat wide muscle that lies in the lateral portion of the root of the tongue.[51] The hyoglossus originates from the lateral aspect of the basihyoid bone and from portions of the stylohyoid and thyrohyoid bones and is innervated by the lateral branch of the hypoglossal nerve.[51] The styloglossus muscle originates at the distal lateral aspect of the stylohyoid bone and travels the length of the tongue, along its lateral aspect.[51] Near the tip of the tongue the paired muscle meets and ramifies with fibers of intrinsic tongue muscles. Styloglossus contraction retracts the tongue. Contraction of the genioglossus muscle protracts the tongue and pulls the basihyoid bone rostrally. Genioglossus also acts with the hyoglossus muscle to depress and retract the tongue. Hyoglossus and genioglossus activity are synchronous with respiration and activity of these muscles correlates well with increases in pharyngeal airway size during breathing.[63–68] Hypoxia, hypercapnia, and airway occlusion caused parallel increases in electrical activity of the protrudor and retractor muscle of the tongue, consistently inducing net retraction and depression of the tongue, improved airflow function and enhanced pharyngeal stability.[64,65] Therefore, it seems that tongue depression may be the critical force needed to dilate and stabilize the nasopharynx.

Many horses perform or race with their tongues tied to the mandible or out of the mouth to stop the horse from getting the tongue over the bit, and in an attempt to improve performance, decrease airway noise, and improve airway function. Tying the tongue out of the horse's mouth does not influence the position of the hyoid apparatus or dimensions of the nasopharynx in anesthetized horses (Fig. 26.15A,B).[69,70] In addition, application of a tongue-tie does not alter airway mechanics in normal, exercising horses, suggesting that application of a tongue-tie does not improve upper airway function or alter position of the hyoid apparatus in normal horses.[69,70] The passive action of pulling the tongue out of the horse's mouth is very different from active muscle contraction. Also, the tongue-tie may cause protrusion of the tongue but not depression of the tongue, and depression of the tongue may indeed be the critical action of the extrinsic tongue muscles that creates upper airway stability and dilation.

Other muscles that attach to the hyoid apparatus include the geniohyoideus, sternohyoideus and sternothyroideus, omohyoideus, and thyrohyoideus. The geniohyoideus muscle is a fusiform, paired muscle that lies on the ventral surface of the tongue.[71] The geniohyoideus originates from the medial surface of the mandible (near the genioglossus' origin) caudal to the symphysis and inserts on the basihyoid bone. The hypoglossal nerve innervates it, and its action is thought to move the hyoid bone rostrally.[71] The omohyoideus, sternohyoideus and sternothyroideus muscles are accessory respiratory muscles that insert on the manubrium and extend cranially. The sternothyroideus inserts on the caudal abaxial aspect of the thyroid cartilage, and the sternohyoideus inserts on the basihyoid bone and the lingual process of the hyoid apparatus. Contraction of these muscles results in caudal traction of the hyoid apparatus and larynx, resulting in dila-

tion of the upper airway.[71] These muscles are innervated by branches of the first and second cervical nerves.[71] Both the sternothyroideus and sternohyoideus muscles are sometimes transected as palliative therapy for horses with dorsal displacement of the soft palate. Following myectomy, translaryngeal and tracheal inspiratory pressures and resistance measurements increase, suggesting that these muscles may act to dilate and stabilize the nasopharynx in normal horses.[72] The effects of myectomy on airway mechanics in horses with upper airway obstructive disease are yet unknown. The omohyoideus muscles originate on the subscapular fascia near the shoulder joint and also insert on the basihyoid bone and the lingual process of the hyoid apparatus. Contraction of these muscles results in caudal traction of the hyoid apparatus and tongue movement other than retraction.[73] The omohyoideus muscles are innervated by branches of the first and second cervical nerves. The omohyoideus muscles have also been transected for treatment of soft palate displacement in conjunction with the sternohyoideus and sternothyroideus muscles but no experimental data exist to investigate the result of omohyoid transection alone or in conjunction with the sternohyoideus and sternothyroideus muscles in horses during exercise.[74]

The *thyrohyoideus* is a flat rectangular muscle attached to the lateral surface of the thyroid cartilage lamina that inserts on the caudal part of the thyrohyoid bone.[71] It is innervated by the hypoglossal nerve and moves the hyoid bone caudally or the larynx rostrally and dorsally.[71] In studies evaluating the electromyographic activity of some 'extrinsic' nasopharyngeal muscles during exercise, Ducharme and co-workers observed decreased thyrohyoideus muscle activity prior to soft palate displacement in one horse. Investigations by Tsukroff et al[75] reveal that transection of a combination of the following muscles results in dorsal displacement of the soft palate in horses: thyrohyoideus, omohyoideus, sternohyoideus and hyoepiglotticus muscles.[75] The displacement observed was associated with a more caudal positioning of the basihyoid bone. In subsequent studies thyrohyoideus muscle resection caused intermittent dorsal displacement of the soft palate in exercising horses.[76] As well, thyrohyoideus muscle prosthesis, created by placing a suture through the basihyoid bone and the thyroid cartilage, alleviates dorsal displacement of the soft palate.[76] These data clearly suggest that thyrohyoideus muscle dysfunction is the likely etiology of intermittent dorsal displacement of the soft palate in horses.

Dorsal pharyngeal constrictors

The action of the dorsal pharyngeal constricting muscles and the stylopharyngeus muscle is responsible for stiffening and dilating the nasopharynx.[77–80] The inferior pharyngeal constrictor (thyropharyngeus muscle), middle pharyngeal constrictor (hyopharyngeus muscle), and superior pharyngeal constrictor (palatopharyngeus and pterygopharyngeus muscles) form the dorsal and caudolateral pharyngeal walls.[78,79] Contraction and shortening of these muscles forms a sphincter, moving the food bolus caudal into the esophagus during swallowing. During breathing, these muscles have tonic and phasic expiratory activities, which helps to support the nasopharynx.[79,80] The major dilating muscle of the dorsal nasopharynx is the stylopharyngeus muscle.[79] This muscle originates on the axial aspect of the distal portion of the stylohyoid bone and courses rostroventrally to ramify in the wall of the dorsal nasopharynx, by passing between the pterygopharyngeus and palatopharyngeus muscles (Fig. 26.16A,B). Contraction of the stylopharyngeus muscles pulls the pharyngeal wall dorsally, to receive the bolus during swallowing.[81] In a similar manner, during breathing, contraction of the stylopharyngeus muscle pulls the nasopharyngeal wall dorsally, thereby supporting the dorsal wall of the nasopharynx and preventing dynamic collapse of this area during inspiration.[82] The glossopharyngeal nerve provides motor innervation to the stylopharyngeus muscle.[81] Bilateral glossopharyngeal nerve anesthesia produces stylopharyngeus muscle dysfunction, dorsal pharyngeal collapse both during nasal occlusion and exercise, and airway obstruction in horses (Fig. 26.17A,B).[83] Therefore, the stylopharyngeus muscle is an important nasopharyngeal dilating muscle in horses and dysfunction of this muscle may be implicated in clinical cases of dorsal nasopharyngeal collapse.[83]

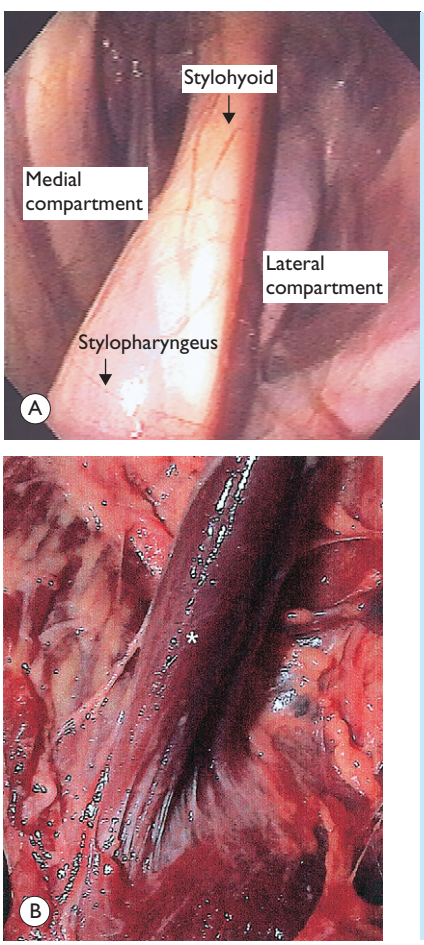


Fig. 26.16 (A) Endoscopic image of the origin of the stylopharyngeus muscle on the axial aspect of the stylohyoid bone within the guttural pouch. (B) Post-mortem dissected specimen showing the stylopharyngeus muscle inserting between the pterygopharyngeus and palatopharyngeus muscles.

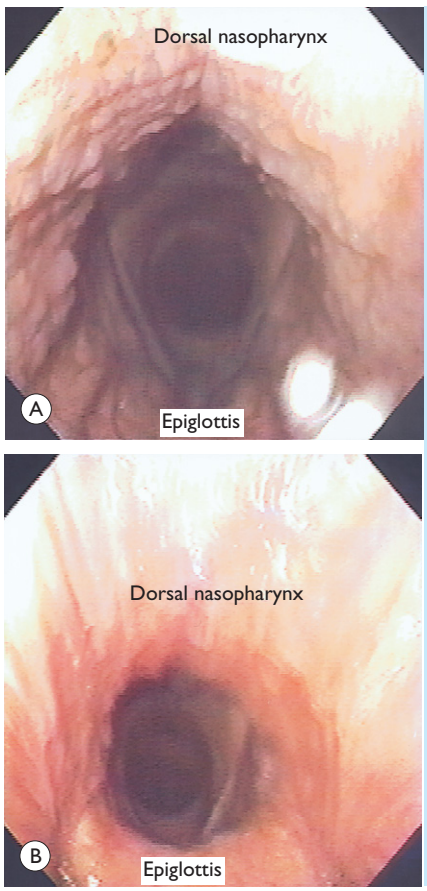


Fig. 26.17 (A) Endoscopic image of the nasopharynx following bilateral glossopharyngeal anesthesia with the nares occluded. Notice how the dorsal nasopharynx collapses. (B). Endoscopic image of the nasopharynx following bilateral glossopharyngeal nerve anesthesia during treadmill exercise (12 m/s). Notice how the dorsal nasopharynx collapses, obstructing the view of the corniculate processes.

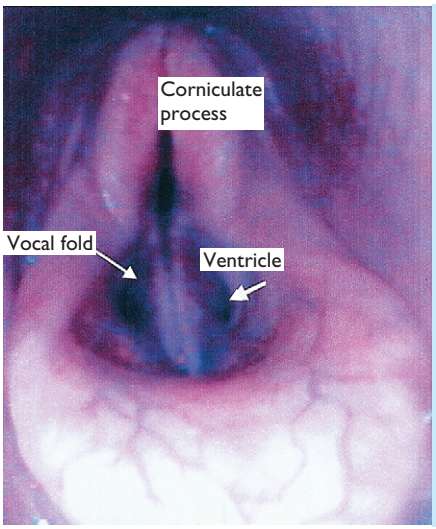


Fig. 26.18 Endoscopic image of the larynx during adduction.

The larynx

The larynx forms the communicating channel between the pharynx and the trachea and functions during breathing, vocalization, and deglutition. The larynx is composed of cartilage and muscle and is covered with a mucous membrane. The laryngeal cartilages include the cricoid, thyroid, and epiglottic cartilages, which are unpaired, and the arytenoid cartilages, which are paired.[84] The cricoid cartilage is shaped like a signet ring and is positioned rostral to the first tracheal ring and connected to the trachea by the cricotracheal membrane. The thyroid cartilage is the largest of the laryngeal cartilages and is situated just rostral to the cricoid cartilage.[84] The arytenoid cartilages form the dorsal border of the rima glottidis. They are triangular in shape with a dorsal muscular process, which serves as the origin for the cricoarytenoideus dorsalis muscle, a ventral vocal process serving as the attachment of the vocal ligament, and the rostral apex which forms the corniculate process.[84] The arytenoid cartilages are positioned on either side of the cricoid cartilage and are connected to it by the cricoarytenoid articulations. The articulation is a diarthrodial joint that allows the arytenoid cartilage to rotate dorsolaterally during abduction and axially during adduction.[84] The mucous membrane covering the epiglottic cartilage reflects off the lateral border of the epiglottis and blends with the mucous membrane covering the corniculate processes of the arytenoid cartilages, forming the aryepiglottic folds. The mucous membrane covers the vocal ligament, forms the vocal folds, and lines the lateral ventricles, forming the laryngeal saccules (Fig. 26.18). These saccules are 2.5 cm deep with a capacity of 5 to 6 ml. They extend between the medial surface of the thyroid cartilage and the ventricularis and vocalis muscles.

The intrinsic laryngeal muscles produce changes in caliber of the rima glottidis by abducting and adducting the corniculate processes of the arytenoid cartilages and the vocal folds and hence altering airway resistance. These actions are accomplished by the contractions of the intrinsic laryngeal muscles. The cricoarytenoideus dorsalis is the principal abductor muscle that widens the laryngeal aperture by abducting the corniculate process of the arytenoid cartilage and tensing the vocal folds. The thyroarytenoideus, arytenoideus transversus, and the cricoarytenoideus lateralis muscles adduct the corniculate processes of the arytenoid cartilages, narrowing the rima glottidis and protecting the lower airway during swallowing.[84] The cricothyroideus muscle receives efferent motor innervation from the external branch of the superior laryngeal nerve, a branch of the vagus nerve, while all other intrinsic laryngeal muscles receive motor innervation from the recurrent laryngeal nerve, which is also a branch of the vagus nerve.[84] Crushing or transection of the left recurrent laryngeal nerve, or perineural anesthesia of the left recurrent laryngeal nerve, results in grade IV laryngeal hemiplegia in horses.[85] However, following experimental crush of the left recurrent laryngeal nerve in ponies, reinnervation of some intrinsic laryngeal muscles is evident.[85] In ponies, recovery of movement of the vocal folds occurred between 2.5 and 8 months, following recurrent laryngeal nerve crush.[85] Electromyographic examinations of the laryngeal muscles and microscopic evaluation of the muscles and the recurrent larygneal nerve reveal that return of function is due to reinnervation.[85] At times, there is evidence of aberrant reinnervation in abductor and adductor muscles.[85]

The epiglottis is principally composed of elastic cartilage and rests on the dorsal surface of the body of the thyroid cartilage and is held there by the thyroepiglottic ligaments. The position of the epiglottis is controlled by the position of the larynx, and hyoid apparatus, and by contraction of the hyoepiglotticus muscle, which is the only muscle that attaches to the epiglottis.[84] The hyoepiglotticus is a bilobed extrinsic laryngeal muscle that originates on the basihyoid bone in horses, and inserts on the ventral body of the epiglottis.[84] In horses, contraction of the hyoepiglotticus muscle pulls the epiglottis toward the basihyoid bone, depressing it against the soft palate, enlarging the airway.[28] The hyoepiglotticus muscle has respiratory-related electromyographic activity in horses that increases with exercise intensity and breathing effort.[28] Furthermore, electrical stimulation of the hyoepiglotticus muscle depresses the epiglottis ventrally against the soft palate, changing the conformation of the epiglottis in some horses (Fig. 26.19A,B).[28] The hyoepiglotticus muscle is likely an upper airway dilating muscle, which functions to enlarge the airway, thereby decreasing airway resistance in exercising horses. In addition to dilating the aditus laryngis, contraction of the hyoepiglotticus muscle stabilizes the epiglottis during inspiration, preventing its prolapse through the rima glottidis. Retroversion of the epiglottis is described clinically in exercising horses and can be created experimentally by anesthesia of the hypoglossal nerves.[86,87] Blockade of these nerves creates hyoepiglotticus dysfunction, and dysfunction of other hyoid muscles including geniohyoideus and genioglossus, and suggests that the clinical problem may be due to paresis of the hyoepiglotticus muscle or other muscles involved in controlling the position of the basihyoid. Active control of epiglottis position by the hyoepiglotticus muscle apparently stabilizes the epiglottis and vigorous recruitment of the muscle activity during inhalation dilates the airway and maintains the nasal breathing route in horses during intense exercise. Conformational changes in the epiglottis that occur during exercise, respiratory stimulation, sedation, or nasal occlusion may not be abnormal, but may be the result of normal activity of the hyoepiglotticus muscle.

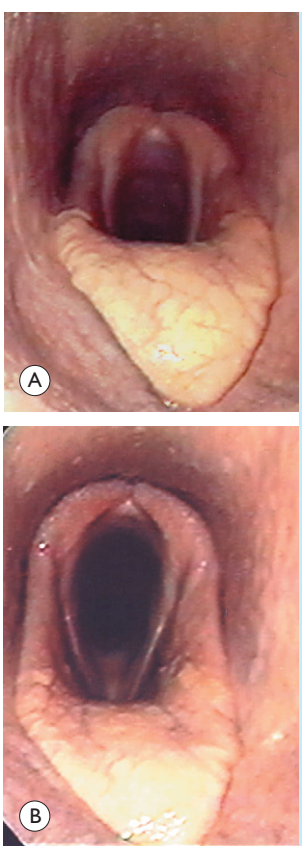


Fig. 26.19
(A) Endoscopic image of the larynx. (B) Endoscopic image of the same larynx during electrical stimulation of the hyoepiglotticus muscle.

Guttural pouches

Physiology

The guttural pouch, or diverticulum of the auditory tube, is unique to the horse and other Perissodactyla. Each pouch has a volume of 300 to 500 mL and communicates with the nasopharynx through the pharyngeal opening of the auditory tube. The guttural pouch is lined with a thin mucous membrane composed of pseudostratified, ciliated epithelium interspersed with goblet cells.[88] Mucous glands and lymphatic nodules are found deep to the epithelial layer. Various immunoglobulin isotypes, including IgGa, IgM, and IgA, have been detected in the guttural pouch mucosa, submucosa, and lymph nodules, suggesting that the guttural pouch has phylactic ability.[89]

Recently, investigators determined that the equine guttural pouches function during selective brain-cooling to maintain blood carried by the internal carotid arteries at a temperature below the core body temperature during hyperthermia, induced by exercise.[88] Blood is supplied to the brain, principally, by the internal carotid arteries, with contributions from the cerebral and occipital arteries. The extracranial portion of the internal carotid artery travels through the medial compartment of the guttural pouch. The temperature of the air within the guttural pouch was fairly constant (37.5 ± 0.05°C) during exercise, and was responsible for cooling the blood within the internal carotid artery by 2°C.[88] The heat transfer from the internal carotid artery to the guttural pouch was minimal at rest but became more efficient with exercise.[88] Therefore, the function of the guttural pouches in the horse seems to be to cool the brain during periods of hyperthermia.[89]

Because of the position of the nasopharyngeal openings of the guttural pouches, changes in nasopharyngeal pressures during inspiration and expiration also affect pressures within the guttural pouches.[90] When airflow through the nasopharynx is 0 L/s the pressure within the guttural pouches is negative, similar to measurements made in the middle ear of humans.[90] After swallowing the nasopharyngeal aperture opens and pressures within the guttural pouches equilibrate with the nasopharynx. Both at rest and during exercise the guttural pouch static pressures are similar to

nasopharyngeal pressures, but slightly out of phase with the respiratory cycle.[90] Movement of the head, chewing, snorting, or swallowing causes changes in pressures simultaneously in both guttural pouches. Therefore, the elevated compliance of the guttural pouch makes it susceptible to pressure changes in the nasopharynx associated with airflow but also with head movement.[90]

Anatomy

The openings of the guttural pouches are within the nasopharynx. The floor of the pouches forms the dorsal aspect of the nasopharynx, and the caudal extent of the guttural pouch is at the level of the parotid salivary glands. The guttural pouches are bordered dorsally by the base of the skull and the atlas, ventrally by the nasopharynx and rostral esophagus, medially by the longus capitis muscle, the rectus capitis ventralis muscle and the median septum, and laterally by many blood vessels and muscles, including the digastric muscles. Retropharyngeal lymph nodes can be identified beneath the guttural pouch membrane on the floor of the medial compartment (Fig. 26.20).

The guttural pouch is divided into medial and lateral compartments by the stylohyoid bone. The caudal portion of the stylohyoid bone articulates with the petrous temporal bone at the base of the skull (Fig. 26.21). Cranial nerves VII (facial) and VIII (vestibulocochlear) exit the cranium near this articulation. The opening from the middle ear into the guttural pouch is with the dorsolateral compartment, near the articulation of the stylohyoid and petrous temporal bones. The medial compartment is approximately twice as large as the lateral compartment and cranial nerves IX (glossopharyngeal), X (vagus), XI (accessory), and XII (hypoglossal), the sympathetic trunk, the cranial cervical ganglion, and the internal carotid artery lie beneath the lining of the medial compartment (Figs 26.22 and 26.23). Cranial nerve X, the sympathetic trunk, and the cranial cervical ganglion are

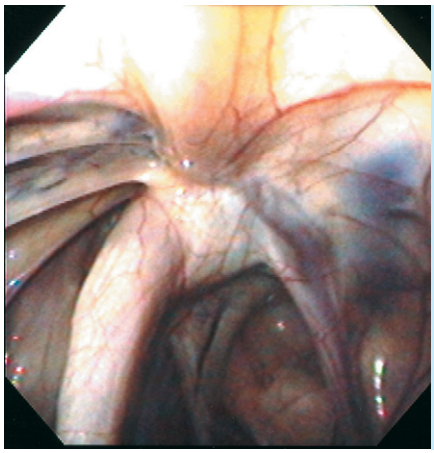


Fig. 26.21 Endoscopic image of the dorsal portion of the right guttural pouch and stylohyoid/petrous temporal bone articulation.

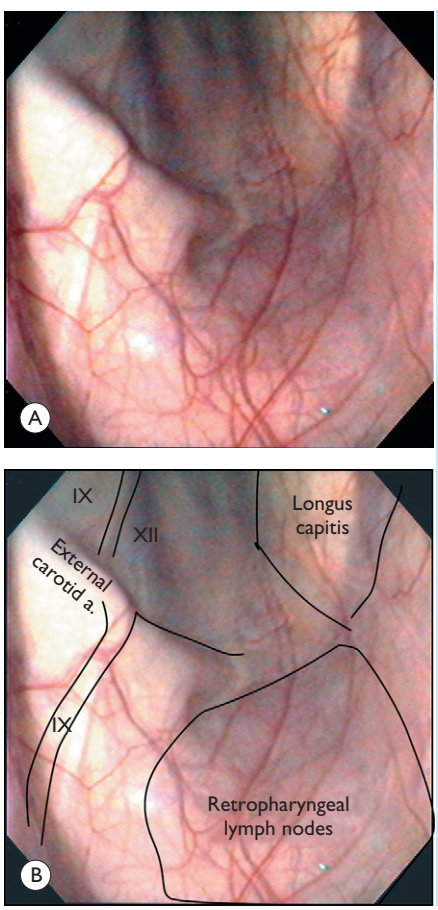


Fig. 26.20 (A) Endoscopic image of the ventral medial compartment of the right guttural pouch. (B) Endoscopic image of the ventral medial compartment of the right guttural pouch with figure labels. Notice how IX (glossopharyngeal nerve) and XII (hypoglossal nerve) course together, caudal to the external carotid artery. XII dives deep to the external carotid artery, and IX travels across the external carotid artery, rostrally in the guttural pouch. a, artery.

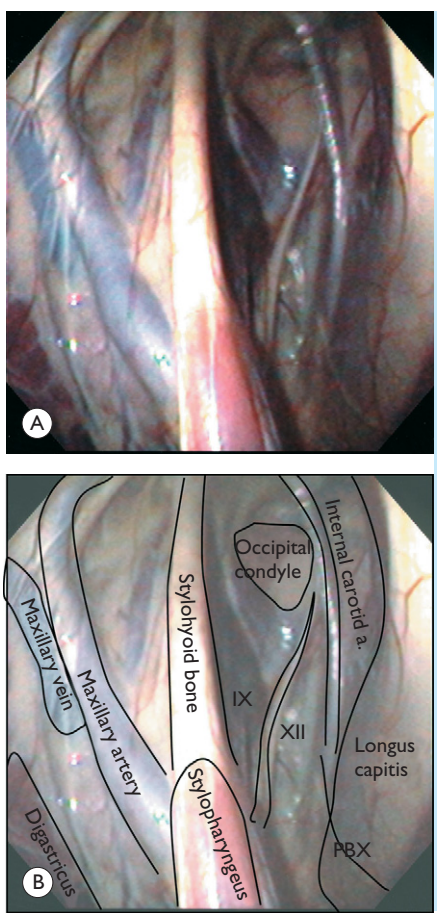


Fig. 26.22 (A) Endoscopic image of the medial and lateral compartments of the right guttural pouch. Medial is the right side of the image. (B) Endoscopic image of the medial and lateral compartments of the guttural pouch with figure labels. IX, glossopharyngeal nerve; XII, hypoglossal nerve; PBX, pharyngeal branch of the vagus nerves. a, artery.

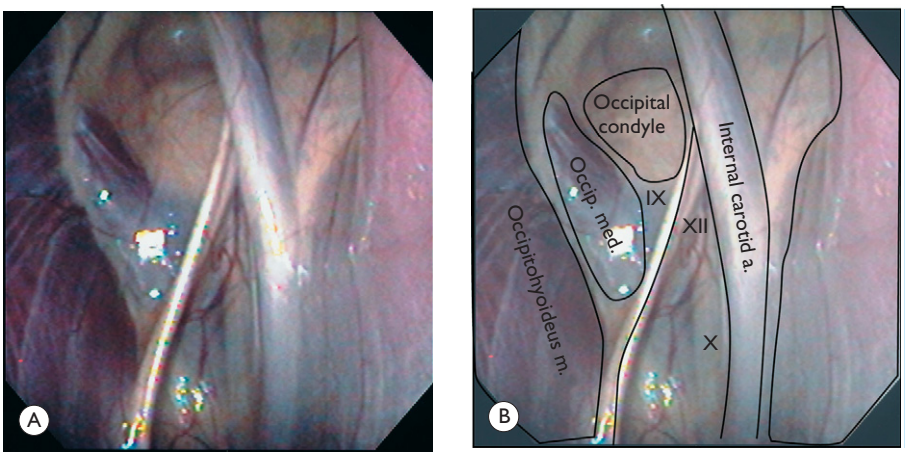


Fig. 26.23
(A) Medial compartment of the right guttural pouch. (B) Medial compartment of the right guttural pouch with figure labels. IX, glossopharyngeal nerve; XII, hypoglossal nerve; X, vagus nerve; a, artery; Occip. med., occipitohyoideus, medial muscle belly.

closely associated with the internal carotid artery. The pharyngeal branch of X is given off near the cranial cervical ganglion and can be seen as it runs rostroventrally in the guttural pouch toward the wall of the dorsal pharynx, where it ramifies with the pharyngeal branch of IX in the pharyngeal plexus. The pharyngeal branch of IX can be identified as it runs rostrally across the ventral aspect of the stylohyoid bone (Fig. 26.24). The maxillary artery is a continuation of the external carotid artery, beyond the origin of the superficial temporal artery, and runs dorsally in the lateral compartment of the guttural pouch. The maxillary vein can be seen lateral to and slightly deep to the external carotid artery. A portion of the digastric muscle can be seen along the ventrolateral wall of the lateral compartment (Fig. 26.25). The levator veli palatini and the tensor veli palatini muscles arise, partially, from the lateral lamina of the auditory tube, and

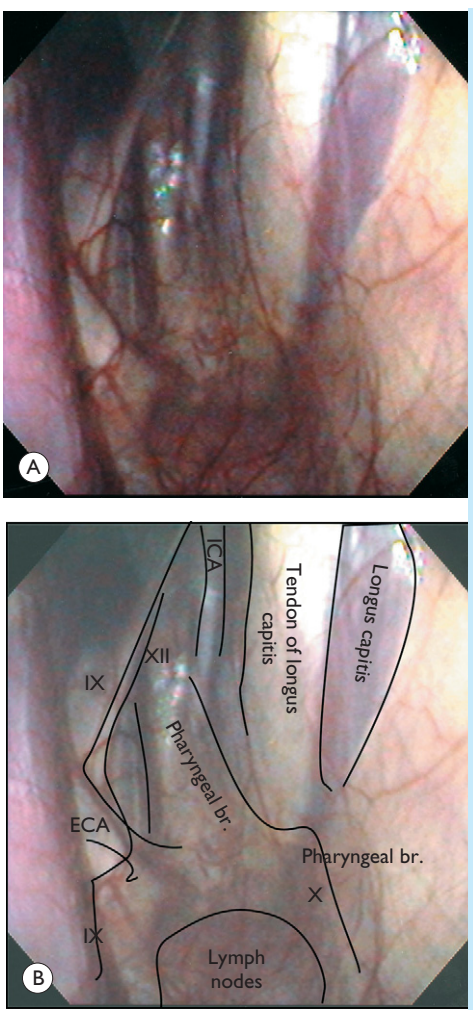


Fig. 26.24
(A) Ventral medial compartment of the right guttural pouch. (B) Ventral medial compartment of the right guttural pouch with figure labels. ICA, internal carotid artery; IX, glossopharyngeal nerve; XII, hypoglossal nerve; ECA, external carotid artery; Pharyngeal br. X, pharyngeal branch of the vagus nerve; Pharyngeal br. IX, pharyngeal branch of the glossopharyngeal nerve.

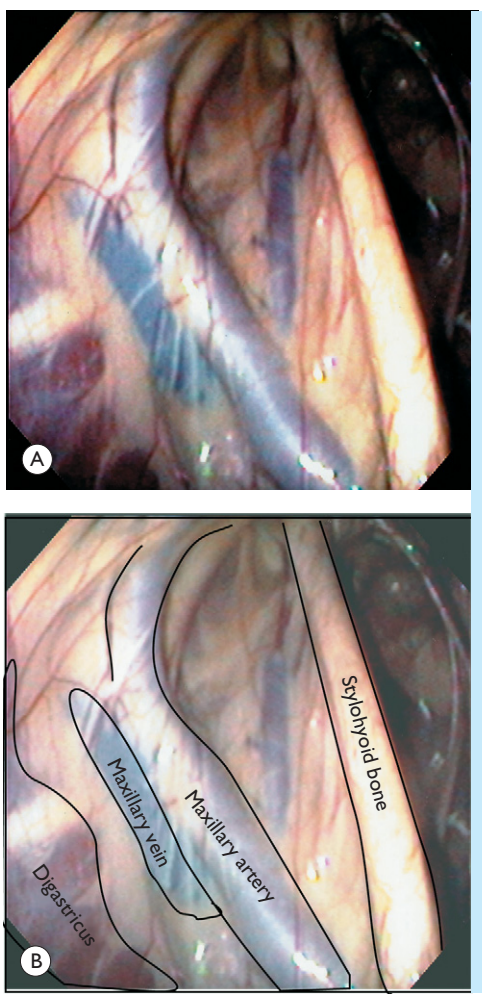


Fig. 26.25
(A) Lateral compartment of the right guttural pouch. (B) Lateral compartment of the right guttural pouch with figure labels.

can be seen within the pouch, as they pass rostrally and ventrally along the lateral lamina, the wall of the nasopharynx, to the soft palate. At the most caudal aspect of the guttural pouch, the occipital condyle can be seen.

References

1. Robinson NE, Sorenson PR. Pathophysiology of airway obstruction in horses: a review. J Am Vet Med Assoc 1978; 172(3):299–304.
2. Olson LG, Strohl KP. The response of the nasal airway to exercise. Am Rev Respir Dis 1987; 1735:356–359.
3. Negus VE. The function of the epiglottis. J Anat 1929; 62:1–8.
4. Fregosi RF, Lansing RW. Neural drive to nasal dilator muscles: influence of exercise intensity and oronasal flow partitioning. J Appl Physiol 1995; 79(4):1330–1337.
5. Niinimaa V, Cole P, Mintz S, et al. The switching point from nasal to oro-nasal breathing. Respir Physiol 1980; 42:61–71.
6. Saibene F, Mongnoni P, Lafortuna CL, et al. Oro-nasal breathing during exercise. Pfuegers Arch 1982; 378:65–69.
7. Erickson BK, Piesdil RC, Erickson HH. Alleviation of exercise induced hypoxemia utilizing inspired 79% helium, 30.95% oxygen. In: Robinson NE, ed. Equine exercise physiology. Davis, CA: ICEEP Publications; 1991; 54.
8. Lumsden J, Derkson FJ, Stick JA, et al. Use of flow-volume loops in evaluating upper airway obstruction in exercising horses. Am J Vet Res 1993; 54:766–774.
9. Rodarte JR, Rehder K. Dynamics of respiration. In: Fishman AP, ed. The respiratory system. Bethesda, MD: The American Physiological Society: 1986; 131–144.
10. West JB. Mechanics of breathing. In: West JB, ed. Respiration physiology, 3rd edn. Baltimore, MD: Williams and Wilkins; 1985; 85–111.
11. Petsche VM, Derksen FJ, Berney CE, et al. Effect of head position on upper airway function in exercising horses. Equine Vet J Suppl 1995; 18:18–22.
12. Mortimore IL, Mathur R, Douglas NJ. Effect of posture, route of respiration, and negative pressure on palatal muscle activity in humans. J Appl Physiol 1995; 79(2):448–454.
13. Giuseppe L, Stanescu D, Dooms G, et al. Head position modifies upper airway resistance in men. J Appl Physiol 1988; 64(3):1285–1288.
14. Krogh A, Lindhard J. The regulation of respiration and circulation during the initial stages of muscular work. J Physiol Lond 1913; 47:112–136.
15. Sullivan J, Fuller D, Fregosi RF. Control of nasal dilator muscle activities during exercise: role of nasopharyngeal afferents. J Appl Physiol 1996; 80:1520–1527.
16. Van der Touw T, O'Neill N, Amis T, et al. Soft palate muscle activity in response to hypoxic hypercapnia. J Appl Physiol 1994; 77:2600–2605.
17. Bartlett D. Effects of hypercapnia and hypoxia on laryngeal resistance to airflow. Resp Physiol 1979; 37:293–302.
18. Van de Touw T, O'Neill N, Brancatisano A, et al. Respiratory-related activity of soft palate muscles: augmentation by negative upper airway pressure. J Appl Physiol 1994; 76:424–432.
19. Wheatley JR, Tangel DJ, Mezzanotte WS, et al. Influence of sleep on response to negative airway pressure of tensor palatini muscle and retropalatal airway. J Appl Physiol 1993; 75:2117–2124.
20. Horner RL, Innes JA, Murphy K, et al. Evidence for reflex upper airway dilator muscle activation by sudden negative airway pressure in man. J Physiol 1991; 436:15–29.
21. van Lunteren E, Van de Graaff WB, Parker DM, et al. Nasal and laryngeal reflex responses to negative upper airway pressure. J Appl Physiol: Respir Environ Exerc Physiol 1984; 56:746–752.
22. Sant'Ambrogio G, Mathew OP, Fisher JT, et al. Laryngeal receptors responding to transmural pressure, airflow and local muscle activity. Respir Physiol 1983; 54:317–330.
23. Mathew OP, Sant'Ambrogio JT, Fisher JT, et al. Respiratory afferent activity in the superior laryngeal nerves. Respir Physiol 1984; 58:41–50.
24. Mathew OP, Sant'Ambrogio G, Fisher JT, et al. Laryngeal pressure receptors. Respir Physiol 1984; 57:113–122.
25. Tsubone H. Mechanoreceptor stimulation in horses. Proceedings of the World Equine Airway Symposium, Guelph, Ontario, Canada, August 1998.
26. van Lunteren E, Cherniak NS. Activity of upper airway muscles during augmented breaths. Respir Physiol 1983; 53:87–98.
27. Brouillette RT, Thach BT. A neuromuscular mechanism maintaining extrathoracic airway patency. J Appl Physiol 1979; 46:772–779.
28. Holcombe SJ, Cornelisse CJ, Berney CE, et al. Electromyographic activity of the hyoepiglotticus muscle and control of epiglottis position in horses. Am J Vet Res 2002; 63(12):1617–1622.
29. Holcombe SJ, Derksen FJ, Stick JA, Robinson NE. Electromyographic activity of the palatinus and palatopharyngeus muscles in exercising horses. Vet Surg 1998; 27(5).
30. Ducharme NG Holcombe SJ. The function of the extrinsic and intrinsic musculature in stabilizing the upper airways. CD Proceeding of 2nd World Equine Airway Society 2001.
31. van Lunteren E, Strohl KP, Parker DM, et al. Phasic volume-related feedback on upper airway muscle activity. J Appl Physiol: Respir Environ Exerc Physiol 1984; 56(3): 730–736.
32. Horner RL, Innes JA, Murphy K, et al. Evidence for reflex upper airway dilator muscle activition by sudden negative airway pressure in man. J Physiol 1991; 436:15–29.
33. Holcombe SJ, Derksen FJ, Berney CE, et al. Effect of topical anesthesia of the laryngeal mucosa on upper airway mechanics in exercising horses. Am J Vet Res 2001; 62(11): 1706–1710.
34. Holcombe SJ, Derksen FJ, Stick JA, et al. Effect of nasal occlusion on tracheal and pharyngeal pressures in horses. Am J Vet Res 1996; 57(9):1258–1260.
35. Pelletier N, Leith DE. Ventilation and carbon dioxide exchange in exercising horses: effect of inspired oxygen fraction. J Appl Physiol 1995; 78:654–662.
36. Bruce EN, Mitra J, Cherniack NS. Central and peripheral chemoreceptor inputs to phrenic and hypoglossal motoneurons. J Appl Physiol: Respir Environ Exerc Physiol 1982; 53(6):1504–1511.
37. McEnvoy RD, Popovic RM, Saunders NA, et al. Effects of sustained and repetitive isocapnic hypoxia on ventilation and genioglossal and diaphragmatic EMGs. J Appl Physiol 1996; 81(2):866–875.
38. Petsche VM, Derksen FJ, Robinson NE. Tidal breathing flow-volume loops in horses with recurrent airway obstruction (heaves). Am J Vet Res 1994; 55(7):885–891.
39. Derksen FJ, Holcombe SJ, Hartmann W, et al. Spectrum analysis of respiratory sounds in exercising horses with experimentally induced laryngeal hemiplegia or dorsal

displacement of the soft palate. Am J Vet Res 2001; 62(5):659–664.
40. Nielan GJ, Rehder RS, Ducharme NG, et al. Measurement of tracheal static pressure in exercising horses. Vet Surg 1992; 21(6):423–428.
41. Dersen FJ, Stick JA, Scott EA, et al. Effect of laryngeal hemiplegia and laryngoplasty on airway flow mechanics in exercising horses. Am J Vet Res 1986; 47:16–20.
42. Mangseth G. Evaluation of tracheal pressures in the running horse. In: Proceedings of the first annual meeting of the Association for Equine Sports Medicine 1984; 74–76.
43. Marlin DJ, Roberts CA. Qualitative and quantitative assessment of respiratory airflow and pattern of breathing in exercising horses. Equine Vet J 1998; 10(4):178–186.
44. Bayly WM, Slocombe RF, Weidner JP, et al. Influence of air movement, facemask design and exercise on upper airway, transpulmonary and transdiaphragmatic pressures in Thoroughbred horses. Cornell Vet 1994; 84(1):77–90.
45. Bayly WM, Schulz DA, Hodgson DR, et al. Ventilatory responses of the horse to exercise: effect of gas collection systems. J Appl Physiol 1987; 63(3):1210–1217.
46. Holcombe SJ, Beard WL, Hinchcliff KW. Effect of a mask and pneumotachograph on tracheal and nasopharyngeal pressures, respiratory frequency, and ventilation in horses. Am J Vet Res 1996; 57(3):250–253.
47. Sauerland EK, Orr WC, Hairston LE. EMG patterns of oropharyngeal muscles during respiration in wakefulness and sleep. Electromyogr Clin Neurophysiol 1981; 21:307–316.
48. Newman S, Road J, Bellemore F, et al. Respiratory muscle length measured by sonomicrometry. J Appl Physiol 1984; 56(3):753–764.
49. Sisson S. Equine mycology. In: Getty R, ed. Sisson and Grossman's The anatomy of domestic animals. 5th edn. Philadelphia: WB Saunders; 1975; 377–379.
50. Olson LG, Strohl KP. The response of the nasal airway to exercise. Am Rev Respir Dis 1987; 135:356–359.
51. Sisson S. Equine digestive system. In: Getty R, ed. Sisson and Grossman's The anatomy of domestic animals. 5th edn. Philadelphia: WB Saunders; 1975; 471–475.
52. Kuehn DP, Folkins JW, Cutting JW. Relationships between muscle activity and velar position. Cleft Palate J 1982; 19:25–35.
53. Moon JB, Smith AE, Folkins JW, et al. Coordination of velopharyngeal muscle activity during positioning of the soft palate. Cleft Palate Craniofac J 1991; 101:1332–1335.
54. Baptiste K. Functional anatomy observations of the pharyngeal orifice of the quine guttural pouch (auditory tube diverticulum). Vet J 1997; 153(3):311–319.
55. Holcombe SJ, Derksen FJ, Stick JA, et al. Effect of bilateral tenectomy of the tensor veli palatini muscle on soft palate function in horses. Am J Vet Res 1997; 58(3):317–322.
56. Trigos I, Ysunza A, Vargas D, et al. The San Venero Roselli pharyngoplasty: an electromyographic study of the palatopharyngeus muscle. Cleft Palate J 1988; 25(4): 385–388.
57. Holcombe SJ, Derksen FJ, Stick JA, Robinson NE. Bilateral nerve blockade of the pharyngeal branch of the vagus nerve produces persistent soft palate dysfunction in horses. Am J Vet Res 1998; 59(4):504–508.
58. DeLahunta A. Veterinary neuroanatomy and clinical neurology. 1st edn. Philadelphia: WB Saunders; 1977; 104–107, 370.
59. Mayhew IG. Large animal neurology: a handbook for veterinary clinicians. 1st edn. Philadelphia: Lea and Febiger; 1989.
60. Holcombe SJ, Derksen FJ, Stick JA, et al. Electromyographic activity of the palatinus and palatopharyngeus muscles in exercising horses. Vet Surg 1998; 27:58.
61. Holcombe SJ. New thoughts on URT anatomy: Relevancy. Proceedings of the 29th annual surgical forum, American College of Veterinary Surgeons, Chicago, IL; 2001; 59–62.
62. Getty R. Equine osteology. In: Getty R, ed. Sisson and Grossman's The anatomy of domestic animals. 5th ed. Philadelphia: WB Saunders; 1975; 336–340.
63. Van de Graaff WB, Gottfried SB, Mitra J, et al. Respiratory function of hyoid muscles and hyoid arch. J Appl Physiol 1984; 57(1):197–204.
64. Fregosi RF, Fuller DD. Respiratory-related control of extrinsic tongue muscle activity. Respir Physiol 1997; 110:295–306.
65. Fuller DD, Williams JS, Janssen PL, et al. Effect of coactivation of tongue protrudor and retractor muscles on tongue movements and pharyngeal airflow mechanics in the rat. J Physiol 1999; 519(2):601–613.
66. Brouillette RT, Bradley TT. Control of genioglossus muscle inspiratory activity. J Appl Physiol 1980; 49(5):801–808.
67. Mathew OP, Abu-Osba YK, Thatch BT. Genioglossus muscle responses to upper airway pressure changes:afferent pathways. J Appl Physiol: Respir Environ Exerc Physiol 1984; 52(2):445–450.
68. McEnvoy RD, Popovic RM, Saunders NA, et al. Effects of sustained and repetitive isocapnic hypoxia on ventilation and genioglossal and diaphragmatic EMGs. J Appl Physiol 1996; 81(2):866–875.
69. Cornelisse CJ, Holcombe SJ, Derksen FJ, et al. Effect of a tongue-tie on upper airway mechanics in horses during exercise. Am J Vet Res 2001; 62(5):775–778.
70. Cornelisse CJ, Rosenstein DS, Derksen FJ, et al. Computed tomographic study of the effect of a tongue-tie on hyoid apparatus position and nasopharyngeal dimensions in anesthetized horses. Am J Vet Res 2001; 62(12): 1865–1869.
71. Sisson S. Equine myology. In: Getty R, ed. Sisson and Grossman's The anatomy of domestic animals. 5th edn. Philadelphia: WB Saunders; 1975; 386–387.
72. Holcombe SJ, Beard WL, Hinchcliff KW, et al. Effect of sternothyrohyoid myectomy on upper airway mechanics in normal horses. J Appl Physiol 1994; 77(6):2812–2816.
73. Castro HA, Resende LA, Berzin F, Konig B. Electromyographic analysis of the superior belly of the omohyoid muscle and anterior belly of the digastric muscle in tongue and head movements. J Electromyogr Kinesiol 1999; 9(3):229–232.
74. Zertuche JML, Turner TA, Colahan PT. Strap muscle myectomy for treatment of idiopathic intermittent dorsal displacement of the soft palate in racing Thoroughbreds. Vet Surg (abstract) 1990; 12:182.
75. Tsukroff S, Ducharme NG, Bertram JE, Hackett RP. Relationship of basihyoid bone and thyroid cartilage in exercising horses. Proceedings of the World Equine Airway Symposium, Guelph, Ontario, Canada, August 1998.
76. Ducharme NG, Hackett RP, Woodie JB, et al. Investigation into the role of the thyrohyoid muscles in the pathogenesis of dorsal displacement of the soft palate. Equine Vet J 2003; 35(3):258–263.
77. Feroah TR, Forster HV, Pan LG, et al. Reciprocal activation of hypopharyngeal muscles and their effect on upper airway area. J Appl Physiol 2000; 88(2):611–626.
78. Kuna ST. Effects of pharyngeal muscle activation on airway size and configuration. Am J Respir Crit Care Med 2001; 164(7):1236–1241.

79. Kuna ST, Smickely JS, Vanoye CR. Respiratory-related pharyngeal constrictor activation on pharyngeal airway function. J Appl Physiol 1999; 86(1):411–417.
80. Kuna ST, Smickley JS, Vanoye CR. Respiratory-related pharyngeal constrictor muscle activity in normal human adults. Am J Respir Crit Care Med 1997; 155(6): 1991–1997.
81. Sisson S. Equine digestive system. In: Getty R, ed. Sisson and Grossman's The anatomy of domestic animals. 5th edn. Philadelphia: WB Saunders; 1975; 475.
82. Feroah TR, Forster HV, Pan L, et al. Effect of slow wave and REM sleep on thyropharyngeus and stylopharyngeus activity during induced central apneas. Respir Physiol 2001; 124(2): 129–140.
83. Tessier C, Holcombe SJ, Derksen FJ, et al. Effect of stylopharyngeus muscle dysfunction on the nasopharynx in exercising horses. Equine Vet J 2003, in press.
84. Sisson S. Equine respiratory system. In: Getty R, ed. Sisson and Grossman's the anatomy of domestic animals. 5th ed. Philadelphia: WB Saunders; 1975; 504–511.
85. Duncan ID, Baker GJ. Experimental crush of the equine recurrent laryngeal nerve: a study of normal and aberrant reinnervation. Am J Vet Res 1987; 48(3): 431–438.
86. Holcombe SJ, Derksen FJ, Stick JA, Robinson NE. Effect of bilateral hypoglossal and glossopharyngeal nerve blocks on epiglottic and soft palate position in exercising horses. Am J Vet Res 1997; 58(9):1022–1026.
87. Parente EJ, Martin BV, Tulleners EP. Epiglottic retroversion as a cause of poor performance in two horses. Equine Vet J 1998; 30:270–272.
88. Baptiste KE, Naylor JM, Bailey J, et al. Physiology: A function for guttural pouches in the horse. Nature 2000; 403: 382–383.
89. Manglai D, Wada R, Kurohmaru M, et al. Distribution of immunoglobulin isotypes and subisotypes in equine guttural pouch (auditory tube diverticulum). J Vet Med Sci 2000; 62(9):1001–1003.
90. Rehder RS. Equine upper airway and guttural pouch pressures during exercise. MS thesis, Cornell University, 1992.

CHAPTER 27

Abnormalities of the upper airway

Susan J. Holcombe and Norm G. Ducharme

Upper airway obstructive diseases can limit athletic performance by decreasing minute ventilation, exacerbating exercise-induced hypoxemia, decreasing maximal oxygen consumption and increasing airway resistance. Such lesions can be dynamic and only apparent during exercise, or static and evident at rest. In concert with a complete history, signalment, and physical examination, endoscopic examination of the upper airway, both at rest and during treadmill exercise, will establish the etiology of the airway obstruction. In addition, imaging modalities such as radiography, ultrasonography, computed tomography, sound analysis, and nuclear medicine can be valuable in diagnosing performance-limiting lesions of the upper airway.

Redundant alar folds (alar fold collapse)

- The alar fold is formed by a thick fold of skin and mucous membrane extending rostrad from the ventral nasal concha.[1]
- Redundant alar folds are an uncommon cause of exercise intolerance and respiratory noise in performance horses.[2,3]
- The diagnosis is made by securing the alar folds dorsally to document decreased respiratory noise and improved exercise intolerance.[2]
- Treatment includes tying the alar folds out of the airway during exercise or alar fold resection.[2,3]

Recognition

History and presenting complaint

Most horses with redundant alar folds make an expiratory fluttering noise during exercise and may be exercise intolerant. Horses exhibit no clinical signs at rest.[2]

Physical examination

No abnormalities are apparent at rest.

Special examination

Other causes of respiratory noise and exercise intolerance should be eliminated by performing an endoscopic examination of the upper airway and evaluating both nasal passages. Confirmation that redundant alar folds are the cause of the airway noise is made by placing a temporary suture through the skin of each nostril, the alar folds, and tying it over the bridge of the nose while the horse exercises (Fig. 27.1).[2] The alar folds may also be held out of the nasal passage manually or with clips. Alleviation of the upper airway noise suggests that redundant alar folds are the cause.[2]

Fig. 27.1
The nose of a horse with rings through the alar folds. The string is used to tie the rings together, pulling the alar fold out of the airway.

Laboratory examination

None is indicated.

Diagnostic confirmation

Absence of noise and improved exercise tolerance during exercise with the alar folds secured out of the nasal passage confirms the diagnosis.[2,3] Differential diagnoses for alar fold collapse include obstructive airway diseases that cause exercise intolerance and abnormal respiratory noise during exercise (Table 27.1).

Treatment and prognosis

Therapeutic aims

The goal of treatment is to remove or secure the alar folds during exercise. The alar folds can be tied out of the airway during exercise or surgically resected.

Therapy

The horse is anesthetized and placed in lateral or dorsal recumbency. The alar fold is exposed by dilating the nostril or incising the lateral ala of the external naris. The alar fold is excised along the lateral margin of the alar cartilage and nasal septum, ending ventral to the ventral concha.[2,3] Usually, 1–2 cm of the cartilaginous portion of the ventral concha is excised. Hemostasis is achieved by placing ligatures and apposing the nasal mucosa and the skin of the nasal diverticulum. If the lateral nasal ala is incised to expose the alar fold, it is closed in two layers.[2,3]

Prognosis

Reportedly, respiratory tract noise improves in 71% of horses following alar fold resection and 88% of horses race after

Table 27.1 Upper airway mechanics measurements and blood gas variables in horses with obstructive upper airway diseases

Disease	Pao_2	$Paco_2$	TIP	TEP	Ziu	Zeu	IF	EF	RF	V_T	$\dot{V}_E$
Normal[132]	71.7 (1.6)	54.7 (1.9)	–42.9 (2.8)	9.2 (3.8)	0.53 (0.02)	0.14 (0.06)	80.4 (4.2)	66.6 (4.3)	84 (4)	22.2 (1.6)	1858 (109)
Normal[51]	75 (2.3)	55 (2.3)	–39 (3.3)	12 (1.4)	0.42 (0.05)	0.18 (0.02)	90 (5.2)	91 (4.1)	109 (11.7)	17.1 (1.7)	1690 (130)
Pharyngeal collapse[131]			–40.8 (4.4)	22.0 (6.6)	0.73 (0.02)	0.46 (0.19)	54.2 (4.0)	55.6 (4.1)	76 (4.0)	16.8	1159.4 (94.1)
DDSP[48]			–18.6 (7.6)	36.2 (11.3)	0.41 (0.11)	0.88 (0.38)	44.5 (9.0)	46.7 (10.4)	57 (9.8)	15 (3.31)	875.2 (114.5)
DDSP[51]	64 (3.6)	66 (4.9)	–29 (3.4)	35 (6.7)	0.33 (0.05)	0.66 (0.11)	66 (3.8)	69 (3.4)	98 (8.2)	13.6 (2.5)	1265 (315)
ILH[64]	53	58 (8.3)	–59.4	21.3 (0.47)	1.52	0.49 (9.0)	42.6	42.7 (9)	70		1106.5 (191.5)
Laryngoplasty + ventriculocordectomy[64]	83	39	–45.1 (8.4)		0.82 (0.14)		55.5 (5.0)		77 (20)		1211.5 (95.4)
Arytenoidectomy + ventriculectomy[88]			–40.0 (4.4)		0.81 (0.10)		48.0 (2.0)				1178.5 (38.6)
Epiglottic retroversion[60]			–35.7 (3.80)	13.3 (2.4)					58 (5)		

TIP, tracheal inspiratory pressure (cmH_2O); TEP, tracheal expiratory pressure (cmH_2O); Ziu, inspiratory impedance (cmH_2O/L/s); Zeu, expiratory impedance (cmH_2O/L/s); IF, peak inspiratory flow (L); EF, peak expiratory flow (L); RF, respiratory frequency (breaths/min); V_T, tidal volume (L); $\dot{V}_E$, minute ventilation (L/min); values in parentheses are standard error of the mean.

surgery.[3] Horses with small nares and narrow nasal passages have a poorer prognosis for performance.[2,3]

Prevention

There is no known prevention.

Etiology and pathophysiology

Etiology

The etiology of redundant alar folds is unknown, but may involve narrow nasal passages and inappropriate function of the transversus nasi muscles.

Pathophysiology

A thick fold of skin forms the alar fold and mucous membrane extending rostrad from the ventral nasal concha.[1] The space dorsal to the alar fold is the false nostril or diverticulum of the nostril while the true nostril that continues caudally to the nasal passage is ventral to the alar fold. When the nostril is dilated, the alar fold is tensed, obliterating the nasal diverticulum.[2] Excessive alar fold tissue or inappropriate nostril dilation may cause the alar fold to collapse across the nostril, causing airway obstruction and exercise intolerance during inhalation, and a fluttering noise during exhalation.

Epidemiology

Standardbred horses and American Saddlebreds may be predisposed to this condition.[3]

Mycotic rhinitis

Recognition

History and presenting complaint

Mycotic rhinitis is rare in horses and occurs most frequently in warm, humid climates. The most common clinical signs include nasal discharge that may or may not be foul smelling, sneezing, and intermittent epistaxis.[2,4] Horses with nasal granulomas may make an abnormal respiratory noise during exercise and show signs of exercise intolerance. If the fungal infection is invasive and involves the paranasal sinuses, extension to the brain and meninges can occur, resulting in cerebral signs such as depression, dementia, ataxia, and recumbency.

Physical examination

Horses with mycotic rhinitis generally have nasal discharge that may be malodorous, and if chronic, they may have alopecia along the ventral aspect of the affected naris.[2] If a nasal granuloma is causing airway obstruction, decreased airflow through the affected nostril is detected by holding the hands over each nostril.

Special examination

Endoscopic examination of the affected nasal passage reveals fungal plaques or granulomas affecting the mucocutaneous junction of the nostril, or mucous membrane of the nasal septum and concha.[2,4,5] Ulceration of the mucosa surrounding the plaque or granuloma may also be seen.[5] If the primary site of infection is the paranasal sinus region, exudate at the nasomaxillary opening within the middle meatus may be evident.

Laboratory examination

Laboratory tests are generally not warranted, but if the infection is chronic, hyperfibrinogenemia may be detected.

Diagnostic confirmation

The diagnosis of fungal rhinitis is confirmed by biopsy and culture of the plaque or mass.[2–6] Fungi that have been reported to cause mycotic rhinitis in horses include *Conidiobolus coronatus*, *Cryptococcus*, *Rhinosporidium*, *Aspergillus fumigatus* and *A. boydii*, *Coccidioides*, and *Pseudallescheria*.[2–7] The presence of septate hyphae or fungal mycelium on cytological examination is indicative of fungal infection.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to eradicate the fungus from the nasal passage.

Therapy

Surgical excision of granulomas and topical as well as systemic antifungal therapy are effective in the treatment of mycotic rhinitis.[2] *Aspergillus fumigatus* is sensitive to natamycin solution applied topically.[4] Nystatin can be added to the natamycin and used topically or intralesionally.[4] Oral itraconazole, 3 mg/kg, orally, twice daily, for 3.5 to 4 months also results in the resolution of *Aspergillus* sp. infection.[6] Topical and intralesional injection of amphotericin B and intravenous sodium iodide or oral potassium iodide is used to treat *Conidiobolus coronatus* infection, but recurrence has been reported.[5]

Prognosis

Mycotic rhinitis due to *Aspergillus* sp. resolves with treatment and recurrence is low.[2,4,6] *Conidiobolus coronatus* resolves with surgical and medical treatment, but does recur.[5,6]

Cryptococcus sp. is an invasive fungus that can infect the paranasal sinuses and invade the brain and meninges.[2,7] Because of the aggressive nature of this fungus, the prognosis is generally poor for resolution, unless a single, non-invasive granuloma is excised.[2,7]

Prevention

No method of prevention is known.

Etiology and pathophysiology

Etiology

Fungi isolated from the nasal cavity of affected horses include *Conidiobolus* spp., *Cryptococcus* spp., *Rhinosporidium*, *Aspergillus* spp., *Coccidioides*, and *Pseudallescheria*.[2–7]

Pathophysiology

Inhalation of fungal spores and colonization of the nasal mucosa is the most likely route of infection, resulting in mycotic rhinitis.

Epidemiology

Mycotic rhinitis is rare, but is most commonly seen in hot, humid climates, such as the southeastern USA and tropical areas.

Progressive ethmoid hematoma (PEH)

- Clinical signs include unilateral epistaxis and respiratory stridor.
- Endoscopy of the nasal passage and inspection of the ethmoid region demonstrates ethmoid hematoma.
- The diagnosis is confirmed by histopathology of the mass.
- Most ethmoid hematomas originate at the ethmoid turbinate, but can originate from the paranasal sinuses.
- Treatment options include surgical excision, either sharply or with a laser, or chemical ablation.
- Recurrence is approximately 43%.

Recognition

History and presenting complaint

Horses with progressive ethmoid hematoma (PEH) have unilateral or bilateral epistaxis, respiratory stridor, variable facial deformity depending on the duration of the condition, and decreased airflow through the affected nostril.[8]

Physical examination

Unilateral nasal obstruction may be diagnosed by holding the hands over each nostril and detecting reduced airflow from the affected nostril. Decreased airflow will generally be detected from the nostril with the most nasal discharge. Facial deformity may also be observed as asymmetric convexity of the facial bones, medial and rostral to the orbit.

Special examination

Endoscopic examination of the upper airway, including both nasal passages, is frequently diagnostic for progressive

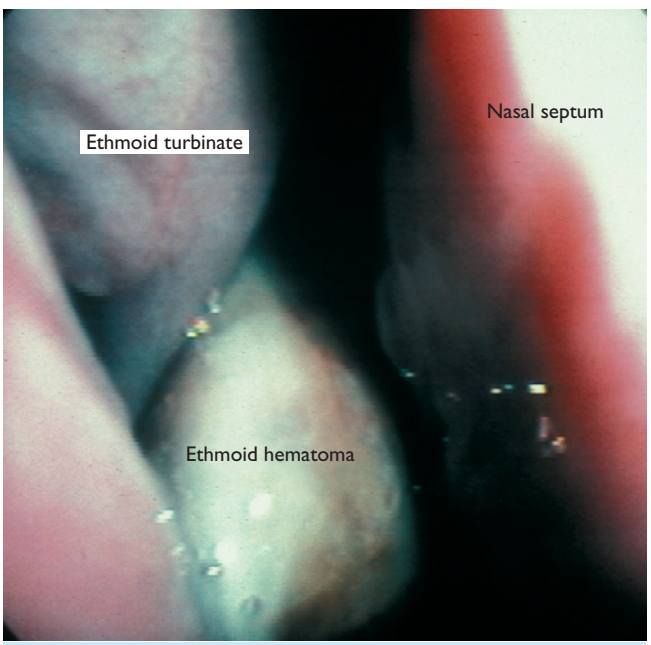


Fig. 27.2
Endoscopic image of an ethmoid hematoma.

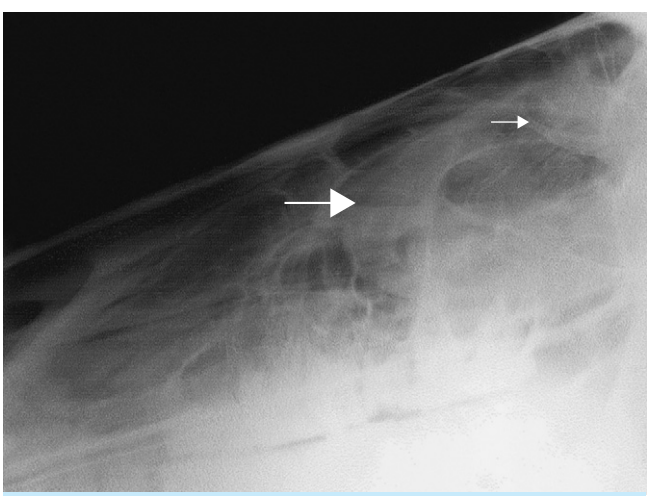


Fig. 27.3
Lateral radiograph of the paranasal sinus region of a horse. The large arrow points to the ethmoid hematoma and the small arrow points to the ethmoid turbinates.

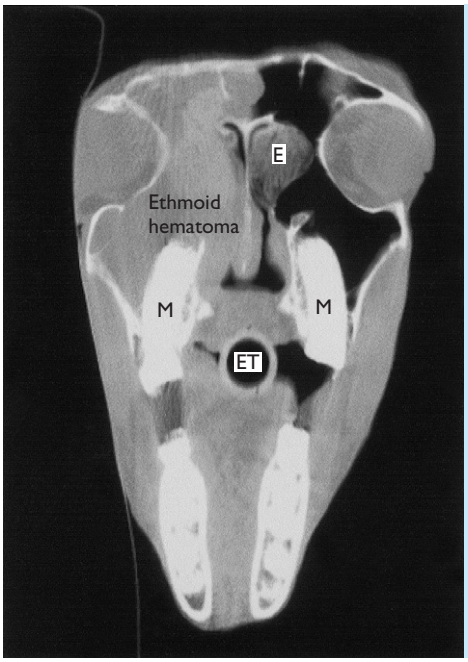


Fig. 27.4 Coronal slice of a computed tomographic image of a horse with an ethmoid hematoma. Notice the left sinus region is occupied by the ethmoid hematoma. E, normal ethmoid turbinate; ET, endotracheal tube; M, molars.

ethmoid hematoma. Ethmoid hematomas originate from the ethmoid turbinate region or paranasal sinuses (Fig. 27.2). The masses are smooth, green to purple in color and may be small and discrete or expansile, invading the entire nasal passage, nasopharynx, or paranasal sinus region.[8,9] If the mass is confined to the maxillary or frontal sinus, serosanguineous fluid will be evident at the nasomaxillary opening, but the mass may be obscured from view.[8,9] Differential diagnoses for progressive ethmoid hematoma include fungal granulomas, neoplasia, and nasal polyps. Biopsy and histopathology is warranted if the etiology of the mass is unknown.

Lateral, dorsoventral, and oblique radiographic projections of the paranasal sinus region are taken to define the anatomic limits of the expansile mass (Fig. 27.3).[10] A discrete, round density overlying the ethmoid labyrinth or within the maxillary or frontal sinus is suggestive of progressive ethmoid hematoma.[10] Fluid lines in the sinuses may be present if secondary sinusitis has occurred. Computed tomography is useful to define the extent of the mass prior to surgical excision (Fig. 27.4).[10]

Laboratory examination

Rarely, horses have evidence of mild, regenerative anemia, though generally blood loss from ethmoid hemotoma is minimal. Depending on the duration, size of the mass, and inflammatory reaction, hyperfibrinogenemia may be present.[11]

Diagnostic confirmation

Differential diagnosis for PEH includes neoplasia, fungal granuloma, nasal polyp, sinus cyst or abscess. Definitive diagnosis is made based on the histopathology of the mass. Ethmoid hematoma is a non-neoplastic angiomatous mass covered by respiratory epithelium and fibrous tissue.[8,9] The parenchyma of the mass is composed of blood, fibrous tissue, hemosiderin laden macrophages, neutrophils and necrotic debris, especially in large, chronic masses, with occasional calcareous deposits.

Treatment and prognosis

Therapeutic aims

The goal of treatment is elimination of the mass. This can be achieved by surgical excision, laser photo ablation, or chemical ablation.[8,9,11,12] Surgical excision of progressive ethmoid hematoma is performed by placing the horse under general anesthesia, in lateral recumbency, with the affected side up.[8,9] Depending upon the location of the mass, a maxillary bone flap or frontal nasal bone flap may be performed to provide access to the maxillary sinuses, or frontal sinuses and nasal cavity, respectively.[8] The mass is resected at its origin by sharp dissection or using Nd:YAG laser.[8,9] Copious hemorrhage is expected and controlled using cold saline and pressure applied with sterile gauze packing. Prior to surgery, it is prudent to have a blood donor available in case blood loss is excessive enough (packed cell volume < 20% following volume resuscitation) to warrant blood transfusion. Photo ablation of the mass using the Nd:YAG laser can be performed in the standing, sedated horse if the mass is accessible via the nasal passage.[9] Treatments are generally performed weekly until the mass has resolved. Alternatively, progressive ethmoid hematomas can be chemically ablated by intralesional injection of formalin.[11,12] In the standing, sedated horse, the mass is injected with 4% formaldehyde or neutral buffered 10% formalin using a transendoscopic 23-gauge retractable needle (Mill-Rose Laboratories, Inc., Mentor, OH) or through an injection apparatus constructed from polyethylene tubing and a 22- or 25-gauge needle.[11,12] The injection apparatus is inserted into the biopsy channel of the endoscope and the mass is injected with formalin until the mass distends.[12] Treatments are repeated every 3–4 weeks until the lesion is obliterated, requiring a mean of 5 treatments, ranging from 1 to 18 treatments.[12]

Complications from surgical excision include severe hemorrhage, chronic sinusitis, surgical site infection, and osteomyelitis of the bone flap.[8] Complications following formalin injection include laminitis, dysphagia, and neurologic disease, if the ethmoid hematoma has eroded through the cribiform plate.[11,12]

Prognosis

Recurrence following surgical excision is 43%, necessitating periodic re-evaluation should the mass recur. Recurrence is slightly higher in horses with bilateral progressive ethmoid hematomas.[8,9,12]

Prevention

There are no known preventive measures.

Etiology and pathophysiology

Etiology

The etiology of PEH is unknown.

Pathophysiology

Progressive ethmoid hematoma is an expanding angiomatis mass originating from the mucosa of the ethmoid conchae or paranasal sinuses. Progressive expansion of the mass occurs due to recurrent hemorrhage and local invasion of tissues. Masses may expand rostroventrally into the nasal passage or nasopharynx, or within the paranasal sinuses.

Epidemiology

Progressive ethmoid hematomas have been reported in horses from 6 months to 20 years old, but are most commonly diagnosed in middle-aged and older horses.[8] Thoroughbred horses are over-represented in case series, though the disease has been reported in many breeds. Bilateral lesions occur 15% of the time.[8]

Sinusitis

- The paranasal sinuses include the frontal, maxillary, sphenopalatine, and dorsal and ventral conchal sinuses.
- Sinusitis can be primary or secondary, and is most commonly associated with dental disease, masses, and trauma.
- Clinical signs of sinusitis include nasal discharge and facial swelling.
- Surgical debridement of the sinus is frequently recommended for treatment of primary or secondary sinusitis.

Recognition

History and presenting complaint

Horses with sinusitis frequently have unilateral or bilateral nasal discharge. If the sinusitis is due to dental disease or fungal infection the discharge may be foul smelling.[13] Horses with primary sinusitis frequently have a history of recent upper respiratory tract infection. If the sinusitis is secondary to a cyst or neoplastic mass, facial swelling and deformity of facial bones may be detected as the mass expands within the sinus.[13,14]

Physical examination

Rarely are horses febrile. Facial swelling may be detected and may be painful to palpation.[13] Deformity of facial bones overlying the sinus may be evident, especially in chronic cases of expansile masses such as sinus cysts and neoplasia.[13,14] Increased respiratory rate and effort is detected if the airway is obstructed. This occurs when the ventral cochal sinus is affected and compresses the ventral meatus.[14] Airflow obstruction may occur if the mass expands into the ventral meatus and is diagnosed by holding the hands over each nostril and detecting reduced airflow from the affected nostril. Epiphora occurs in horses with sinusitis if the nasolacrimal duct is compressed by a mass or swelling in the surrounding tissues.[13] Hair loss may be detected on the horse's face if the epiphora is chronic.

Special examination

Techniques used to diagnose sinusitis include radiography, computed tomography, sinoscopy, endoscopy, and nuclear medicine.[13,14] Generally at least four views of the skull are taken if sinusitis is expected, including the left and right oblique, lateral, and dorsoventral views. The left and right oblique views help to confirm which side of the head is affected. Fluid lines (Fig. 27.5), masses within the sinuses (Fig. 27.6) and periapical tooth root abscessation and abnormal alveolar bone can frequently be detected radiographically. Computed tomography is performed to localize the lesion more accurately in cases of secondary sinusitis. Sinus cysts, dental disease, neoplasia, ethmoid hematoma, mycotic granulomas, polyps, and epidermal inclusion cysts can cause secondary sinusitis and frequently require surgical removal.[13,14] The information gained from the computed tomographic scan aids in surgical planning and the surgical approach. Sinoscopy is performed in the sedated, standing horse by inserting a flexible endoscope or arthroscope through a trephine in the frontal, rostral maxillary, or caudal maxillary sinus.[15] Fluid is aspirated from the sinus and submitted for culture and cytology and the

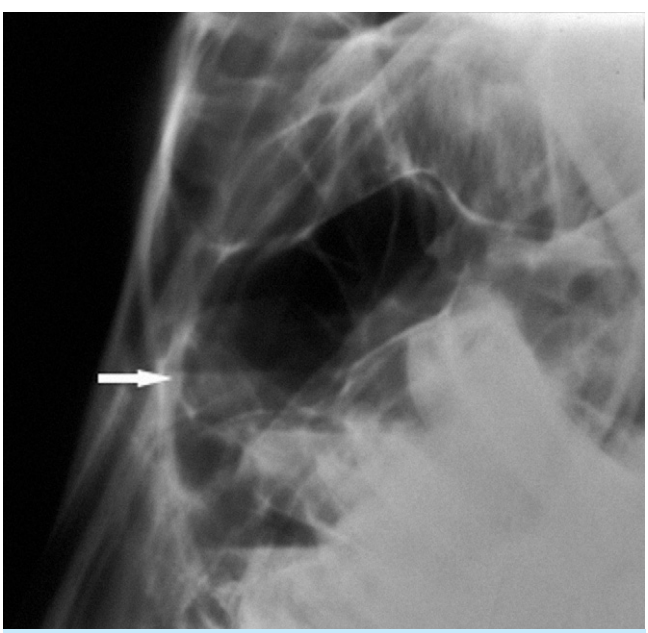


Fig. 27.5
Lateral radiograph of the paranasal sinus region of a horse with sinusitis illustrating the fluid line (arrow) within the maxillary sinus.

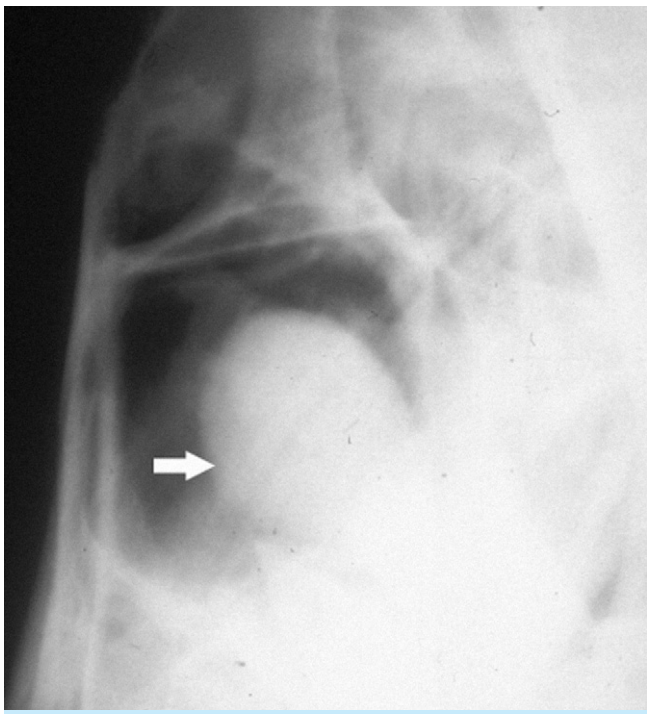


Fig. 27.6
Lateral radiograph of the paranasal sinus region of a horse with a mass (arrow) within the maxillary sinus.

sinus can be irrigated to evacuate exudate. The sinuses can be explored and masses or tooth root abscesses identified and biopsied by use of this technique. Endoscopic examination of the nasal passages is useful in cases of sinusitis to confirm that the exudate is coming from the nasomaxillary opening of the middle meatus. The specific origin of the exudate and inciting cause cannot be determined by endoscopy alone. Nuclear medicine is rarely used in cases of sinusitis, but can be used to confirm infected apical tooth roots. Despite radiography and computed tomography, identifying the affected tooth can at times be difficult. White blood cell scan is performed to help localize the infected tooth because the radiolabeled white blood cells can be imaged surrounding the infected tooth root.

Laboratory examination

The results of laboratory tests on blood are generally normal. Fluid aspirates are submitted for culture and sensitivity.

Diagnostic confirmation

The diagnosis of primary sinusitis is made based on a history of previous upper respiratory tract infection, nasal discharge originating from the paranasal sinus region, evidence of fluid within the sinuses on radiographs or computed tomography, and the absence of a secondary cause of the sinusitis.[13,14] Secondary sinusitis is diagnosed based on the presence of an inciting cause of the sinusitis, such as apical tooth root abscess, sinus cyst, neoplastic mass, ethmoid hematoma, mycotic granuloma, polyp, or trauma and facial bone fracture into the sinus.[13,14] Conformation of the etiology of secondary sinusitis is made by sinoscopy, biopsy, or surgical exploration of the sinus.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to rid the sinus of infection and remove the inciting cause in cases of secondary sinusitis.

Therapy

The results of culture and sensitivity of fluid aspirated from the sinus dictate the appropriate antimicrobial therapy necessary to treat the sinusitis. Because primary sinusitis frequently is a sequela to upper respiratory tract infection, *Streptococcus* spp. are frequently isolated. Penicillin or trimethoprim sulfonamides are appropriate antibiotics to use in the treatment of primary sinusitis, prior to receipt of culture results. In addition to systemic antibiotics, repeated lavage of the sinus with balanced polyionic solution decreases the exudate and dilutes the organisms and inflammatory mediators within the sinus.[13,14] A chronic irrigation system can be placed following sinus centesis. Sinus centesis can be performed at the cranial or caudal maxillary sinus or frontal sinus. A point 2.5–3 cm dorsal to the facial crest and 3 cm rostral to the medial canthus marks the placement for centesis of the caudal maxillary sinus;[14] 2.5–3 cm dorsal to the facial crest and 3 cm caudal to the infraorbital foramen permits access to the cranial maxillary sinus.[14] Centesis of the frontal sinus is performed at a site midway between the medial canthus of the eye and the midline of the head.[14] Following aseptic preparation, a 2–3 mL bleb of local anesthetic is injected subcutaneously at the chosen site. A stab incision is made through the skin and subcutaneous tissue and a 2 mm Steinmann pin in a Jacob's chuck is used to drill a hole into the sinus. Sterile polyethylene tubing is fed through the centesis site and fluid is aspirated using a needle and syringe attached to the tubing. Next, a chronic irrigation system can be placed through the centesis site into the sinus and sutured in place. An extension set works well. The chronic irrigation system permits irrigation of the sinus with 1–3 liters of solution two to four times daily until there is no longer production of exudate.

The goal of treating secondary sinusitis is to treat the primary cause. Depending upon the location, sinus cysts, ethmoid hematomas, neoplasia, polyps, and infected teeth can be approached surgically through a maxillary bone flap or frontal nasal bone flap.[14,16] Because the sinuses are highly vascular, copious hemorrhage can occur. Hemorrhage is controlled during surgery by lavaging the site with cold saline and applying pressure to the bleeding area. Occasionally, but rarely, vessels can be located and ligated. After the mass has been removed, continuous pressure is applied to the area using stallion gauze packing placed within the sinus. The end of the packing is exited through a hole in the dorsal or ventral conchal sinus and then out the nose. The packing is pulled in 36 to 48 hours.

Prognosis

The prognosis for recovery from primary sinusitis, sinus cysts, trauma, and dental disease is good.[13,17] Complications can include chronic drainage from the sinus, recurrence of the cyst if a portion of the cystic lining was left within the sinus, oral nasal fistulas from tooth extraction, incisional infection and sequestration of the bone flap overlying the sinus. Prognosis for most neoplastic masses within the sinus resulting in sinusitis is poor due to the expansile, invasive, and metastatic nature of the tumors. Recurrence of ethmoid hematoma is 43%.[2]

Prevention

There is no known prevention.

Etiology and pathophysiology

Etiology

Sinusitis can result from a primary infection within the sinus, frequently secondary to an upper respiratory tract infection. Sinusitis can also occur secondary to an apical tooth root abscess, sinus cyst, neoplasia, trauma and fracture of facial bones, ethmoid hematoma, and fungal granuloma.[13,14]

Epidemiology

The prevalence of sinusitis is approximately 1.06%.[18]

Rostral and dorsal pharyngeal collapse

- Horses with nasopharyngeal collapse usually are normal at rest.
- The diagnosis of nasopharyngeal collapse is made during treadmill endoscopic examination.
- There is no known treatment for nasopharyngeal collapse.
- Clinical signs of nasopharyngeal collapse, in some horses, will resolve with time.
- Horses with hyperkalemic periodic paralysis are at risk for developing nasopharyngeal collapse.

Recognition

History and presenting complaint

Various degrees of nasopharyngeal collapse may cause exercise intolerance and respiratory noise in exercising horses.

Physical examination

This is normal in the resting horse.

Special examination

Endoscopic examination of the nasopharynx and larynx is generally normal. If the nares are manually occluded during the examination, the lateral walls, dorsal aspect of the nasopharynx, or rostral portion of the soft palate may collapse into the airway to an abnormal degree in affected horses, especially horses with hyperkalemic periodic paralysis (HYPP).[19,20] In normal horses, the roof of the nasopharynx projects into the

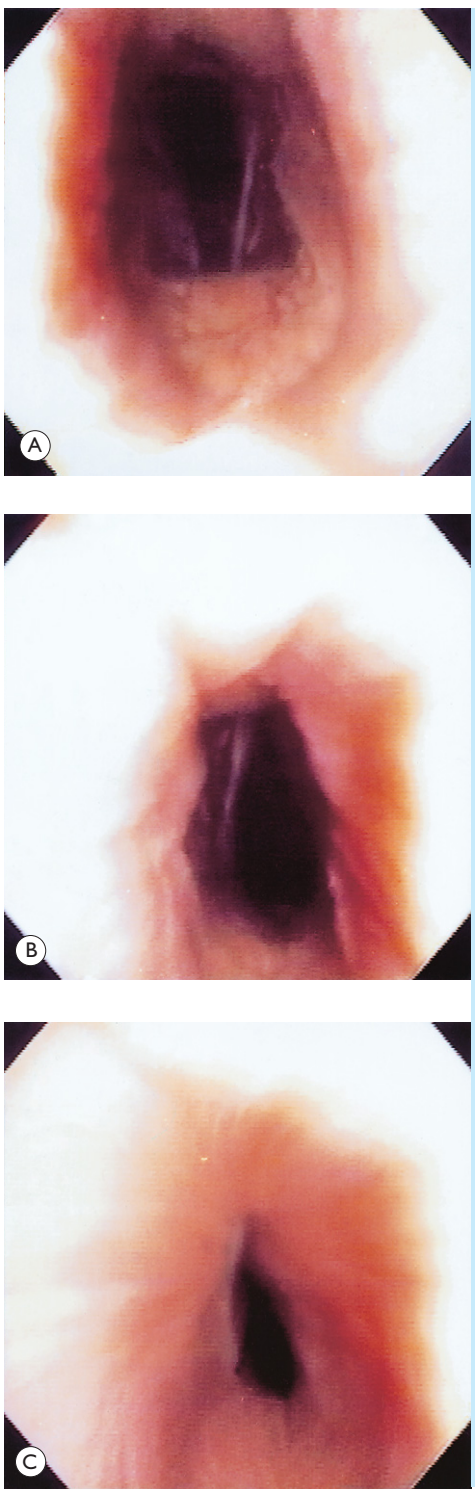


Fig. 27.7 Endoscopic images of the nasopharynx of an exercising horse showing progressive nasopharyngeal collapse. Collapse is apparent in the first frame (A) and increases with increasing duration of exercise on the treadmill (B, C).

lumen of the nasopharynx minimally at the end of expiration due to positive end-expiratory pressure within the guttural pouches. The floor of the guttural pouch forms the roof of the nasopharynx. At rest, the pressure in the guttural pouches is in phase with the pressure in the nasopharynx.[21] During exercise, the pressures are not in phase, such that peak expiratory pressure within the guttural pouch lags behind peak expiratory nasopharyngeal pressure, resulting in some degree of dorsal pharyngeal collapse at end expiration.[21] Nasopharyngeal collapse is most accurately diagnosed during treadmill endoscopic examination. Some horses show signs of nasopharyngeal collapse during resting endoscopic examination, but have normal nasopharyngeal function during exercise. Similarly, horses with exercise intolerance and respiratory noise during exercise may be normal at rest, exhibiting signs of disease during treadmill endoscopy (Fig. 27.7).

Laboratory examination

None is indicated.

Diagnostic confirmation

Differential diagnoses for nasopharyngeal collapse include dynamic upper respiratory diseases that cause exercise intolerance and abnormal respiratory noise during exercising, such as dorsal displacement of the soft palate. Evaluating the horse's airway function during exercise can lead to a definitive diagnosis of nasopharyngeal collapse.

Treatment and prognosis

Therapeutic aims

The goal of treatment is to resolve the nasopharyngeal collapse.

Therapy

There is no current treatment for nasopharyngeal collapse. Horses are exercised with their tongues tied and wearing figure eight nosebands in an attempt to help 'stabilize' the airway. Occasionally, the disease is self-limiting and horses recover normal function without treatment. If the horse has suffered from a respiratory viral infection or pharyngitis, alleviating the airway inflammation may improve nasopharyngeal function within a few weeks to months. Horses that are HYPP positive respond to acetazolamide therapy.[19,21]

Prognosis

The prognosis is usually unfavorable, especially in horses with underlying disease such as HYPP. The condition resolves in some horses.

Prevention

There is no known prevention.

Etiology and pathophysiology

Etiology

The disease is associated with HYPP in some horses. However, in most cases the etiology of pharyngeal collapse is not known.

Pathophysiology

Nasopharyngeal collapse may result from some form of exercise-induced guttural pouch tympany or neuromuscular lesion involving the muscles that support the dorsal nasopharynx.[19] Horses should be evaluated for neuromuscular or primary muscle disorders, such as equine protozoal neuropathy, selenium and vitamin E deficiency, hyperkalemic periodic paralysis, or upper respiratory inflammatory disease.[19,20]

Epidemiology

The epidemiology of this condition has not been described. However, this disease is most frequently diagnosed in young race horses, which may be due to the speed and intensity at which they compete. As well, nasopharyngeal collapse is frequently recognized in horses with HYPP, and rather than being a distinct entity, represents a muscle group affected by the disorder.

Retropharyngeal abscesses

Recognition

History and presenting complaint

Horses with retropharyngeal abscessation frequently have palpable swelling in the throat region, nasal discharge, abnormal respiratory noise during exercise, dorsal displacement of the soft palate, and exercise intolerance. If the airway obstruction is severe, horses may show signs of

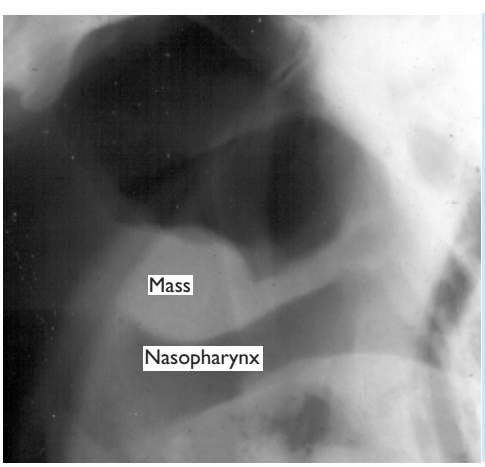


Fig. 27.8 Lateral radiograph of the pharyngeal region of a horse with an abscessed retropharyngeal lymph node causing collapse of the dorsal nasopharynx.

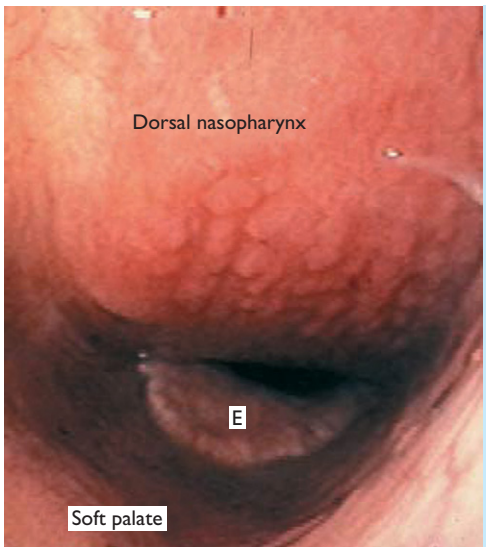


Fig. 27.9 Endoscopic image of the nasopharynx of a horse with abscessed retropharyngeal lymph nodes. Notice how the dorsal nasopharynx is collapsed, such that the larynx cannot be seen. E, epiglottis.

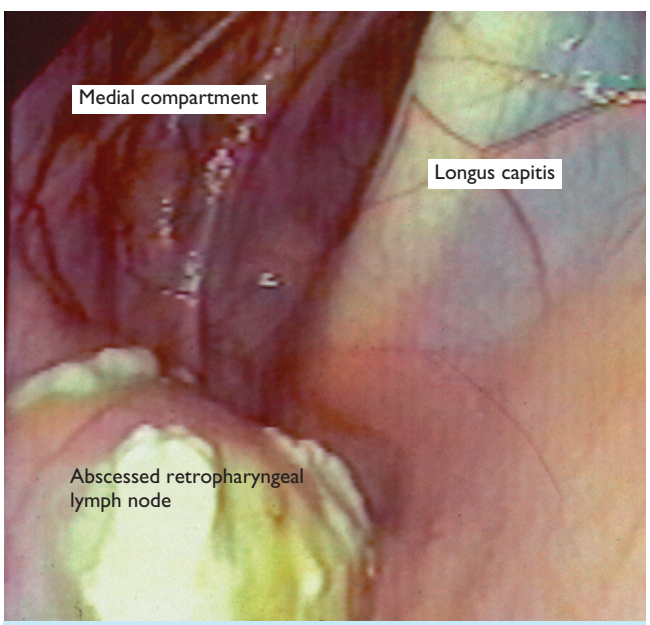


Fig. 27.10 Endoscopic image of the medial compartment of the guttural pouch. Notice the abscessed retropharyngeal lymph node.

respiratory distress at rest, including respiratory stridor, increased respiratory rate and effort, and anxiety. Additional clinical signs include dysphagia, inappetance, and depression.

Physical examination

Palpation of the throat in the area of Viborg's triangle may reveal swelling that can be painful. Pressure in this area can cause the horse to make stridorous upper airway noise. If the horse is dysphagic, feed material and saliva may be seen at the nares. If the horse is in respiratory distress, stridorous breathing and increased respiratory effort may be apparent.

Special examination

Radiography of the throat area reveals soft tissue density in the retropharyngeal region, dorsal to the pharynx and on the floor of the guttural pouch (Fig. 27.8). Compression of the dorsal nasopharynx by the abscessed retropharyngeal lymph node is evident during endoscopic examination of the upper airway (Fig. 27.9). Depending upon the size and location of the abscess, the enlarged lymph node may be best seen within the guttural pouch, on the floor of the medial compartment (Fig. 27.10) Ultrasonographic examination of the throat will show increased soft tissue density containing hyperechoic fluid, or purulent exudates.

Laboratory examination

Results of complete blood count frequently show leukocytosis and neutrophilia with regenerative left shift, and lymphocytosis. Some horses will have hyperfibrinogenemia.

Diagnostic confirmation

The diagnosis is confirmed by aspiration of material from the affected lymph node and culture of the exudate. Retropharyngeal lymph node abscesses are most frequently caused by *Streptococcus* spp., particularly *Streptococcus equi*.

Treatment and prognosis

Therapeutic aims

The goal of therapy is resolution of the abscess.

Therapy

If the horse is in respiratory distress an emergency tracheotomy is performed. Briefly, an area 20 cm long and 15 cm wide at the junction of the proximal and middle thirds of the trachea is clipped and aseptically prepared. Tracheal rings can be palpated in this area. The skin is anesthetized by subcutaneous injection of local anesthetic (lidocaine (lignocaine) or mepivacaine hydrochloride) in a linear pattern in the area of the incision or in a curved pattern proximal to the incision. A 10–12 cm linear incision is made through the skin, subcutaneous tissue, and cutaneous trunci sharply with a scalpel along the midline. The fascial plane dividing the right and left sternohyoid muscles is sharply incised with a scalpel, Metzenbaum scissors, or the muscle bellies can be moved to the side, exposing the tracheal rings. A scalpel is inserted between two tracheal rings, in the middle of the incision, by stabbing the blade through the tracheal ligament, attaching the two tracheal rings. Without removing the blade, the ligament is cut 50% to the left, turned within the trachea, and cut 50% to the right, taking care to only transect the ligament. Before removing the scalpel blade from the tracheal lumen, a Kelly hemostat is inserted into the tracheal lumen, identifying the opening in the tracheal lumen. As the hemostat is removed from the lumen, the tracheostomy tube is inserted. The tube must be secured such that when the

horse moves its head and neck, the tube lumen is not obstructed and the tube is not dislodged from the trachea.

Because most retropharyngeal lymph node abscesses are caused by streptococcal species, penicillin, 22 000–44 000 IU/kg, or sulfamethoxazale-trimethoprim, 15 mg/kg, is administered for 7 to 10 days. Judicious use of non-steroidal anti-inflammatory medication is appropriate. If the lymph nodes are large, surgical drainage may be required. Following general anesthesia, the horse is positioned in dorsal recumbency. A modified Whitehouse approach is performed on the affected side, exposing the abscessed lymph node. Confirmation of the abscess is made by inserting a needle into the mass and aspirating material from the lymph node that can be submitted for culture and antibiotic sensitivity. A stab incision is then made in the lymph node and the purulent material evacuated. The incision is left open, to heal by second intention, and the site is lavaged with saline or dilute tamed iodine solution twice daily.

Prognosis

The prognosis for return to normal function within 4 to 5 months following retropharyngeal lymph node abscess is excellent, or approximately 90%.[22]

Prevention

Decreased exposure to horses infected with *Streptococcus equi* minimizes the occurrence of retropharyngeal lymph node abscess formation. Prophylactic vaccination against *S. equi* may limit retropharyngeal lymph node abscess formation, but vaccination is not without risk.

Etiology and pathophysiology

Etiology

Most retropharyngeal lymph node abscesses are caused by streptococcal species, principally *S. equi.*

Epidemiology

Retropharyngeal lymph node abscesses are most commonly seen in horses less than 1 year old, and in horses infected with *S. equi.*

Dorsal displacement of the soft palate (DDSP)

Recognition

History and presenting complaint

Horses with intermittent dorsal displacement of the soft palate (DDSP) are exercise intolerant and make an abnormal expiratory noise during exercise. The displaced soft palate

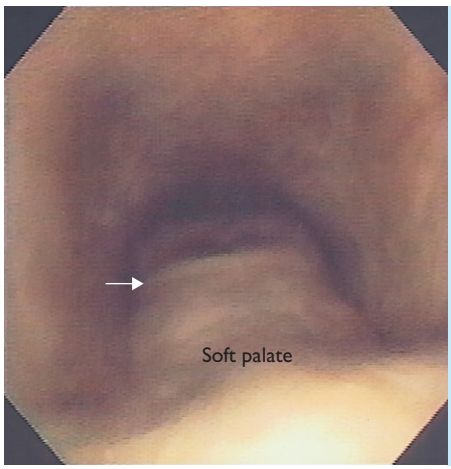


Fig. 27.11 Endoscopic image of a horse with dorsal displacement of the soft palate while exercising on a treadmill. Notice how the soft palate billows dorsally in the airway, obstructing the rima glottidis. Arrow, caudal free margin of the soft palate.

billows dorsally during exhalation as air flows beneath the soft palate (Fig. 27.11). The noise associated with DDSP is a 'snoring noise', and is caused by fluttering of the caudal margin of the soft palate. In approximately 30% of horses with DDSP, noise is not reported.[23,24] The importance of either noise production or exercise intolerance is dependent on the activity of the horse. This is an uncommon disease of show horses and generally affects the horse's performance because of the noise production. However, horses that perform with the head and neck flexed, such as upper level dressage horses and Saddlebreds, suffer exercise intolerance with DDSP due to the more negative inspiratory pressure and airway resistance that occurs with head and neck flexion.[25] Dorsal displacement of the soft palate is more common in race horses, especially 2–4-year-olds.[26–28] The exercise intolerance is often described by trainers and riders or drivers as 'choking down' or 'hitting a wall' because DDSP causes significant expiratory obstruction that limits minute ventilation. Mouth breathing during exhalation is recognized by fluttering of the cheeks as air is diverted underneath the soft palate through the mouth, and is a specific sign that a horse has displaced its soft palate dorsal to the epiglottis. Occasionally coughing during exercise is reported in association with the disease. Coughing is a symptom of upper respiratory infection and these types of infection have been associated with the onset of DDSP in some cases.

Physical examination

Because intermittent DDSP is a dynamic obstructive airway disease that occurs during exercise, most horses are normal at rest. If the soft palate displacement is persistent and associated with dysphagia, feed material may accumulate in the airway, the horse may cough, and have clinical signs of aspiration pneumonia. The primary complaint in these horses is dysphagia and aspiration, which is quite different from the population of horses with intermittent DDSP, exercise intolerance, and respiratory noise.

Some horses with intermittent DDSP have a history of upper respiratory infection. These horses may have nasal discharge, coughing, and enlarged retropharyngeal and submandibular lymph nodes. If the horse had previous surgery in an attempt to treat the DDSP, evidence of such surgery

includes indentation in the cervical musculature, where a sternothyrohyoid myectomy was performed. It is more difficult to identify horses that have excision of the caudal margin of the soft palate or sternothyroid tenectomy and myectomy at the muscle's origin. Clipping the hair over the ventral aspect of the cricoid cartilage may permit identification of a surgical scar indicative of prior laryngotomy procedure.

Special examination

Watching and listening to the horse exercise at a racetrack and witnessing the described abnormal noise and exercise intolerance of the horse may be helpful in diagnosing DDSP. The noise is somewhat specific in that it occurs during expiration and has a snoring character, quite different from inspiratory noises associated with laryngeal hemiplegia and other dynamic inspiratory airway abnormalities. Endscopic examination of the nasopharynx and larynx at rest is important to assess nasopharyngeal function and rule in or out other causes of abnormal airway noise and exercise intolerance, such as laryngeal hemiplegia or epiglottic entrapment. Initially, the nasopharynx is examined in the unsedated horse as the horse breathes normally. Examination of both guttural pouches may be helpful if upper airway infection is suspected. Stimulating the horse to swallow permits assessment of the function of nasopharyngeal muscles and may cause the horse to displace its soft palate. Dorsal displacement of the soft palate is recognized by the dorsal position of the caudal edge of the soft palate obstructing the view of the epiglottis (Fig. 27.12). Occluding the horse's nares for 20–60 seconds, forcing the horse to breathe against the obstruction, may stimulate increased activity in upper airway muscles and induce DDSP. The interpretation of induced DDSP during nasal occlusion is difficult because a percentage of horses that displace the soft palate during nasal occlusion show no evidence of DDSP during endoscopic examination while the horse runs on the treadmill.[26,27] As well, horses that do not displace at rest do displace during treadmill examination. The caudal aspect of the soft palate can be examined by passing the scope in the proximal trachea which induces DDSP in most horses. After withdrawing the endoscope, the caudal edge of the soft palate can be examined for evidence of cyst, masses or prior staphylectomy. During endoscopy, the most important signs indicative of DDSP are (1) the ease with which DDSP can be induced by nasal occlusion, (2) how readily the horse is able to correct it by swallowing, and (3) how many attempts (swallows) are required to replace the caudal edge of the soft palate in its subepiglottic position. Endoscopic examination of the nasopharynx while the horse runs on the treadmill permits identification of DDSP as it occurs during exercise. Some horses will make the characteristic 'snoring' noise and open mouth breathing during exhalation can also be detected.

In some horses, permanent displacement of the soft palate is present such that the epiglottic cartilage cannot be examined. It is important to evaluate the epiglottis morphology as well as its function; for instance, subepiglottic masses and epiglottic deformity can result in DDSP. If permanent displacement is present, there are a few techniques that can be used to evaluate the structure and integrity of the epiglottis. Sometimes removing the twitch will relax the horse and allow it to reposition the soft palate appropriately. Sedation may permit replacement of the soft palate.[29] In the standing, sedated horse, following application of local anesthetic to the nasopharynx, bronchoesophageal forceps can be passed in one nostril and used to un-entrap the epiglottis from the soft palate. Evaluation of the epiglottic cartilage and the position of the soft palate can be performed using radiography (Fig. 27.13). Finally, an oral endoscopic examination can be performed on the horse following sedation or general anesthesia and application of a mouth speculum. If the horse is anesthetized, manual palpation of the epiglottic cartilage and soft palate can also be performed.

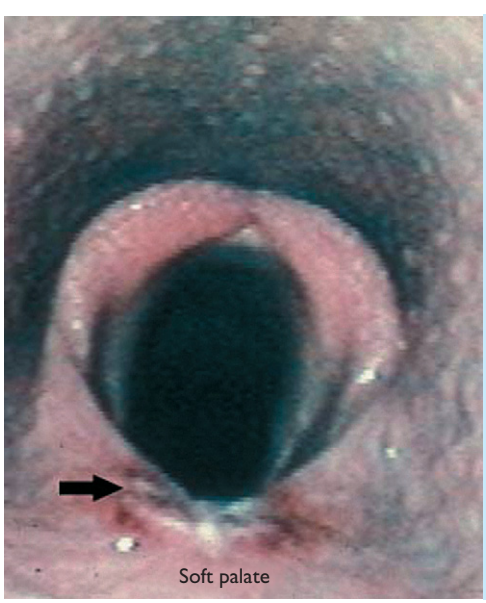


Fig. 27.12 Endoscopic image of the nasopharynx of a horse with dorsal displacement of the soft palate. Notice the ulcer (arrow) at the caudal free margin of the soft palate.

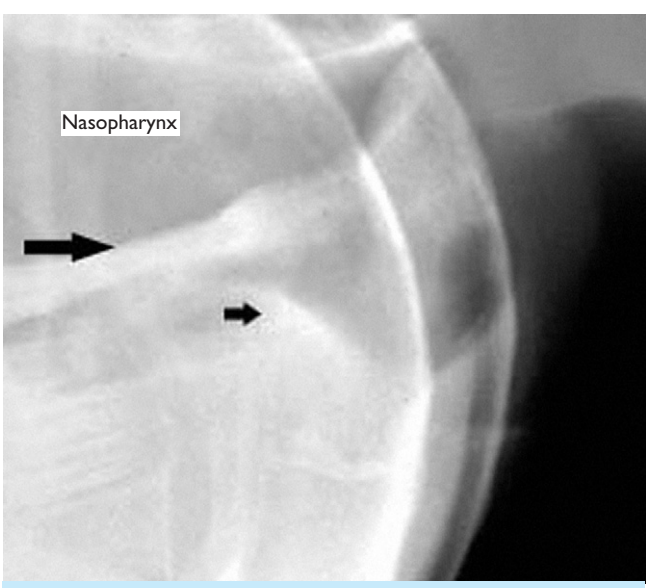


Fig. 27.13 Lateral radiograph of the pharyngeal region of a horse with persistent dorsal displacement of the soft palate. Notice the epiglottis (small arrow) positioned ventral to the soft palate (large arrow).

Diagnostic confirmation

Because horses with DDSP are normal at rest, with clinical signs occurring only during exercise, the diagnosis can be very difficult to confirm. The best way to diagnose DDSP is during endscopic examination of the nasopharynx while the horse runs on the treadmill. However, not all horses exhibit signs of DDSP during treadmill exercise. As well, because the clinical signs are similar to many other obstructive upper airway diseases, DDSP can be easily missed or overdiagnosed.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to prevent DDSP from occurring. Because the etiology of DDSP is unknown, this can be a difficult task.

Therapy

In 2-year-old horses or any horse that has active or previous upper airway inflammation, the initial therapy should focus on decreasing the upper airway inflammation. Medical therapy can be instituted unless a structural abnormality, such as epiglottic deformity, entrapment, or soft palate cyst or mass, is present. If bacterial upper airway infection is diagnosed, systemic antibiotics (usually penicillin G, ceftiofur or sulfamethoxazole-trimethoprim) may be administered with non-steroidal anti-inflammatory drugs. Upper airway inflammation is treated in a plethora of different ways, including systemic administration of corticosteroids (dexamethasone), non-steroidal anti-inflammatory medication, topical anti-inflammatory throat sprays such as glycerin, dimethyl sulfoxide, and nitrofurazone, systemic administration of interferon, and guttural pouch lavage with balanced polyionic solutions with or without dimethyl sulfoxide and corticosteroids. Oral interferon alpha (50–200 IU/day for 10 days to 2 weeks) is sometimes prescribed. An appropriate treatment regimen for moderate to severe nasopharyngeal inflammation, without bacterial infection, might include treatment first with systemic corticosteroids such as prednisolone or dexamethasone and topical anti-inflammatory throat spray for 2 to 4 weeks. A common throat spray administered at the rate of 20 cc, orally, every 12 hours consists of: glycerin 250 mL, 250 mL DMSO 90%, nitrofurazone 500 mL, prednisolone 50 mL (25 mg/mL). Horses should be rested (light training without fast speed work) for 10–30 days and the upper airway function re-evaluated periodically. Normal function may not return for 3–4 months, if the cause of the DDSP was neuromuscular dysfunction related to airway inflammation.

Tack modifications such as the use of a bit that keeps the tongue under it (i.e., a 'W' bit, Serena bit), tongue-ties and the figure eight noseband are traditional approaches (although unproven) that might be of value in reducing the occurrence of DDSP. There is no evidence to support the use of a tongue-tie in the prevention of DDSP or improvement of airway mechanics in exercising horses.[30–32]

Owners and trainers of 2-year-old horses should consider waiting until the following year before pursuing any surgical treatment as maturity may alleviate the need for treatment. In addition, 2-year-olds have a high prevalence of pharyngitis that has been associated with DDSP due to inflammation of the nerves and perhaps muscles that stabilize the soft palate.[33]

Surgical treatment alternatives are numerous and include staphylectomy or trimming the caudal free margin of the soft palate, various strap muscle resections (sternohyoid, sternothyroid, and omohyoid alone or in combination), epiglottic cartilage augmentation, and various tension palatoplasty procedures.[34–40] These procedures are performed by some surgeons alone or in various combinations.

The goal of staphylectomy is to remove a thin section of the caudal free edge of the soft palate.[40] If an ulcer is present at the caudal margin of the soft palate, resection of the ulcerative tissue via staphylectomy is recommended. The mechanism by which this procedure is therapeutic is unknown. Some suggest that staphylectomy stiffens the free edge of the soft palate or perhaps enlarges the pharyngeal ostium.[40] Following the surgical procedure, systemic antibiotic therapy is continued for 7 days and anti-inflammatory medication is continued for 3–7 days. The laryngotomy incisions should be cleaned twice daily until they are healed (approximately 3 weeks). The horse can begin training 2–3 weeks later. Some surgeons close the thyrohyoid membrane at the time of surgery, which dramatically decreases the discharge from the incision. Others close the entire laryngotomy incision, eliminating the need for postoperative wound care.[41] Complications following primary closure of a laryngotomy incision include subcutaneous emphysema, incisional discharge, postoperative fever, incisional abscessation, seroma, and subcutaneous edema.[41]

Complications of staphylectomy include dysphasia, coughing, aspiration, pneumonia, and permanent DDSP.[40] The most common complication is infection at the laryngotomy site, which usually responds to wound care and antibiotics. Staphylectomy is traditionally done through a laryngotomy, but can be performed with the horse standing by use of a laser. The section of soft palate removed should be minimal as the major complication of this procedure is nasal regurgitation of feed and water. If resection is too extensive, the soft palate no longer contacts the ventral surface of the epiglottis, forming a communication between the oropharynx and nasopharynx, such that feed material from the oropharynx reaches the nasopharynx prior to or during swallowing. Furthermore, if the caudal free edge of the soft palate is rostral to the epiglottic cartilage, expiratory airflow reaches the ventral surface of the soft palate, lifting the soft palate and leading to displacement.

The goal of the resection of the sternothyroideus and sternohyoideus muscles is to prevent caudal retraction of the larynx from the caudal edge of the soft palate.[34] The most common myectomy is the sternothyrohyoid myectomy, which can be performed in the standing, sedated horse with local anesthetic applied at the surgical site.[34] Additionally, some surgeons also resect a section of the omohyoid muscles. Complications are usually minor and include incisional seromas or abscesses requiring appropriate drainage. There is a report of one horse exsanguinating following this

procedure.[34] This latter complication is more common if the omohyoid muscles are removed. Long-term complications were thought to be only cosmetic in nature associated with the lack of strap muscle at the surgery site. However, in experimental horses with normal airway function, resection of the sternothyroid and sternohyoid muscles has been observed to result in a less dynamically stable nasopharynx at exercise as measured by an increase in inspiratory tracheal pressure.[42]

The Llewellen procedure combines the staphylectomy and myectomy, but the sternothyroideus tendon is transected through the laryngotomy site, as it inserts on the thyroid cartilage.[35] Following the staphylectomy portion of the Llewellen procedure, some surgeons elect to remove 4–7 cm of the sternohyoideus muscles that are easily accessed via the laryngotomy incision.

Epiglottic augmentation was developed because epiglottic flaccidity is implicated in the pathogenesis of DDSP. The purpose of the procedure is to stiffen the horse's epiglottis.[36,43] With the horse under general anesthesia, the subepiglottic tissue is injected with Teflon paste (Mentor Polytef paste for injection, Mentor O&O, Inc., 3000 Long Water Dr, Norwell, MA 02061) as the epiglottis is retroverted through a laryngotomy incision. Postoperatively, the resulting fibrosis and granulomatous reaction in response to the Teflon contributes to a thicker and less flaccid epiglottis.[43] The frequent lack of availability of the Teflon paste in recent years has diminished the use of this technique, which is usually performed in combination with a sternothyroid myectomy and a staphylectomy. For 5–7 days following epiglottic augmentation, the epiglottis may look swollen and red, and may, in fact, be entrapped. Some horses have persistent soft palate displacement for 5–14 days following surgery. Horses are treated with systemic antibiotics and anti-inflammatory medication for 2 weeks after surgery and can begin training within 6–8 weeks. Complications include dysphasia, permanent soft palate displacement, coughing, Teflon granulomas, and epiglottic entrapment.

Tension palatoplasty was introduced during the 1990s to reduce the dorsal billowing of the soft palate by stiffening the ventral aspect of the soft palate.[37–39] Rostral stability of the soft palate might be important in the overall stability of the soft palate during exercise and in the prevention of intermittent dorsal displacement of the soft palate. The popularity of these procedures has diminished because of the finding that, in experimental horses, rostral palate stability may not be important in prevention of DDSP.[44] Furthermore, results in clinical patients were comparable to that of other techniques.

Three techniques have been described to stiffen the soft palate. In the original technique, under general anesthesia using an oral approach with long-handled scissors, a section of oral palatine mucosa and submucosa (starting 1–2 cm caudal to the hard palate) is resected.[37] Care must be taken not to invade the entire palate as a palatal fistula could occur. Tension on the palate is obtained by re-apposing the edges of the palatal mucosa and closing the defect created. Stiffening has also been done using thermal cautery applied at the same location.[38] Alternatively, the procedure can be done with the horse standing, applying thermal cautery to the nasopharyngeal mucosa of the rostral palate.

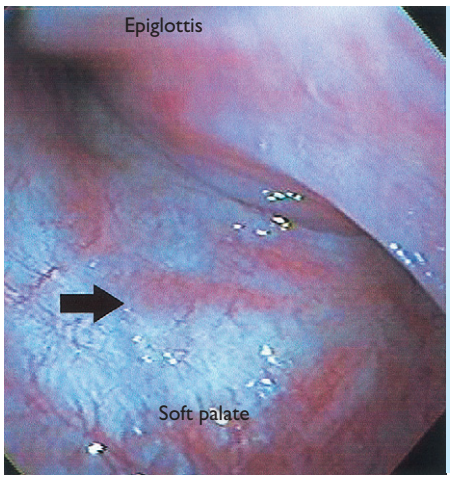


Fig. 27.14 Endoscopic image of the soft palate of a horse following laser surgery. Notice the white, scarred area (arrow).

Tension palatoplasty has also been performed at the caudal aspect of the soft palate using the laser.[39] This procedure was proposed as an alternative for staphylectomy and performed in conjunction with a sternothyroid myectomy and tenectomy. Briefly, horses are restrained in stocks and sedated. Using endoscopic guidance, the caudal margin of the soft palate is anesthetized by use of topical local anesthesia. A 600 μm bare fiber is passed through the biopsy channel and directed at the caudal free edge of the soft palate. Using 15 watts of power and contact technique, the fiber was applied for 1–2 seconds at 2–4 mm intervals along the entire free edge of the palate and extending approximately 1.5 cm rostrally.[39] Horses are treated intraoperatively with phenylbutazone (6 mg/kg intravenously) and topical throat spray, and discharged with instructions to hand walk for 3 days prior to returning to jogging or galloping. Postoperative medications consisted of intranasal throat spray for 14 days, phenylbutazone (4 mg/kg by mouth) for 5 days, and a decreasing regime of oral prednisolone for 14–21 days. If an endoscopic examination at 1 week indicated normal healing of the soft palate, horses were returned to full training (Fig. 27.14).[39]

Finally, a new procedure is being developed based on the finding of the results of experimentally created dysfunction of the thyrohyoid muscle.[45] The surgical procedure restores the function of the thyrohyoid muscles using sutures as prostheses to displace the larynx rostrally and slightly dorsal to the basihyoid bone. A clinical trial is currently underway and further discussion is pending validation of the surgical procedure in a clinical population with naturally occurring DDSP (Ducharme NG, Cornell University, personal communication).

Prognosis

The prognosis following treatment is approximately 60 ± 10%. According to trainers and veterinarians recurrence frequently occurs 3–6 months after surgery. Reported success rate for epiglottic augmentation is 66%.[46] Staphylectomy has a 59% success rate, defined as improved racing performance.[40] Horses will have their first race start approximately 16 weeks after surgery.[40] Reported success for the sternothyrohyoid myectomy is 58–60%.[34,40] Horses have their first

race start approximately 10 weeks following surgery. Reported success rate for the Llewellen procedure is 60%.[35] Following transendoscopic laser cauterization of the caudal margin of the soft palate, combined with sternothyroid myectomy and tenectomy, 92% of horses raced successfully.[39]

Etiology and pathophysiology

Etiology

The cause of intermittent DDSP is unknown. However, many theories exist to explain the etiology of this condition, some based on research and data and others on speculation. Dorsal displacement of the soft palate occurs when the soft palate displaces dorsal to the epiglottis, billowing in the nasopharynx creating expiratory obstruction. This event occurs during inspiration, expiration, and swallowing and probably has multifactorial etiology.[47] Some theories focus on dysfunction of the nerves and muscles controlling the soft palate function, and others are directed at the stability and proximity of the epiglottis and larynx to the soft palate. The stability of the nasopharynx is obtained by complex coordination of skeletal muscles and a multitude of conditions affecting these muscles, such as hyperkalemic periodic paralysis and equine protozoal myeloencephalopathy, can result in DDSP during exercise.[20]

The thyrohyoideus is a flat rectangular muscle attached to the lateral surface of the thyroid cartilage lamina that inserts on the caudal part of the thyrohyoid bone. It is innervated by the hypoglossal nerve and moves the hyoid bone caudally or the larynx rostrally and dorsally. In studies evaluating the electromyographic activity of some 'extrinsic' nasopharyngeal muscles during exercise, Ducharme et al observed decreased thyrohyoideus muscle activity prior to soft palate displacement in one horse. Bilateral resection of the thyrohyoideus muscles causes intermittent DDSP during exercise in horses.[45] The specific function of the thyrohyoideus muscle in preventing DDSP is not well understood, but because contraction of the thyrohyoideus muscles apposes the larynx and basihyoid bone, the position of the larynx relative to the soft palate is probably important in the pathogenesis of DDSP.

Neuromuscular dysfunction of the structures controlling the position of the soft palate has been implicated as a cause of this disease, and may occur due to inflammation of the upper airway. The pharyngeal branch of the vagus nerve, and other nerves important in the coordination of nasopharyngeal function, course through the guttural pouch. Specifically, the pharyngeal branch of the vagus nerve provides motor innervation to the palatinus and palatopharyngeus muscles, two muscles that control the position of the caudal portion of the soft palate. Desensitizing the pharyngeal branch of the vagus nerve bilaterally causes persistent DDSP and dysphagia in horses.[48] Biopsies taken of the palatinus muscle from horses with DDSP showed evidence of chronic denervation included fiber type grouping, mild atrophy, moth eaten fibers and target fibers.[49]

Epiglottic hypoplasia may cause DDSP because the epiglottis is not rigid enough to maintain its position dorsal to the soft palate.[49] No conclusive evidence exists to support epiglottic hypoplasia as the cause of DDSP, and its association with DDSP and poor racing performance has not been confirmed.[50] However, epiglottic malformation or chondritis may result in permanent or persistent DDSP.

Pathophysiology

Dorsal displacement of the soft palate is an expiratory obstructive syndrome that causes increased expiratory impedance, decreased minute ventilation, hypoxia, and hypercarbia (Table 27.1).[48,51] When the soft palate displaces dorsal to the epiglottis during exercise, it billows dorsally and ventrally during the respiratory cycle. During inhalation, the soft palate is located ventrally (still dorsal to the epiglottis). During exhalation, the soft palate displaces dorsally, thus diverting the flow of air through the oropharynx and mouth. This flow pattern is associated with more negative peak tracheal pressure and increased expiratory impedance.[47,48,51] During inhalation, it is less clear whether the less negative atmospheric pressures are associated with decreased airway resistance due to oral breathing as two studies revealed different results.[47,48,51]

Prevention

Preventing DDSP is difficult because the etiology of this disease is unknown. However, aggressive, timely treatment of upper airway inflammation and appropriate vaccination against upper respiratory tract viruses may decrease the chances of horses developing intermittent DDSP.

Epidemiology

Dorsal displacement of the soft palate (DDSP) is a performance-limiting upper airway condition in horses that was identified in 1.3% of 479 horses examined endoscopically at rest.[52] The prevalence of this disease is likely to be higher because DDSP is a dynamic condition that occurs during intense exercising, making the diagnosis at rest and, even during treadmill exercise, difficult.

Epiglottic entrapment

- Epiglottic entrapment occurs when redundant aryepiglottic tissue envelops the epiglottis.
- Epiglottic entrapment can be an incidental finding during endoscopic examination of the larynx and not associated with clinical signs.
- The entrapping aryepiglottic tissue can be smooth or edematous and ulcerated.

Recognition

History and presenting complaint

Horses with epiglottic entrapment may have exercise intolerance and make an abnormal respiratory noise during exer-

cise but rarely cough or are dysphagic. Some affected horses do not display any abnormalities.

Physical examination

This is generally normal. Horses with severely ulcerated, swollen entrapping aryepiglottic membrane may be dysphagic and have signs of aspiration pneumonia, though this is rare.

Special examination

Endoscopic examination reveals that the epiglottis is in its normal position dorsal to the soft palate but is encased in aryepiglottic tissue. The normal serrated edge of the epiglottis and its vascular pattern are obscured by the entrapping membrane. The aryepiglottic tissue can be smooth, fitting tightly around the epiglottis, or swollen and ulcerated (Fig. 27.15A, B). Occasionally, the epiglottis is entrapped by the aryepiglottic tissue intermittently, during exercise or swallowing. In these cases, the diagnosis may be made during endoscopic examination with the horse running on a treadmill or may be apparent on a lateral projection radiograph of the larynx. Radiographically, the entrapment appears as excessive soft tissue density surrounding the epiglottis. Radiography can be useful if the soft palate is persistently displaced, due to the entrapment, and the epiglottis and entrapping aryepiglottic membrane cannot be seen during endoscopic examination performed transnasally.

Laboratory examination

Laboratory examination is normal, but none is usually indicated.

Diagnostic confirmation

Differential diagnoses for epiglottic entrapment include dynamic upper airway lesions that cause exercise intolerance and abnormal respiratory noise during exercise. A definitive diagnosis of epiglottic entrapment is made by endoscopic examination.

Treatment and prognosis

Therapeutic aims

The goal of treatment is to relieve the entrapment.

Therapy

Transaxial division of the entrapping aryepiglottic membrane can be performed by use of a hooked bistoury through the mouth with the horse under general anesthesia (Fig. 27.16).[53] This same procedure is sometimes performed transnasally on standing, sedated horses, but is not recommended because of the risk of soft tissue damage.[54] Lacerations of the nasopharynx, soft palate, and epiglottis have occurred during transaxial division of the entrapping aryepiglottic tissue performed

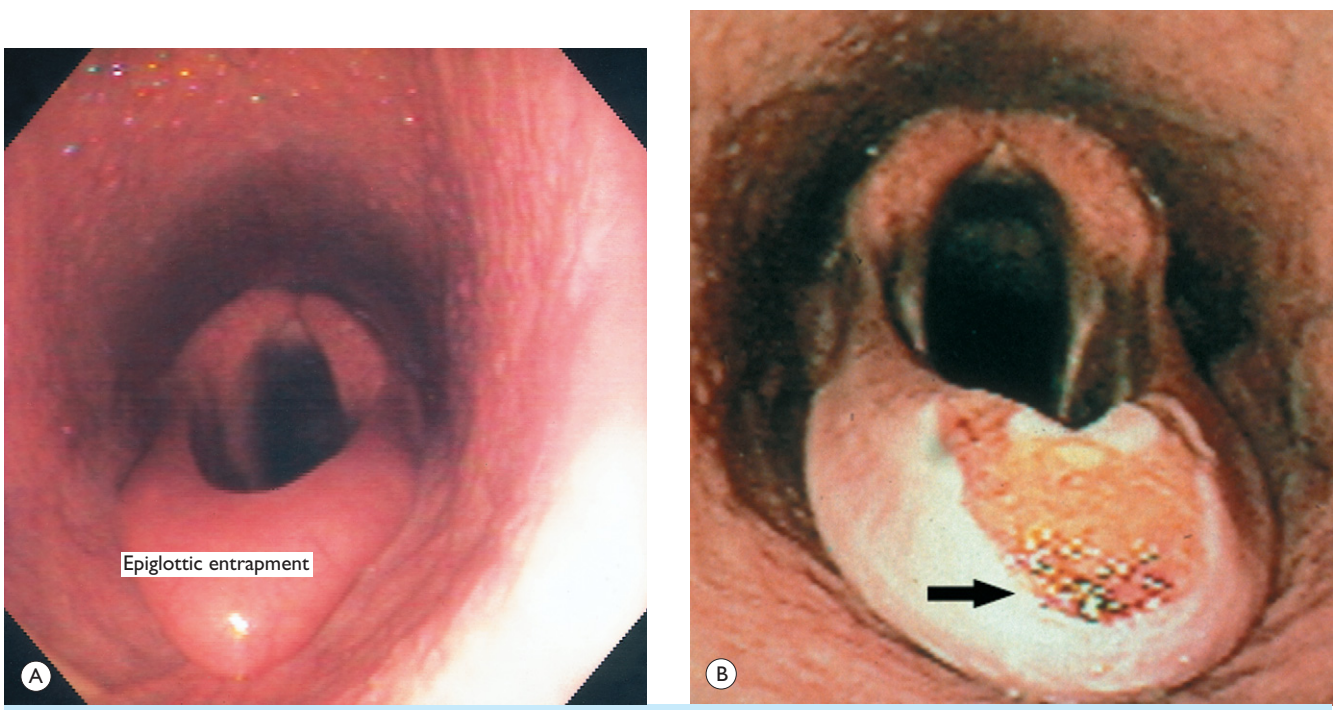


Fig. 27.15
(A) Endoscopic image of the larynx of a horse with epiglottic entrapment. Notice that the epiglottis is encased in the aryepiglottic membrane such that the vascular pattern on the dorsal surface of the epiglottis and the serrated margin of the epiglottis is not visible. (B) Endoscopic image of the larynx of a horse with an epiglottic entrapment. Notice the ulcerated area (arrow) of the entrapping aryepiglottic tissue.

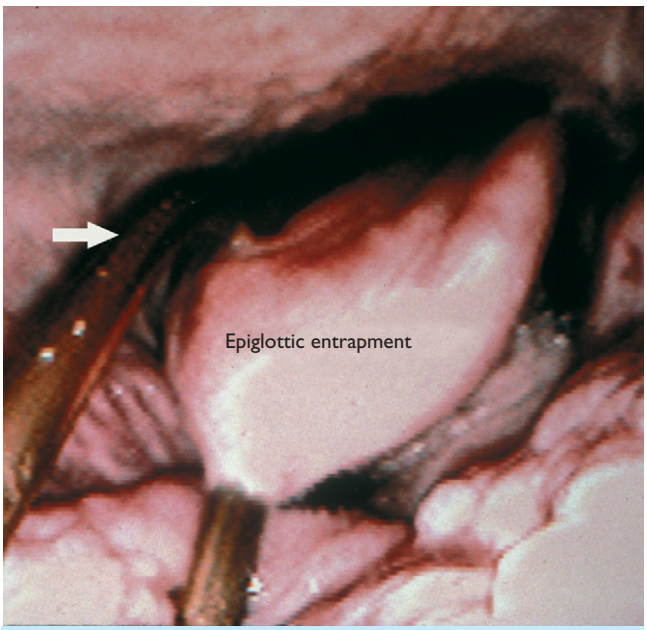


Fig. 27.16
Endoscopic image through the mouth of a horse where an entrapping aryepiglottic membrane is being excised using a hooked bistoury (arrow) with the horse under general anesthesia.

through the nose in standing horses if the horse swallows or moves. Such complications can be career or life ending. The entrapping membrane can also be divided by use of the Nd:YAG laser in standing, sedated horses.[55] Following axial division of the aryepiglottic membrane, topical and systemic anti-inflammatory therapy are recommended in an attempt to prevent re-entrapment of the epiglottis. A topical anti-inflammatory solution (furacin, dexamethasone, DMSO, glycerin) can be sprayed into the throat twice daily using an infusion pipette and judicious use of oral phenylbutazone or flunixin meglumine is recommended for 7 to 10 days. If the aryepiglottic membrane is ulcerated and swollen, the membrane can be resected through a laryngotomy incision, following general anesthesia of the horse.[53]

Prognosis

Eighty-two percent of horses have a positive outcome following transoral axial division of the aryepiglottic tissue; 5–10% of horses have recurrence of the entrapment after surgery, and 10–15% of horses develop dorsal displacement of the soft palate following correction of epiglottic entrapment.[53,55] The prognosis for a positive outcome following resection of the aryepiglottic tissue through a laryngotomy incision is 27%. The large discrepancy in outcome compared to horses with simple axial division may be due to the severity of the ulceration of aryepiglottic tissue and possible epiglottic deformity or chondritis of the epiglottic cartilage that may develop secondary to the entrapment.

Prevention

There is no known preventive measure.

Etiology and pathophysiology

Etiology

The etiology is unknown.

Pathophysiology

Aryepiglottic tissue is areolar, mucous membrane that attaches along the free margin of the epiglottis and continues between the lateral edges of the epiglottis to the corniculate processes of the arytenoid cartilages. This mucous membrane is somewhat redundant along the ventral surface of the epiglottis. The manner by which the entrapment occurs is unknown, but it may be precipitated by airway inflammation and specifically inflammation of the aryepiglottic tissue. It has been suggested that horses with epiglottic hypoplasia, diagnosed by use of endoscopy or radiographic measurement of the thyroepiglottic length, are predisposed to epiglottic entrapment.[49] Standardbred and Thoroughbred horses with epiglottic entrapment have a shorter epiglottis than do horses of the same breed without entrapment.[49]

Epidemiology

Between 0.74 and 2.1% of race horses have epiglottic entrapment.[52,56] As many as 8% of horses with a complaint of upper airway obstruction have epiglottic entrapment.[57]

Epiglottic retroversion

- Epiglottic retroversion is a rare cause of exercise intolerance and abnormal respiratory noise in horses.
- Epiglottic retroversion is diagnosed during treadmill examination with the horse running on a treadmill.
- When the epiglottis retroverts, it prolapses through the rima glottidis, causing airway obstruction.
- Epiglottic retroversion is probably due to damage to the hyoepiglotticus or geniohyoideus muscle, or branches of the hypoglossal nerve.

Recognition

History and presenting complaint

Epiglottic retroversion is a rare condition that causes abnormal respiratory noise during exercise and exercise intolerance.[58,59]

Physical examination

The physical examination is normal.

Special examination

Epiglottic retroversion is diagnosed during treadmill endoscopic examination.[58,59] At rest, the nasopharynx and larynx of af-

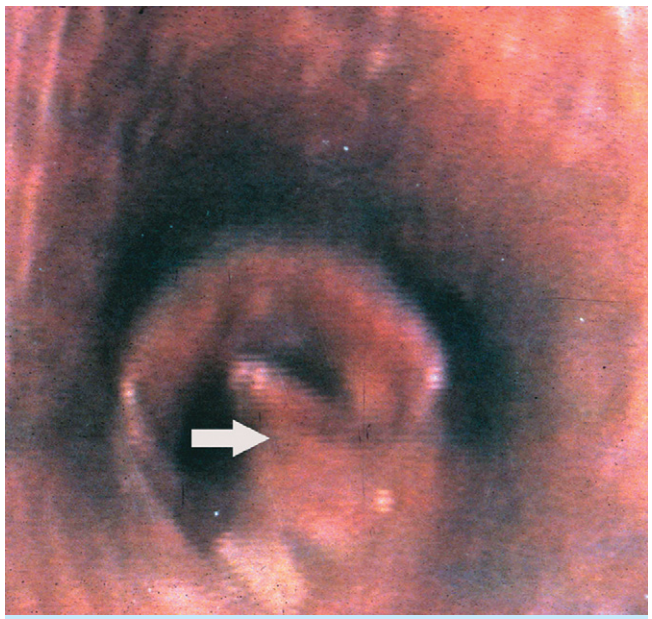


Fig. 27.17
Endoscopic image of the larynx of a horse running on a treadmill. Notice that the epiglottis (arrow) is retroverted through the rima glottidis, exposing the ventral surface of the epiglottis.

fected horses is normal during endoscopic examination. During treadmill endoscopy, the epiglottis lifts dorsally off of the soft palate during inspiration such that the ventral surface of the epiglottis faces rostrally and is readily seen on endoscopic examination. As airflows increase as treadmill speed increases, the epiglottis retroverts through the rima glottidis, such that the ventral surface of the epiglottis is seen (Fig. 27.17). Epiglottic retroversion causes dynamic airway obstruction in affected horses (Table 27.1).

Laboratory examination

Laboratory examination is normal; though none is usually indicated.

Diagnostic confirmation

Differential diagnosis of epiglottic retroversion includes those diseases that cause abnormal respiratory noise during exercise and exercise intolerance (Table 27.1). The diagnosis of epiglottic retroversion is definitively made during treadmill endoscopic examination.

Treatment and prognosis

Therapeutic aims

The goal of treatment is to stabilize the epiglottis and prevent it from obstructing the airway during inspiration.

Therapy

Little is described of treatment for epiglottic retroversion. Treatment of two horses is described, with one horse racing successfully after epiglottic augmentation with polytetrafluoroethylene (Teflon), and another horse showing no improvement.[59]

Prognosis

Prognosis is excellent for life, but guarded for athletic endeavors.[58,59]

Prevention

There are no known preventive measures, though care should be taken when performing surgery ventral to the epiglottis so as not to damage nerve supply or muscles in this area.

Etiology and pathophysiology

Etiology

The cause of epiglottic retroversion is unknown.

Pathophysiology

Epiglottic retroversion has been produced experimentally by bilaterally anesthetizing the hypoglossal nerves and by anesthesia of the geniohyoideus muscle, suggesting that trauma or dysfunction of the hyoepiglotticus or geniohyoideus muscle are implicated in the pathogenesis of epiglottic retroversion.[60]

Epidemiology

Because so few cases have been reported, the epidemiology of this disease is unknown.

Subepiglottic cyst

Recognition

History and presenting complaint

Coughing, abnormal respiratory noise, and exercise intolerance are clinical signs of subepiglottic cyst in mature horses. Dysphagia may occur in younger horses or horses with a very large cyst.[58]

Physical examination

Physical examination is usually normal. If the horse is dysphagic, coughing and aspiration pneumonia may be evident.

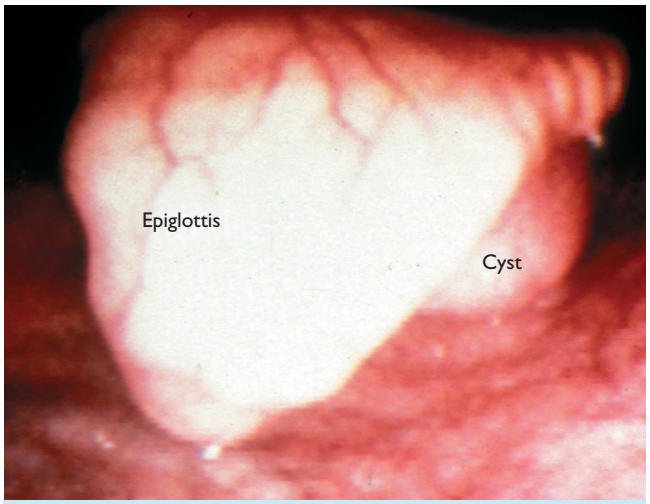


Fig. 27.18
Endoscopic image of the epiglottis of a horse with a subepiglottic cyst.

Special examination

Endoscopic examination of the larynx and nasopharynx is generally diagnostic for subepiglottic cyst (Fig. 27.18) The cyst is round, pale pink to red, covered with mucosa, and generally seen beneath the epiglottis. Occasionally, the cyst can only be seen in the nasopharynx during swallowing or intermittently during exercise, and remains beneath the soft palate in the oropharynx.

Laboratory examination

None is indicated unless there is a suspicion of aspiration pneumonia.

Diagnostic confirmation

Endoscopic examination is diagnostic for subepiglottic cyst. Following resection, the cyst can be submitted for histopathologic analysis if there is any concern that the cyst may instead be a neoplastic mass.

Treatment and prognosis

Therapeutic aims

The goal of treatment is removal of the cyst.

Therapy

Subepiglottic cysts can be excised through a laryngotomy incision with the horse in dorsal recumbency under general anesthesia.[58] The cyst is positioned beneath the laryngotomy incision by retroverting the epiglottis. The aryepiglottic mucosa is incised and the cyst is dissected free and removed. The incision in the aryepiglottic tissue is allowed to heal by second intention. Alternatively, the cyst can be excised along with the overlying mucosa by application of a snare device made with obstetrical wire threaded through an infusion pipette in an anesthetized horse.[58] Care must be taken to remove the entire cyst and minimal amount of aryepiglottic tissue. Subepiglottic cysts can also be excised using an Nd:YAG or diode laser in standing, sedated horses or horses under general anesthesia.[58]

Prognosis

The prognosis for return to function and resolution of coughing is good to excellent. Recurrence is rare, unless the entire cyst is not removed.

Prevention

There is no known preventive measure.

Etiology and pathophysiology

Etiology

Subepiglottic cysts may be either acquired, especially in older horses, or congenital in foals. The cysts may develop from remnants of thyroglossal ducts, but this has not been substantiated.

Pathophysiology

Airway obstruction and abnormal respiratory noise result from the cyst flipping dorsally across the rima glottidis, causing airway obstruction.

Epidemiology

Subepiglottic cysts are most frequently diagnosed in young racing horses, both Standardbreds and Thoroughbreds, but have been identified in foals and older horses. There is no known breed predisposition.[58]

Axial deviation of the aryepiglottic folds

- Axial deviation of the aryepiglottic folds has been diagnosed in racing Thoroughbreds, Standardbreds, and Arabians.[61]
- This disease is probably associated with racing because of the high speeds at which the horses perform.
- Diagnosis of axial deviation of the aryepiglottic folds is made during endoscopic examination of the horse running on a treadmill.
- Treatment includes rest and anti-inflammatory therapy or surgical removal of the aryepiglottic folds.

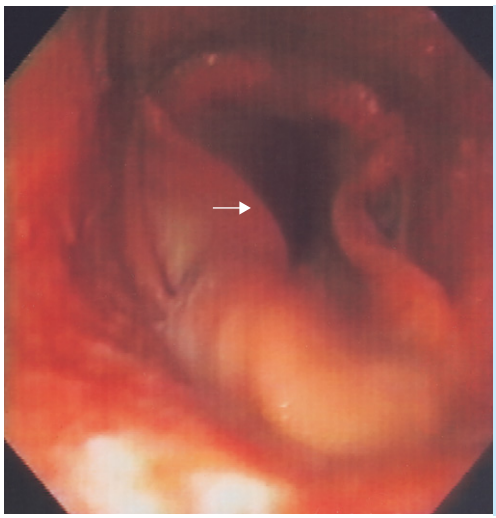


Fig. 27.19 Endoscopic image of the larynx of a horse with aryepiglottic fold collapse (arrow). This image was taken while the horse was running on the treadmill.

Recognition

History and presenting complaint

Horses with axial deviation of the aryepiglottic folds are exercise intolerant and make an abnormal respiratory noise during exercise.[61]

Physical examination

Physical examination is normal.

Special examination

Axial deviation of the aryepiglottic folds is only diagnosed during endoscopic examination of horses running on a treadmill (Fig. 27.19). During intense exercise, the aryepiglottic tissue that connects the corniculate portions of the arytenoid cartilages to the lateral edge of the epiglottis collapses axially across the rima glottidis during inspiration.[61]

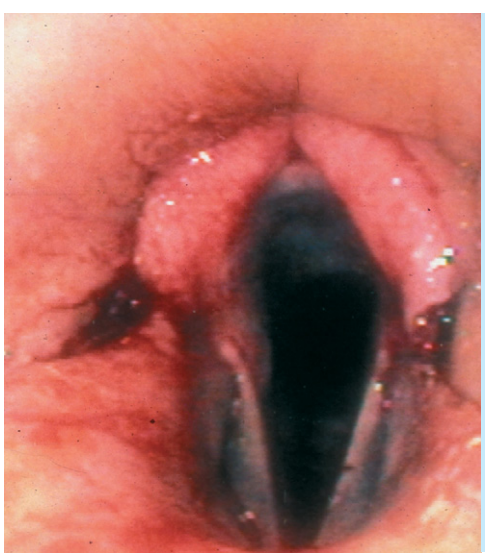


Fig. 27.20 Endoscopic image of the larynx of a horse following resection of the aryepiglottic folds.

The obstruction is dynamic and worsens as exercise intensity increases.

Laboratory examination

Laboratory examination is normal; none is usually indicated.

Diagnostic confirmation

Differential diagnosis of axial deviation of the aryepiglottic folds includes dynamic obstructive upper airway diseases that cause abnormal respiratory noise and exercise intolerance. The definitive diagnosis of axial deviation of the aryepiglottic folds is made during endoscopic examination with the horse running on a treadmill.[61]

Treatment and prognosis

Therapeutic aims

The goal of treatment is to alleviate the dynamic airway obstruction by stabilizing the aryepiglottic folds.

Therapy

Treatment for axial deviation of the aryepiglottic folds includes surgical resection of the aryepiglottic tissue between the lateral edge of the epiglottis and the corniculate processes of the arytenoid cartilages (Fig. 27.20). This can be accomplished using an Nd:YAG or diode laser, with the horse sedated and standing or under general anesthesia.[61] Alternatively, horses can be rested and treated with topical anti-inflammatory throat spray and systemic anti-inflammatory medication.[61]

Prognosis

Seventy-five percent of horses that had surgery and 50% of horses that were rested had objective improvement in performance.[61]

Prevention

There is no known method of prevention.

Etiology and pathophysiology

Etiology

The cause of this condition is unknown.

Pathophysiology

The aryepiglottic tissue that attaches the lateral aspect of the corniculate process of the arytenoid cartilage to the lateral edge of the epiglottis collapses dynamically across the rima glottidis during intense exercise, resulting in inspiratory airway obstruction.

Epidemiology

Axial deviation of the aryepiglottic folds has been diagnosed in racing Thoroughbreds, Standardbreds, and Arabians.[61] This disease is likely associated with racing because of the high speeds at which the horses perform.

Epiglottitis

- Epiglottis is inflammation of the epiglottic mucosa, and at times, the tip of the epiglottic cartilage.
- Treatment includes rest and systemic and topical anti-inflammatory therapy.
- Complications of epiglottitis include epiglottic entrapment and deformity of the epiglottic cartilage.
- The prognosis for return to athletic endeavors following epiglottitis is excellent.

Recognition

History and presenting complaint

Most horses have a history of exercise intolerance, abnormal respiratory noise during exercise, and coughing. Occasionally, horses have evidence of airway obstruction at rest, dysphagia, and anorexia.[62]

Physical examination

Generally, physical examination is normal, unless the horse is dysphagic or coughing. Coughing can be easily elicited by laryngeal palpation. Dysphagic horses may have clinical signs of aspiration pneumonia or rhinitis.[62]

Special examination

Epiglottitis is diagnosed by endoscopic examination of the horse's larynx at rest. The epiglottis is swollen and dark pink to purple. The mucosa on the surface of the epiglottis and the aryepiglottic tissue beneath the epiglottis is frequently swollen and may be ulcerated. Frequently, the tip of the epiglottic cartilage is visible and may be surrounded by granulation tissue.[62]

Laboratory examination

Complete blood count and serum chemistry values are usually normal.

Diagnostic confirmation

Differential diagnosis of epiglottitis includes epiglottic entrapment, subepiglottic cyst and other dynamic airway diseases that cause exercise intolerance, abnormal respiratory noise during exercise, and coughing.

Treatment and prognosis

Therapeutic aims

The goal of treatment is to resolve inflammation of the epiglottis.

Therapy

Horses should be rested for a minimum of 14 days. Topical administration of furacin-DMSO-glycerin-prednisolone solution is applied transnasally twice daily for 10 days to 2 weeks.[62] Systemic anti-inflammatory medication such as phenylbutazone, flunixin meglumine, or dexamethasone is recommended for 10 to 14 days. If aspiration pneumonia is suspected, broad-spectrum antimicrobial therapy is recommended.[62] Endoscopic examination of the airway should be repeated in 2 weeks.

Prognosis

Prognosis for return to performance is excellent. Complications resulting from epiglottitis occur in approximately 28% of cases and include epiglottic deformity, which can occur if the epiglottic cartilage is exposed and chondritis occurs.[62] Also, epiglottic entrapment can occur following epiglottitis due to the subepiglottic inflammation.[62]

Prevention

There is no known prevention.

Etiology and pathophysiology

Etiology

The etiology of epiglottitis is unknown, though speculative causes include trauma due to poor quality hay, dorsal displacement of the soft palate, and the presence of a foreign body, respiratory tract infection, and allergic reaction.

Pathophysiology

Respiratory noise and dysphagia are caused by swelling of the epiglottis with subsequent partial occlusion of the airway and abnormal function of the epiglottis.

Epidemiology

Epiglottitis is diagnosed frequently in race horses but has been seen in older brood mares.[62]

Laryngeal hemiplegia

- Laryngeal hemiplegia almost always affects the left side of the larynx and its cause is unknown.

- Laryngeal hemiplegia is frequently diagnosed during endoscopic examination of the larynx at rest, but treadmill endoscopy may be required.
- Horses with laryngeal hemiplegia may cough due to aspiration of food material because the laryngeal adductor function is compromised.
- The current surgical therapy of choice includes laryngoplasty with ventriculocordectomy.

Idiopathic laryngeal hemiplegia (ILH) has been recognized in horses for several centuries. Much of the information about this disease was obtained from anatomic and histopathologic studies as well as dynamic and airway mechanics studies during exercise. Despite what is known, there remains a great deal of speculation and controversy concerning the etiology of ILH and the diagnosis and treatment of horses affected with this disease.

Recognition

History and presenting complaint

Horses with ILH or 'roarers' have a history of making an inspiratory noise during exercise and/or poor performance. The term 'roaring' describes an unnatural sound 'rattling, snoring, and whistling' during inspiration.[63] The noise is heard only during exercise, immediately after exercise during hyperpnea, or when the horse is startled (grunt test). These horses also have abnormal vocalization. Many horses are unaffected until 5–6 years of age such that a history of normal breathing during exercise followed by progressively more noisy breathing is often reported. The noise starts as a hoarse whistling which increases to a louder roaring as exercise intensity increases and the condition progresses. Exercise intolerance experienced by horses with ILH is associated with decreased ventilation due to laryngeal collapse.[64,65] The degree of impairment reflects a combination of factors such as degree of laryngeal collapse, athletic capacity, and the length and intensity of competition. Horses performing lower levels of work, such as show hunters and trail horses, may not experience exercise intolerance. The presence of the inspiratory noise during exercise may be the major complaint for this group of horses.

Physical examination

A thorough examination may help to identify the causes of the disease, though the majority of cases of laryngeal hemiplegia are idiopathic. The throat area is visually inspected for signs of trauma or deformity. Horner's syndrome can accompany laryngeal hemiplegia that results from perivascular injection of caustic substances or trauma involving the jugular furrow, due to the close proximity of the jugular vein, recurrent laryngeal nerve, and sympathetic trunk. Horner's syndrome is recognized based upon clinical signs of unilateral ptosis, miosis, dropped eyelid and sweating near the base of the ear, due to loss of sympathetic innervation. An important characteristic of Horner's syndrome is dilation of the vascular bed of the ipsilateral nasal cavity. Sympathetic nerve damage causes the horse to lose its ability to constrict the nasal vascular bed leading to reduced airflow that can be detected manually.

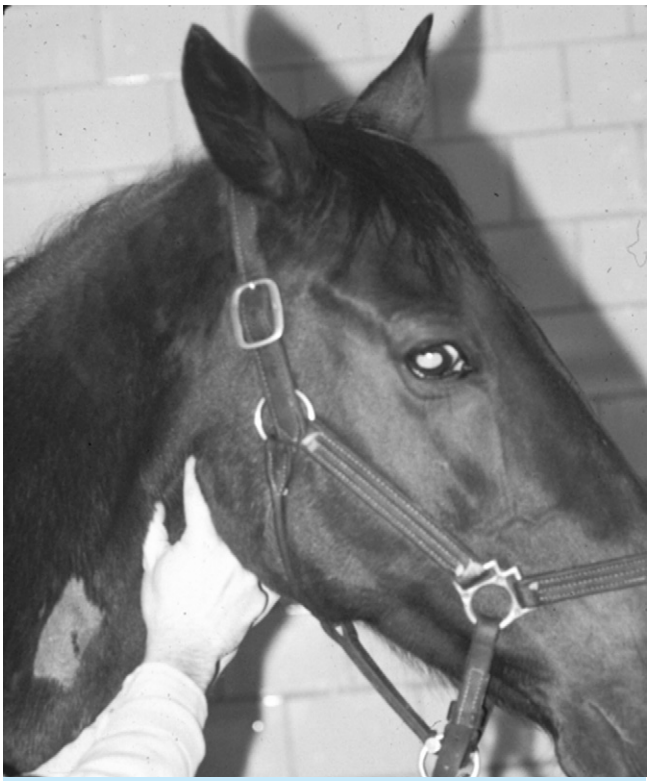


Fig. 27.21
Illustration of laryngeal palpation technique.

The larynx is palpated for evidence of atrophy of the cricoarytenoid dorsalis muscle. This is best done by standing at the shoulder of the horse and using the index fingers to palpate the dorsal aspect of the cricoid cartilage for symmetry (Fig. 27.21), then moving one finger to the muscular process and determining again the symmetry between the left and right side. If the cricoid and/or muscular processes of the arytenoid cartilage are more prominent on one side (usually the left), atrophy of the cricoarytenoid dorsalis muscle and ILH is suspected. This test is somewhat crude, and those inexperienced at palpating this area may find it inaccurate.

Historically, the absence of arytenoid cartilage adductor movement can be identified by the thoracolaryngeal reflex ('slap test').[66] While standing on the left side of the horse, one could place two to three fingers of the left hand on the lateral aspect of the larynx, and using the right hand, slap the wither area. A positive slap test will elicit a contraction of the adductor muscles and a 'twitching' can be felt over the side of the larynx. The procedure is then reproduced on the contralateral side. This test can also be performed during endoscopic examination of the larynx, but the slap test has a poor correlation with laryngeal function.[66]

Listening to the abnormal respiratory sounds that the horse makes during exercise can be helpful in the diagnosis of the ILH. Horses with ILH tend to make a 'grunt' sound and/or a hoarse whistling noise during inspiration. Occasionally ILH

is followed by dorsal displacement of the soft palate so open mouth breathing and a 'gurgling noise' is heard, but this is rare.

Special examination

The diagnosis of ILH is made by endoscopic examination of the larynx at rest, although in a proportion of horses, treadmill videoendoscopy is necessary to confirm the diagnosis. Alternatively, the horse's larynx can be assessed endoscopically immediately after cessation of exercise, though this type of examination is not as specific as treadmill endoscopy. Endoscopic examination permits assessment of the laryngeal anatomy as well as function. Laryngeal function, including adduction and abduction of the corniculate processes of the arytenoid cartilages and vocal folds, can be assessed during nasal occlusion and after swallowing. The ability of the arytenoid cartilages to abduct normally is critically assessed to determine signs of idiopathic laryngeal hemiplegia/hemiparesis. At least 40% of Thoroughbred and other large breed horses have movements of the laryngeal cartilages that are not consistently symmetrical or synchronous. Terms such as 'weak', 'paretic', 'partially paralyzed', 'flutter', and 'hesitation' have been applied to the arytenoid function of these horses. These variations in arytenoid movements are classified in unsedated horses at rest using the grading system (Table 27.2).[67] During exercise, the laryngeal grade can also be classified (Fig. 27.22). The results of studies correlating the grade of laryngeal function at rest with function during exercise suggest that horses with resting grade I or II laryngeal function have full arytenoid abduction at exercise and are normal. Approximately 75% of grade III horses have partial or complete collapse during exercise.[68,69] All horses with resting grade IV laryngeal function have significant collapse of the left hemilarynx during treadmill exercise (Fig. 27.23).[68,69] Therefore, the asynchrony of arytenoid cartilage movement is inconsequential and should not be used as the basis for diagnosis of laryngeal dysfunction or surgical intervention. The diagnosis of idiopathic

Table 27.2 Laryngeal grading system for horses examined at rest

Laryngeal grade	Description
I	Synchronous full abduction of both arytenoid cartilages during inspiration or breath holding or after swallowing
II	Asynchronous full abduction of the left arytenoid cartilage (hesitation, flutter or delay) can be achieved and maintained during inspiration or breath holding or after swallowing
III	Asynchronous abduction of the left arytenoid cartilage (hesitation, flutter or delay). Substantial movement is present but full abduction cannot be achieved and maintained during inspiration or breath holding or after swallowing
IV	No appreciable abduction of left arytenoid cartilage

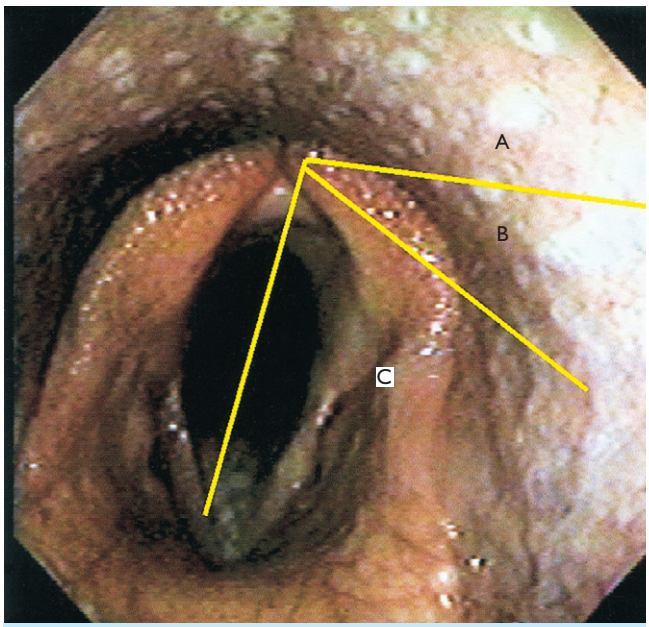


Fig. 27.22
Endoscopic image of a larynx showing the position of the corniculate process of the arytenoids cartilage for each grade of laryngeal position. Zone A represents the position (maximal abduction) for grades I and II; Zone B represents the position for grade III (partial abduction); Zone C represents the position for grade IV laryngeal hemiplegia, or complete paralysis with no abduction.

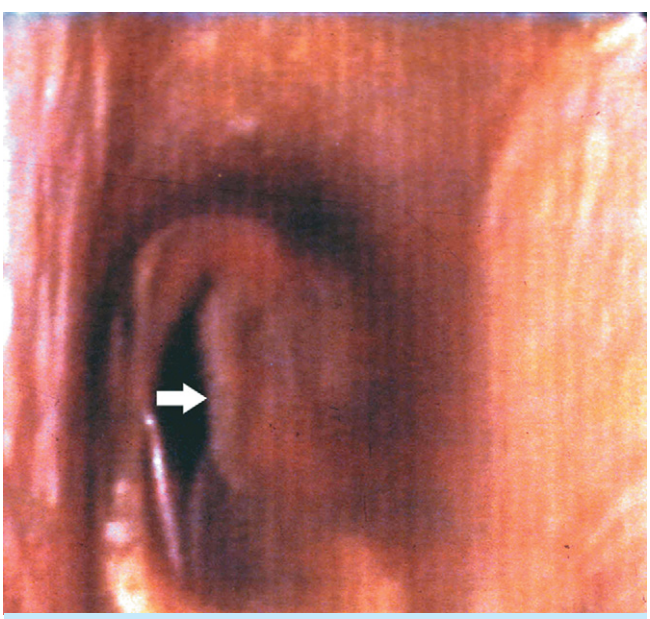


Fig. 27.23
Endoscopic image of the larynx of a horse with grade IV idiopathic laryngeal hemiplegia while the horse is running on the treadmill. Notice how the left arytenoid collapses across the rima glottidis (arrow).

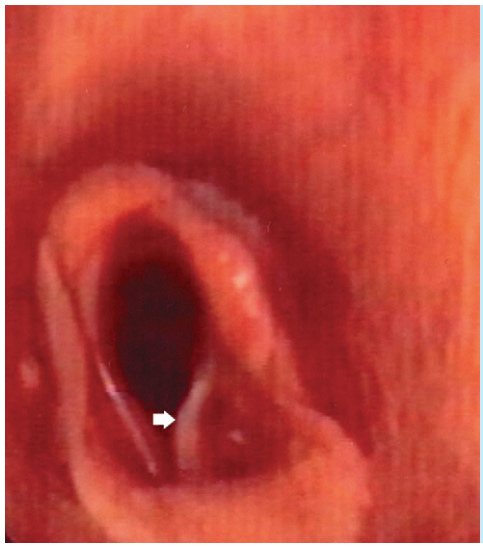
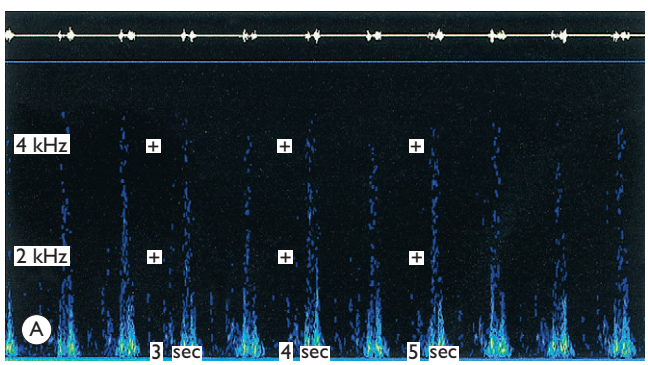


Fig. 27.24 Endoscopic image of the larynx of a horse with grade III idiopathic laryngeal hemiplegia and vocal fold collapse. Notice how the left vocal fold collapses across the rima glottidis (arrow).



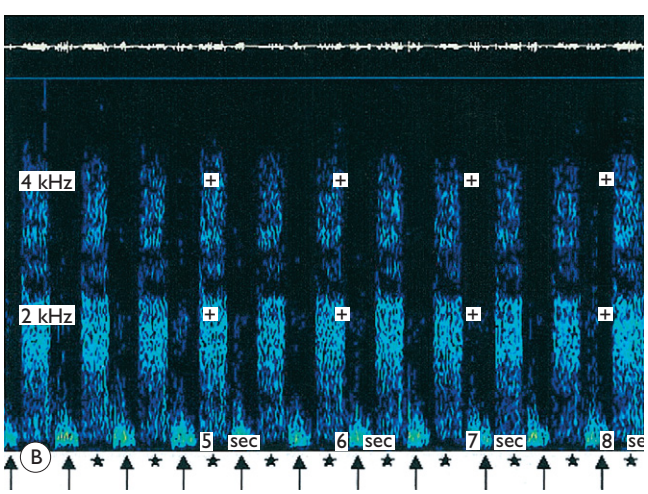


Fig. 27.25
(A) Spectrogram of respiratory sounds from a horse with normal upper airway function. Time is on the abscissa, frequency on the ordinate. Sound level increases with brightness of the color (black indicates no sound). Inspiration is indicated by a star, expiration by an arrow. The top line of the graph is sound pressure level, a measure of sound intensity. (B) Spectrogram of respiratory sounds for a horse with laryngeal hemiplegia. Notice the formants of inspiratory noise centered at 0.3, 1.6, and 3.8 kHz.

laryngeal hemiplegia is made based upon the inability of the horse to abduct the arytenoid cartilages and maintain abduction during exercise.

Treadmill endoscopic examination is useful in horses with grade III ILH because the degree of arytenoid abduction can be assessed and the optimum treatment prescribed. Horses with partial arytenoid collapse during exercise often have the same or better degree of arytenoid abduction than that obtained after a laryngoplasty.[70] These horses frequently have vocal cord collapse (Fig. 27.24), obstructing the ventral aspect of the rima glottidis, with little collapse of the arytenoid cartilage. Therefore, sacculectomy or vocal cordectomy, or ventriculocordectomy, rather that laryngoplasty, might more accurately alleviate the obstruction.

Sound analysis can be helpful in the diagnosis of laryngeal hemiplegia.[24,71] Joint time-frequency analysis of airway sounds during exercise may help quantitate the upper airway sounds of horses such that ILH can be diagnosed during exercise without access to videoendoscopy. From sounds recorded during exercise, laryngeal hemiplegia is identified by the presence of sound throughout inhalation and exhalation and the presence of three frequency bands centered on 0.3 kHz, 1.6 kHz and 3.8 kHz are seen during inhalation (Fig. 27.25A, B).[24]

In the laboratory, airway mechanics can be measured, accurately assessing the degree of laryngeal function and dysfunction.[64,65,72] In addition, blood gas measurements can help to determine the degree of ventilation compromise caused by laryngeal hemiplegia.[65] Typically, horses with laryngeal hemiplegia develop worsening exercise-induced hypoxemia (Pao_2 = 53 torr) and hypercapnia ($Paco_2$ = 53 torr) compared with control values (Pao_2 = 69 torr and $Paco_2$ = 44 torr).[65]

Electrodiagnostic testing of the thoracolaryngeal reflex latency and velocity has been shown to have no correlation with endoscopic examination, and therefore, is not useful in the assessment of laryngeal function.[6]

Treatment and prognosis

Therapeutic aims

The goal of therapy is to restore the diameter of the rima glottidis and to prevent dynamic collapse of the vocal cord and arytenoid cartilage during inspiration, minimizing resistance to airflow. The problem resides in the fact that the larynx has both digestive and respiratory functions. The arytenoid cartilage must fully abduct (larynx must be fully dilated) during strenuous exercise and fully adducted (larynx must fully close) during swallowing. Therefore, treatments aimed at permanently increasing the diameter of the rima glottidis tend to interfere with laryngeal adduction during swallowing and protection of the airway.

Therapy

The treatment of laryngeal hemiplegia was first described by Günther in 1866. He evaluated the effects of various types of arytenoidectomy and ventriculectomy.[63] These treatments

were failures, probably due to surgical techniques that were state-of-the-art at the time. In 1907, Williams introduced the ventriculectomy.[73] This treatment was later modified by Sir Hobday who improved the technique by creating a laryngotomy that did not invade (incise) the thyroid and/or cricoid cartilage and performed the ventriculectomy bilaterally.[73] Quinlan and Morton (1957) further modified the technique by adding the cordectomy to the procedure.[74] The current laryngoplasty technique was first described in 1970.[75] Although some minor variations in the surgical technique have been developed since its original description, the basic principle remains the same. Specifically, one or two prosthetic sutures are placed between the caudodorsal aspect of the cricoid cartilage and the muscular process of the arytenoid cartilage, mimicking the action of the dorsal cricoarytenoid muscle. Various types of arytenoidectomies, both partial and subtotal arytenoidectomy, were introduced in the early 1980s.[76] Partial arytenoidectomy, or removal of all parts of the arytenoid cartilage except the muscular process, achieves the best mechanical result, optimizing the area of the rima glottidis.[76,77] The neuromuscular pedicle graft procedure is the most recent surgical treatment for ILH and is performed by grafting neuromuscular bundles composed of the first cervical nerve and omohyoideus muscle to the atrophied cricoarytenoideus dorsalis muscle or by anastomosing branches of the first cervical nerve to the abductor branch of the left recurrent laryngeal nerve.[78,79] The omohyoideus muscle is a secondary muscle of respiration and contracts during intensive breathing efforts. Therefore, following these procedures, there is no change in laryngeal function or the aperture of the rima glottidis at rest, which minimizes aspiration, but first cervical nerve and omohyoideus muscle activity during intense exercise causes arytenoids abduction.[78,79]

The value of surgical therapy for ILH depends on whether the complaint is exercise intolerance, noise production, or both. Ventriculochordectomy is effective in reducing airway noise and stabilizing the arytenoid cartilage during exercise, but does not improve airway mechanics in horses with ILH as well as other surgical procedures.[64,80,81] Therefore, ventriculocordectomy is the recommended surgical therapy of choice for horses with ILH that produce an abnormal airway noise during exercise, while performing at low intensity.[73,81] Also, ventriculocordectomy or cordectomy is the surgical treatment of choice for horses with vocal fold collapse.

Laryngoplasty or laryngeal prosthesis is the current standard surgical treatment for horses with grade IV laryngeal hemiplegia. Laryngoplasty reduces the high inspiratory upper airway impedance measured in horses with experimentally induced left laryngeal hemiplegia.[64,72,80] The value of adding the ventriculectomy and ventriculocordectomy to further improve the size of the rima glottidis after laryngoplasty is controversial. Ventriculocordectomy or ventriculectomy improves the size of the rima glottidis and, therefore, is routinely performed in addition to laryngoplasty.[82–85] However, ventriculectomy or ventriculocordectomy with laryngoplasty yields no improvement in airway mechanics compared with laryngoplasty alone as evaluated with airway impedance measurement or flow-volume loop analysis in horses with experimentally created ILH.[64] Ventriculocordectomy with laryngoplasty does improve ventilation compared with laryngoplasty alone based upon blood gas measurements.[86] However, the controversial addition of ventriculocordectomy or ventriculectomy to the laryngoplasty procedure as surgical therapy for horses with grade IV ILH may be resolved as follows. First, airway impedance measurements and flow-volume loop analysis suggest that airway function is normal following laryngoplasty. However, clearly the size of the rima glottidis of a horse with grade IV ILH following laryngoplasty is smaller than the rima glottidis of a normal horse. In fact, in the clinical population of horses with grade IV ILH and laryngoplasty, the left arytenoid cartilage is rarely in a maximally abducted position.[70] Indeed, despite the fact that the majority of horses have the arytenoid cartilage abducted to approximately 80% of maximal abduction immediately after surgery, 6 weeks later that degree of abduction decreases to just above the resting position.[70] The rima glottidis is not restored to normal size after surgery yet airway mechanics are comparable to those measured in normal horses, suggesting that upper airway mechanics testing is relatively insensitive to small changes in function that may, indeed, lead to larger changes in performance. This is consistent with the results in the clinical population of horses where successful performance is restored by laryngoplasty and ventriculocordectomy, but at a lower level. In addition, a population of horses with laryngeal hemiplegia treated with laryngoplasty alone later develop dynamic collapse of the vocal folds, which may occur because of the relaxation of the laryngoplasty and paramedian position of the corniculate process of the arytenoid cartilage.

Partial arytenoidectomy is performed in some horses for treatment of ILH but these horses fail to return to their previous level of competition.[87] Furthermore, although airway mechanics measurements are improved following partial arytenoidectomy, impedance values are significantly higher than those of horses treated with laryngoplasty or those of normal horses.[88]

Laryngeal reinnervation returns upper airway mechanics during exercise to normal, but the time required for successful reinnervation is 9 to 12 months.[78] Therefore, this procedure is generally reserved for yearlings or performance horses other than race horses.[78]

The current treatment of choice for horses with grade IV laryngeal hemiplegia is the placement of a laryngeal prosthesis, or laryngoplasty and a ventriculocordectomy.

Prognosis

The clinical results of treatment of laryngeal hemiplegia with collapse of the upper airway (grade III and IV) are highly dependent on the activity of the horse. Horses used for show and jumping have a 90% chance of returning to their same level of function, while the prognosis is worse for race horses, approximately 60–70%.[70,82,85] Age at which the race horse had a laryngoplasty performed may affect prognosis. Two-

year-old horses respond less favorably to surgery than do older horses.[83–85] It is likely that the difference is due to the unknown level of performance in untested 2-year-old race horses, where approximately 30% of the population reaches the racetrack during the fall of their 2nd year.

Complications of the laryngoplasty include (1) continued exercise intolerance and respiratory noise in 30 to 40% of horses during exercise, (2) chronic coughing due to abduction of the left arytenoid cartilage and the resulting inability of the larynx to protect the trachea from aspiration of ingesta in 20 to 40% of horses, and (3) loosening of the prosthetic suture(s) and loss of an initial degree of abduction in approximately 10% of horses.[77,82–85]

Etiology and pathophysiology

Anatomical considerations

The recurrent laryngeal nerve exits the caudal brainstem as part of the vagus nerve (cranial nerve X) and descends along the trachea dorsal to the common carotid artery with a different course between the left and right recurrent laryngeal nerves. The right recurrent laryngeal nerve leaves the vagus nerve at the level of the second rib turning around the costocervical trunk before ascending toward the larynx. The left recurrent laryngeal nerve leaves the vagus nerve as the latter crosses the aortic arch. The left recurrent laryngeal nerve then runs around the concavity of the aortic arch before ascending toward the larynx. Both recurrent laryngeal nerves ascend cranially, ventral to the common carotid artery, to innervate all intrinsic muscles of the larynx except for the cricothyroid muscles, which are innervated by the ipsilateral external branch of the cranial laryngeal nerve.

The nerve cell bodies of the neurons of the recurrent laryngeal component of the recurrent laryngeal nerves were recently mapped in horses.[89] They were found to be in similar locations in the nucleus ambiguus as in small laboratory species.[89] This new information may allow more precise evaluation of the status of the nucleus ambiguus in horses affected with ILH. The microscopic appearance of the peripheral nerve has been well described.[90,91] At the proximal aspect of the recurrent laryngeal nerve, there are large myelinated axons that innervate the intrinsic laryngeal muscles and cervical esophagus. There are also a large number of unmyelinated axons arranged in large fascicles that are either sensory or postganglionic autonomic fibers. Mostly large myelinated axons with a few unmyelinated axons remain at the distal extremity of the nerve.[90,91]

Pathology

Idiopathic laryngeal hemiplegia is a peripheral neuropathy characterized by a distal loss of large myelinated fibers (distal axonopathy) and neurogenic atrophy of the intrinsic laryngeal muscles supplied by the recurrent laryngeal nerve.[90–94] Histologically, sections of the cricoarytenoideus dorsalis muscle exhibit fiber type grouping intermixed with atrophic fibers, suggestive of denervation and reinnervation.[94] Interestingly, there is a preferential atrophy of the adductor muscles in some horses so adductor deficit of the left arytenoid cartilage is observed despite normal abductor function in affected horses.[93] In addition, although the disease affects preferentially the left recurrent laryngeal nerve, there are some mild pathological lesions found in the right recurrent laryngeal nerve and associated right intrinsic laryngeal muscles.

There is not a perfect correlation between nerve and muscle histopathology and clinical disease or the degree of arytenoid dysfunction.[90,91,94] Horses with a clinical laryngeal grade IV (true laryngeal hemiplegia) have marked pathological lesions. Likewise, there is a good clinical correlation between adductor muscle lesions and their loss of adductor function. Many horses have histopathological lesions with no clinical signs of disease.[90,94] Horses with left-sided ILH can have histopathologic evidence of right-sided lesions without right-sided clinical signs. This subclinical disease and its progression are not well understood. The progression from laryngeal grade I to grade IV is variable. Some horses show no progression in their laryngeal grade and stay at laryngeal grade III for years while others progressed over a period of 2 to 4 months from normal to grade IV.[95,96]

Etiology

As indicated by its name, the etiology of ILH is unknown. Anatomically, the course of the left recurrent laryngeal nerve around the aorta, combined with the pathological appearance of the nerve, is suggestive of a compressive lesion, and led to the theory that the aortic pulse against the recurrent laryngeal nerve might be involved in the pathological process. Experimentally, constricting sutures were placed around the recurrent laryngeal nerve and a mixed array of abductor and adductor axons were affected along the course of the nerve, which is quite different that what is seen in the clinical disease.[91,93]

Risk factors for ILH include gender, breed, size, and perhaps genetics. Male horses are over-represented, as are Thoroughbred and draft horses.[97,98] Horses greater than 16 hands have a higher incidence of ILH and the disease is rarely reported in ponies.[97–99] There may also be a genetic basis for ILH.[99]

Additional causes of ILH included perivascular injections with caustic substances, heart base tumors or other thoracic masses, exposure to organophosphates or lead, thiamine deficiency, and guttural pouch infections, and various neurologic diseases such as equine lower motor neuron disease.

Arytenoid chondritis

- Arytenoid chondritis has three clinical presentations that include mucosal ulceration, granulation tissue formation, and cartilage deformity and airway obstruction.
- Clinical signs during exercise mimic those seen in idiopathic laryngeal hemiplegia.

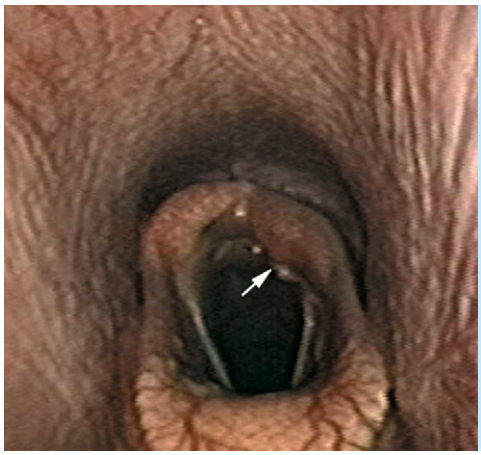


Fig. 27.26 Endoscopic image of the larynx of a horse with 'kissing lesions' on the axial aspect of the mucosa covering the corniculate processes of the arytenoid cartilages (arrow).

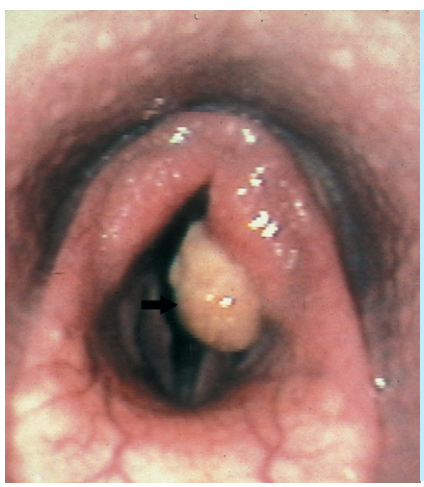


Fig. 27.27 Endoscopic image of the larynx of a horse with arytenoid chondritis. Notice the granulation tissue (arrow) protruding from the left arytenoids.

- Endsocopic examination is diagnostic for arytenoid chondritis.
- Once the arytenoid cartilage is abscessed and deformed, the treatment is surgical arytenoidectomy.

Recognition

History and presenting complaint

Horses affected only with ulcerative lesions of the mucosa on the axial surface of the corniculate processes of the arytenoid cartilages (Fig. 27.26) are generally asymptomatic at rest and during exercise. The lesions are identified during endoscopic examination for reasons unrelated to abnormal airway function. Horses with granulation tissue originating from the arytenoid cartilage and protruding into the lumen of the rima glottidis (Fig. 27.27) or horses with severe arytenoid cartilage abscessation and deformity (Fig. 27.28) have clinical signs of exercise intolerance and upper respiratory noise very similar to horses with laryngeal hemiplegia. If the abscess within the cartilage is large enough, the arytenoid cartilage may be deformed such that it causes severe obstruction of the rima glottidis. Horses with severe airway obstruction due to the deformed, abscessed arytenoid cartilage show signs of respiratory distress such as difficulty breathing or dyspnea and inspiratory wheezing.

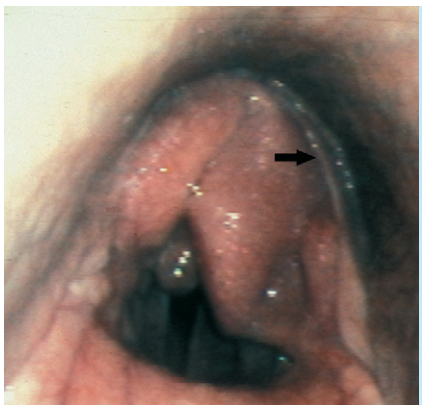


Fig. 27.28 Endoscopic image of the larynx of a horse with severe arytenoid chondritis. Notice the severely deformed left arytenoid cartilage, causing rostral displacement of the palatopharyngeal arch (arrow).

Physical examination

Palpation of the throat and larynx is usually normal. The larynx has a normal contour and asymmetry of the cricoarytenoideus dorsalis muscles is not detected, as in idiopathic laryngeal hemiplegia. Rarely will there be perilaryngeal swelling associated with infection of the arytenoid cartilage. If upper respiratory infection is still present, a horse with ulceration of the mucosa covering the arytenoid cartilage may cough.

Horses that have arytenoid chondritis characterized by granulation tissue formation protruding from the arytenoid cartilage, with or without cartilage deformity, may be exercise intolerant and make an abnormal inspiratory noise during exercise. If the airway obstruction is severe enough to cause airway obstruction at rest, aspiration of feed contents may occur, accompanied by coughing and signs of aspiration pneumonia, though this is rare. Depending upon the severity of respiratory distress, a tracheostomy may be warranted before further diagnostic evaluation is performed.

Special examination

Endoscopic examination of the larynx is frequently diagnostic for arytenoid chondritis. The morphology of the arytenoid cartilages and the integrity of the overlying mucosa should be evaluated, as well as any purulent exudates that may be draining from the cartilage (Fig. 27.29). In addition, it is important to assess the degree of arytenoid movement. If a tracheostomy has been performed, the endoscope can be passed retrograde through the tracheostomy site to further evaluate the morphology of the arytenoid cartilage (Fig. 27.30).

Radiographic examination can also help to identify enlarged or mineralized arytenoid cartilage.

Treatment and prognosis

Therapeutic aims

If mucosal ulceration of the arytenoid cartilage is the only abnormality and the morphology and function of the ary-

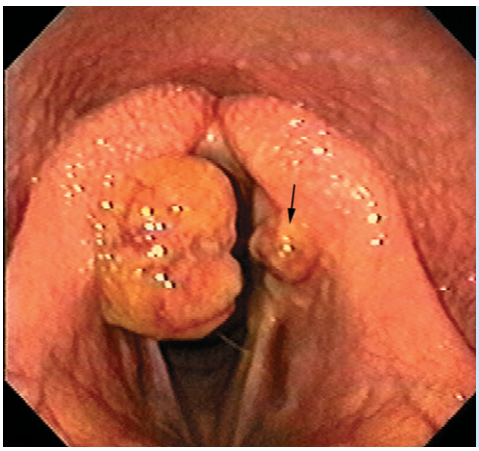


Fig. 27.29 Endoscopic image of the larynx of a horse with arytenoid chondritis. Notice the purulent exudate draining from the abscessed cartilage (arrow).

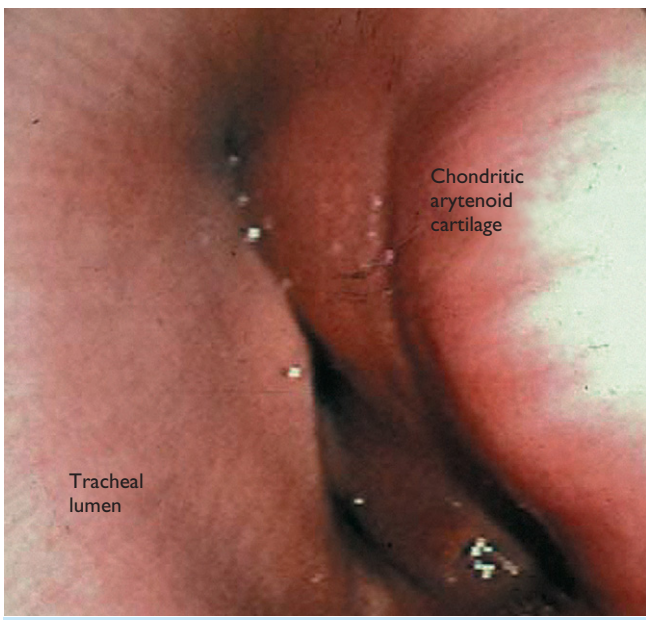


Fig. 27.30 Endoscopic image of the lumen of the larynx of a horse with arytenoid chondritis. Notice the abscessed arytenoid cartilage bulging into the laryngeal lumen. The image was taken by passing the endoscope retrograde, through the tracheotomy site.

tenoids are normal, the goal of treatment is to reduce the local inflammation and prevent bacterial invasion of the arytenoid cartilage. Systemic and topical anti-inflammatory and antimicrobial therapy form the basis of treatment in these cases. Granulation tissue protruding from the arytenoid cartilage is removed sharply or with a laser, and if no abnormality of the arytenoid cartilage or its function is detected, systemic and topical anti-inflammatory and antimicrobial therapy are prescribed.[100] In chronic cases where the arytenoid cartilage is deformed, abscessed, and dysfunctional, the goal of treatment is to restore the diameter of the rima glottidis by surgical removal of the granuloma and the arytenoid cartilage.[101–103]

Therapy

Ulceration of the mucosa covering the arytenoid cartilage is a subclinical finding that is important because the ulcer can serve as an entrance for bacterial invasion into the arytenoid cartilage, potentially leading to abscessation and deformity of the arytenoids.[104] Treatment consists of local therapy with an anti-inflammatory throat spray (glycerin 250 mL, 250 mL DMSO 90% and nitrofurazone 50 mL of a 25 mg/mL solution) applied using a 10-French infant feeding tube placed through the nose to the nasopharynx, 20 cc, twice daily. Systemic antibiotics are prescribed for 3 weeks (trimethoprim sulfa, 15 mg/kg, p.o. q 12 h) and a non-steroidal anti-inflammatory drug (phenylbutazone or flunixin meglumine) for 7–10 days. Endscopic re-evaluation of the larynx should be performed in 3 weeks, with lesions usually healing in 3–6 weeks.

Protruding buds of granulation tissue with normal arytenoid cartilage abduction are treated with surgical resection of the lesion and medical treatment of the resulting mucosal defect as described above. Endoscopic re-evaluation should be performed in 3 weeks and again in 2 to 3 months to determine if the lesion recurs or the process extends into the arytenoid cartilage, resulting in chondritis and cartilage deformity.

In acute cases of unilateral arytenoid chondritis, medical treatment as described above is initiated. The abscessed cartilage is probed to determine if surgical drainage is possible.[100] To accomplish this, the horse is sedated and, via endoscopy, local anesthetic is liberally applied to the laryngeal mucosa. The ventral throat area is clipped and aseptically prepared and local anesthetic is injected subcutaneously 5 to 7 cm on ventral midline. A #15 blade is used to make a stab incision through the skin, muscle, and cricothyroid membrane. A 5 mm trochar is placed through the stab incision and the cricothyroid membrane into the lumen of the larynx. An 18-gauge needle is placed through the mucosal defect into the arytenoid cartilage in the area where the granulation tissue was resected. A curette is used to enlarge the opening, initiating drainage of purulent exudate. This procedure is performed with endoscopic guidance in a standing, sedated or anesthetized horse. Following drainage of the abscess, the lesion may regress completely with return of full cartilage abduction. In bilateral cases, even a return to motion of one of the arytenoid cartilages would significantly increase the prognosis for athletic soundness as unilateral arytenoidectomy is more successful and has less morbidity than bilateral arytenoidectomy.

In chronic cases of arytenoid chondritis or if following drainage of the abscess, the arytenoid cartilage function failed to return, an arytenoidectomy is performed. Two types of arytenoidectomy can be performed: partial and subtotal arytenoidectomy.[101–103] The partial arytenoidectomy includes removal of all portions of the arytenoid cartilage except the muscular process of the arytenoid cartilage. Subtotal arytenoidectomy involves removal of the body of the arytenoid cartilage, leaving the muscular and corniculate processes. Subtotal arytenoidectomy has been shown to yield minimal improvement in airway diameter because the unsupported corniculate process collapses into the rima glot-

tidis during inhalation.[105] However, it preserves best the protective mechanism of the larynx and is associated with less aspiration of feed material. Partial arytenoidectomy provides the best improvement in airway diameter, with a small risk of aspiration of feed material.[106] Therefore, if the goal of therapy is restoration of athletic performance, unilateral partial arytenoidectomy is recommended. Following arytenoidectomy, the horses should be fed and watered from the ground to minimize tracheal contamination.

Prognosis

The prognosis for resolution of mucosal ulcers with medical therapy, without the progression to arytenoid chondritis, is excellent. Horses treated with medical therapy for granulation tissue protruding from the arytenoid have a 30% chance of developing arytenoid chondritis. The prognosis for pasture soundness or light riding following arytenoidectomy is very good.[103] In rare cases, tracheal aspiration of feed material occurs at times, resulting in aspiration pneumonia. Bilateral arytenoidectomy has a less favorable prognosis because the potential for aspiration of feed and laryngeal stenosis is increased.[107]

Experimentally, in horses with laryngeal hemiplegia airway mechanics are improved but do not return to normal following partial arytenoidectomy.[106] There is little clinical data available documenting the prognosis for athletic soundness for horses with arytenoid chondritis treated with arytenoidectomy.[101–103,107] For horses with laryngeal hemiplegia, the prognosis for athletic soundness is very similar whether they are treated with laryngoplasty or partial arytenoidectomy.[103]

Etiology and pathophysiology

Etiology

The arytenoid cartilages are a pair of laryngeal cartilages that articulate with the cricoid cartilage. This articulation is the fulcrum for arytenoid cartilage abduction and adduction. The arytenoid cartilage has two processes: the vocal process where the vocal ligament is attached and the muscular process where the cricoarytenoid dorsalis muscle (the laryngeal abductor muscle) inserts (Fig. 27.31).[1] The comma-shaped corniculate process is attached to the apex of the arytenoid cartilage and forms the dorsal border of the rima glottidis.

Arytenoid chondritis develops following trauma to the mucosa of the arytenoid cartilage and invasion of bacteria into the cartilage. In humans, cattle, and presumably horses trauma occurs following severe coughing episodes where the arytenoid cartilages contact each other during these marked adduction episodes, creating contact ulcers.[104,108] During marked adduction, the point of contact of the arytenoid cartilage is a few millimeters proximal to the vocal process. Therefore, an acute upper respiratory infection (i.e. laryngitis) can be an initiating cause of arytenoid chondritis. Inflamed, swollen laryngeal mucosa may be more susceptible to trauma and the development of contact ulcers. Other causes include iatrogenic damage to the mucosa of the arytenoid cartilage during nasogastric intubation, endoscopy, or by coarse feed material.

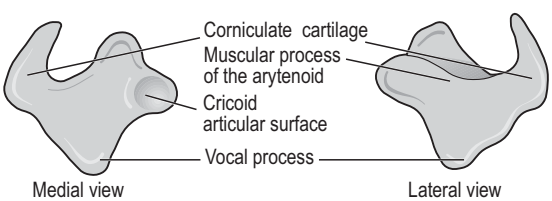


Fig. 27.31
Illustration of the anatomy of the arytenoid cartilage.

Pathophysiology

Arytenoid chondritis has three clinical presentations affecting one or both arytenoid cartilages: mucosal ulceration, granulation tissue projecting in the lumen of the larynx, and arytenoid cartilage abscessation, deformity and dysfunction. Following ulceration of the arytenoid cartilage mucosa, local bacterial invasion of the body of the arytenoid cartilage causes a superficial chondritis resulting in the production of granulation tissues and a fistulous tract. If the infection extends deeper in the body of the cartilage, an abscess may form, and enlargement and deformation of the arytenoid cartilage, and lack of movement result.

The physical presence of the granulation tissue protruding into the rima glottidis causes a static luminal obstruction during both inspiration and expiration. When the cartilage is deformed and immobile, dynamic inspiratory obstruction occurs.

Prevention

Prevention of this syndrome is difficult. Preventing trauma to the arytenoid cartilage by minimizing nasogastric intubation and endoscopic examination is prudent. Treatment of mucosal ulceration and granulation tissue can prevent further bacterial invasion of the cartilage and more severe chondritis from developing.

There has been one report of an association in Thoroughbred horses of equine lymphocyte antigen A9 and chondritis suggesting a possible genetic predisposition to this disease.[109]

Rostral displacement of the palatopharyngeal arch – fourth and sixth branchial arch defect or cricopharyngeal–laryngeal dysplasia

- Rostral displacement of the palatopharyngeal arch results most commonly from laryngeal cartilage malformation.
- Rarely are horses affected at rest but show signs of exercise intolerance and abnormal respiratory noise during exercise.

- Surgical correction is usually unsuccessful due to the cartilage deformity, which most commonly involves the thyroid cartilage.
- Rostral displacement of the palatopharyngeal arch occurs secondarily in horses with arytenoid chondritis, due to deformity of the arytenoid cartilage.

Recognition

History and presenting complaint

Horses affected with rostral displacement of the palatopharyngeal arch are usually asymptomatic at rest and this condition may be diagnosed during routine endoscopic examination of the larynx in yearling horses. Clinical signs are observed during strenuous exercise, frequently when training is instituted. Clinical signs include poor performance and an inspiratory noise the severity of which is related to the severity of the congenital malformation. The character of the inspiratory noise resembles that heard in horses with laryngeal hemiplegia except that it is generally less intense and shorter in duration. In a recent review of 60 cases, 83% of horses made abnormal inspiratory noise, 22% had involuntary aerophagia, 17% had nasal discharge and coughing, and 3% reported tympanic colic.[110]

Physical examination

The most common cause of rostral displacement of the palatopharyngeal arch is congenital malformation of the laryngeal cartilages. The larynx should therefore be palpated in order to detect abnormalities of the laryngeal cartilages. The most common abnormality is deformation of the wing(s) of the thyroid cartilage.[110] The deformity produces a gap between the thyroid and cricoid cartilages that can be easily palpated. Palpation of the muscular processes of the arytenoid cartilages is important because a less prominent or impalpable muscular process suggests arytenoid and/or thyroid cartilage malformation. Paralaryngeal cyst can occur and cause bulging of the lamina of the thyroid cartilage that can be felt unilaterally or bilaterally round the larynx.

Special examination

Endoscopic examination of the larynx is performed to diagnose rostral displacement of the palatopharyngeal arch. The position of the palatopharyngeal arch rostral to the corniculate process of the arytenoid cartilage is pathognomonic for rostral displacement of the palatopharyngeal arch (Fig. 27.32). In addition, the abductor function of the arytenoid cartilages should be carefully evaluated. In a significant proportion of horses affected with rostral displacement of the palatopharyngeal arch, incomplete abduction of one arytenoid cartilage (usually the right) is seen. Endoscopic examination of the airway while the horse is running on a treadmill is performed to assess arytenoid function when abnormal arytenoid cartilage movement is detected during endoscopic examination in the resting horse.

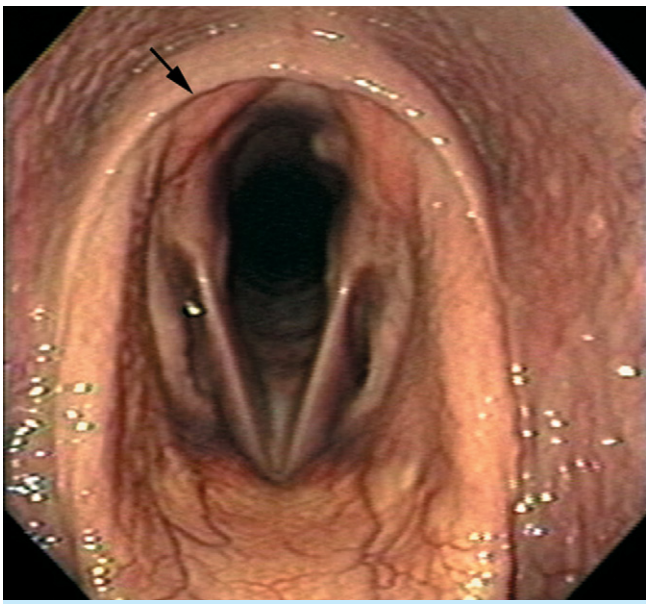


Fig. 27.32
Endoscopic image of the larynx of a horse with rostral displacement of the palatopharyngeal arch. Notice how the palatopharyngeal arch (arrow) protrudes over the corniculate processes of the arytenoid cartilages.

Radiography of the throat is helpful because horses with rostral displacement of the palatopharyngeal arch frequently have an anomaly of the cricopharyngeal sphincter, which is seen radiographically as a continuous column of air between the nasopharynx and the esophagus. The presence of redundant tissue dorsal to the corniculate processes of the arytenoid cartilages is suggestive of rostral displacement of the palatopharyngeal arch. Computer tomography can help identify cartilage malformation and detect paralaryngeal cysts.

Diagnostic confirmation

The diagnosis is made by a combination of laryngeal palpation, radiography and videoendoscopic examination of the upper airway.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to restore airway patency during strenuous exercise. The redundant palatopharyngeal arch can be resected. However, since the cause of the redundant palatopharyngeal arch is laryngeal cartilage deformation, the actual cause of the redundant tissue is not treated. If one of the arytenoid cartilages cannot abduct, procedures used to treat horses with laryngeal hemiplegia will be ineffective in this instance because the cartilages are malformed. If a laryngeal cyst is causing the cartilage malformation, the cyst can be removed.

Therapy

If a laryngeal cyst is present, it should be removed using the lateral laryngeal approach used for laryngoplasty. However, cyst removal does not ensure return of normal abductor function of the arytenoid cartilage. This is because multiple concomitant laryngeal deformations are usually present. Partial arytenoidectomy can be performed in an attempt to maximize the lumen of the airway. Laryngoplasty is generally unsuccessful at abducting the arytenoid cartilage because deformities usually include absence of a normal muscular process. This combined with thyroid cartilage abnormality diminishes any possible movement at the arytenoid cricoid articulation.

Prognosis

The prognosis for athleticism is guarded, but is related to the degree of laryngeal cartilage malformation.

Prevention

Because this congenital malformation is probably heritable, avoiding breeding affected horses will limit occurrence.

Etiology and pathophysiology

Etiology

There is little information on the embryology of horses as it relates to formation of the larynx and nasopharynx. It is, however, well known that the human larynx and its intrinsic musculature, and laryngeal nerves originate from a combination of the fourth and sixth branchial arches.[111,112] Specifically, the cranial laryngeal nerve originates from the fourth branchial arch and the recurrent laryngeal from the sixth branchial arch. The epiglottic cartilage develops separately as it originated from the hypobranchial eminence.

Rostral displacement of the palatopharyngeal arch is a congenital anomaly most commonly seen in Thoroughbreds, which is part of a greater syndrome associated with fourth and sixth branchial arch defects.[110] Abnormalities seen with this congenital disease include absence of cricopharyngeal muscles, deformed thyroid cartilage resulting in an increased space between the thyroid and cricoid cartilage, abnormality of the cricopharyngeus and thyropharyngeus muscles, absence or small muscular process of the arytenoid cartilage, presence of paralaryngeal cyst(s) and associated deformation of laryngeal cartilage.[110,113–116] Vertical displacement of the lamina of the thyroid cartilage over the muscular process of the arytenoid cartilage can occur, and this deformity prevents arytenoid cartilage abduction. The right side of the larynx is most frequently affected but the deformities can occur bilaterally or on the left side.[110]

Rostral displacement of the palatopharyngeal arch can also be seen unilaterally with arytenoid chondritis or following partial arytenoidectomy. This is thought to be due to the physical loss of the corniculate process of the arytenoid cartilage, caudal to which the palatopharyngeal arch membrane normally sits.

Pathophysiology

Most of the clinical signs associated with rostral displacement of the palatopharyngeal arch are respiratory in origin and are due to obstruction of the rima glottidis. More rarely associated abnormality of the cricopharyngeal sphincter leads to dysphagia and aerophagia, which can cause tympanic colic in some horses.

Airway obstruction is caused by collapse of the arytenoid cartilage across the rima glottidis with minimal contribution from the palatopharyngeal arch. This occurs for several reasons including the absence of the muscular process of the arytenoid cartilage, the insertion of the cricoarytenoideus dorsalis muscle, preventing abduction of the arytenoid cartilage. The absence of the cricothyroid articulation leads to caudal displacement of the arytenoid cartilage instead of abduction.[110] Vertical displacement of the thyroid lamina prevents caudolateral displacement of the muscular process of the arytenoid cartilage, a process needed for abduction of the arytenoid cartilage.

When rostral displacement of the palatopharyngeal arch occurs following partial arytenoidectomy, this presentation is unlikely to be of any clinical significance. Decreased performance in horses treated with partial arytenoidectomy may justify endoscopic examination of the larynx with the horse running on the treadmill to determine if dynamic obstruction of the airway due to unilateral collapse of the palatopharyngeal arch membrane occurs.

The digestive dysfunction is rare and caused by regurgitation of esophageal contents back into the nasopharynx due to deficiency in the musculature of the cricopharyngeal sphincter. Regurgitation of feed material back into the nasopharynx and trachea can result in coughing and nasal discharges.[110,116] In addition, aerophagia created by the deficient cricopharyngeal sphincter has been reported to result in tympanic colic.[110]

Guttural pouch mycosis

Recognition

History and presenting complaint

The most common clinical sign of guttural pouch mycosis is severe epistaxis caused by erosion of the internal carotid artery, external carotid artery and/or maxillary artery. Other clinical signs include mucopurulent or hemorrhagic nasal discharge, coughing, dysphagia caused by cranial nerve damage (IX and X), unilateral laryngeal hemiplegia, Horner's syndrome (ptosis, miosis, unilateral facial sweating), parotid pain, tongue paresis, and head shaking.[117–119] Endoscopic examination of the nasopharynx may reveal hemorrhage from one or both nasopharyngeal openings.

Physical examination

Physical examination findings vary depending upon the chronicity of the hemorrhage. If the horse has recently bled severely due to erosion of a major artery within the guttural pouch by a mycotic plaque, the horse will show clinical signs of hypovolemic shock, including sweating, tachycardia, weak peripheral pulses, pale mucous membranes, and cold ears and muzzle. Occasionally, if the mycotic plaque forms over cranial nerves, such as branches of the vagus nerve or the sympathetic trunk, the horse may have clinical evidence of dysphagia and aspiration pneumonia or Horner's syndrome.[117–119] Tongue paresis can occur presumably due to hypoglossal nerve involvement.[120]

Special examination

Endoscopic examination of the nasopharynx and guttural pouches is diagnostic for guttural pouch mycosis.[117,118] Following hemorrhage, a blood clot will protrude from the affected pouch. If the disease is bilateral or the fungus has eroded through the median septum, clots may form at both guttural pouch openings. Inspection of the affected guttural pouch reveals a single fungal plaque or multiple plaques associated with the major arteries of the guttural pouch, including most commonly the internal carotid artery, but also the external carotid artery, and the maxillary artery (Fig. 27.33).[119]

Laboratory examination

Horses may be anemic if guttural pouch hemorrhage is severe or chronic.

Diagnostic confirmation

Differential diagnosis for guttural pouch mycosis includes other conditions that would result in guttural pouch hemorrhage, the most common being avulsion of the longus capitis muscle from the basisphenoid bone, or trauma.[121] Biopsy and culture of the fungal plaque confirms the diagnosis.

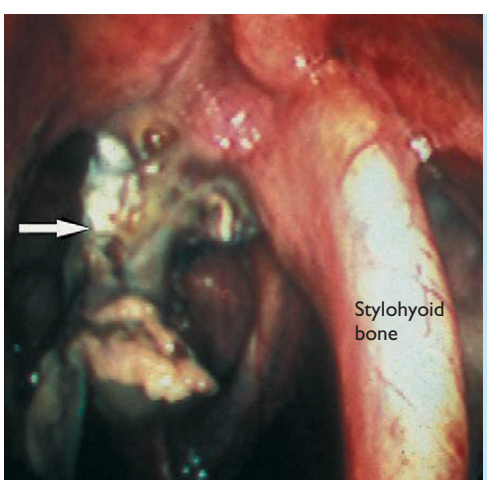


Fig. 27.33 Endoscopic image of the guttural pouch of a horse with guttural pouch mycosis. Notice the gray to black mycotic lesion (arrow).

Treatment and prognosis

Therapeutic aims

The goals of treatment are to prevent life-ending hemorrhage and eradicate the fungal infection from the guttural pouch.

Therapy

Medical treatment of guttural pouch mycosis includes topical application of non-irritating antifungal agents that are effective against *Aspergillus* spp., such as itraconazole and enilconazole.[122] Medical therapy may be initiated if hemorrhage has not occurred and the fungal plaques do not involve any blood vessels. If vascular structures are involved, which is most common, the goal of surgical therapy is to occlude the affected arteries.[117,118] Most simply, the common carotid artery on the affected side can be ligated with the horse standing. This may decrease the hemorrhage, but horses are still at risk for fatal hemorrhage due to collateral circulation through the circle of Willis and the palatine arteries.[118] Alternatively, a combination of internal, external and palatine artery ligation and balloon angioplasty using venous thrombectomy catheters can be performed.[117,118] This technique alleviates the possibility of continued hemorrhage but may result in blindness on the affected side as a result of ischemic optic neuropathy.[123] Affected vessels can also be occluded by use of detachable balloons (Yocan Medical Systems, 4 Spirea Ct, Thornhill, Ontario 13T2W1, Canada) or transarterial coil embolization (Cook Inc., Bloomington, IN). Briefly, the horse is anesthetized and positioned in lateral recumbency with the affected side up. The common carotid artery is carefully isolated and elevated, permitting catheterization with an 18-gauge angiographic needle and an introducer system.[117] Under fluoroscopic guidance, an angiogram is performed by injecting 10 to 20 mL of iohexol:heparinized saline, diluted 1:2, in order to accurately identify the internal, occipital, external, and maxillary arteries, and any aberrant branches of these vessels.[117] Dacron-fiber-covered, stainless steel occluding spring embolization coils are introduced into the internal carotid artery at the level of the basisphenoid bone to prevent retrograde flow from the circle of Willis.[117] Following occlusion of the rostral portion of the internal carotid artery, embolization coils are then placed in the rostral portion of the vessels to prevent normograde blood flow. If the external carotid or maxillary arteries are affected, embolization coil vascular occlusion is performed in the maxillary artery just before the alar foramen, and in the external carotid artery, just after it bifurcates from the linguofacial artery. The common carotid artery is ligated at the site of catheterization.[117]

Prognosis

Approximately 50% of horses that bleed severely die from fatal hemorrhage. If appropriate vascular occlusion is successful, the prognosis for life is excellent. Fungal plaques generally resolve without antifungal medication, 30 to 60 days following vascular occlusion. Dysphagia, unilateral laryngeal hemiplegia, and Horner's syndrome may resolve over 6 to

8 months, or may be permanent. Potential complications related to the surgical procedures include unilateral blindness, cerebral ischemia, and recurrent hemorrhage.[117–119]

Prevention

There is no known method of prevention.

Etiology and pathophysiology

Etiology

The etiology is unknown, but *Aspergillus* spp. is frequently cultured from the diphtheritic plaques.

Pathophysiology

The fungal plaques grow within the guttural pouch, and if they erode through the walls of the internal, external, or maxillary arteries, life-threatening hemorrhage can ensue. Ligation of the common carotid artery or only proximal ligation of affected arteries frequently leads to subsequent hemorrhage due to retrograde flow of blood through the circle of Willis to the erosion in the internal carotid artery, and flow of the blood through the palatine artery to the maxillary and external carotid arteries.[119]

Epidemiology

There is no known geographical predisposition nor age, breed, sex, or occupational predilection for guttural pouch mycosis.

Avulsion of the longus capitis/rectus capitis ventralis muscles

Recognition

History and presenting complaint

Horses with avulsion or rupture of the longus capitis and rectus capitis ventralis muscles usually have a history of trauma, such as falling over or being tied and pulling free.[121] Occasionally, (one case) the trauma may occur as a result of the horse throwing its head and neck overzealously. Affected horses may have bilateral epistaxis, swelling or thickening in the throatlatch area, and may be ataxic or exhibit other signs of neurologic dysfunction.[121]

Physical examination

Horses will often have bilateral epistaxis, may be ataxic or have cranial nerve deficits, and swelling in the area of Vyborg's triangle.[121] Affected horses may have signs of vestibular disease (head tilt, falling, ipsilateral weakness, circling), facial nerve injury (palsy of facial muscles, inability to blink, creased lacrimation and keratitis sicca) and cerebral dysfunction (depressed mentation).

Special examination

Endoscopic examination of the nasopharynx reveals collapse of the dorsal nasopharynx due to the hematoma formation within the dorsal and medial tissues of the guttural pouch and blood or blood clots at the nasopharyngeal openings of the guttural pouches. Within the guttural pouch, hemorrhage and hematoma formation are evident along the medial wall (Fig. 27.34). Lateral radiographic projections of the guttural pouch region show soft tissue density within the guttural pouch compression of the dorsal nasopharynx, and avulsion fracture of the basisphenoid bone (Fig. 27.35).

Laboratory examination

Laboratory examination is normal or there is evidence of hemorrhage.

Diagnostic confirmation

Differential diagnosis for avulsion of the longus capitis and rectus capitis ventralis muscles is guttural pouch mycosis.

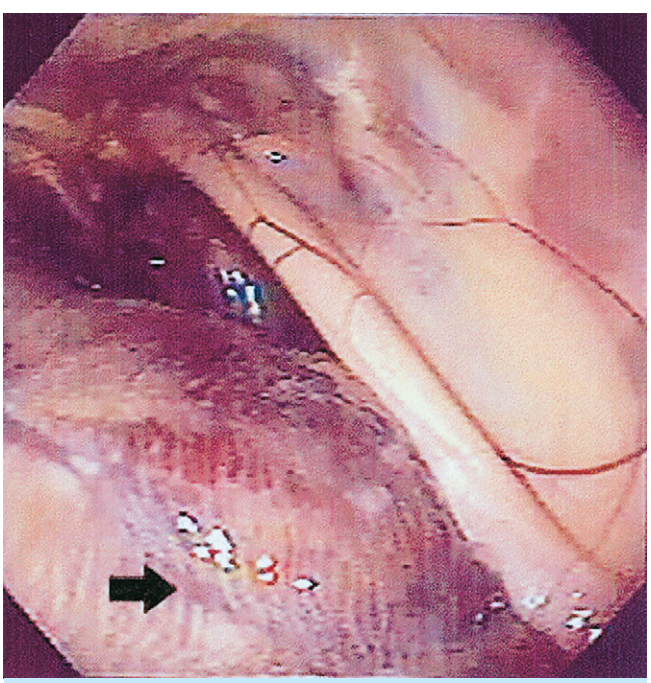


Fig. 27.34
Endoscopic image of the guttural pouch of a horse that avulsed the longus capitis and rectus capitis muscles from the basisphenoid and basioccipitus bones at the base of the skull. Notice the large hematoma (arrow) within the medial compartment of the guttural pouch.

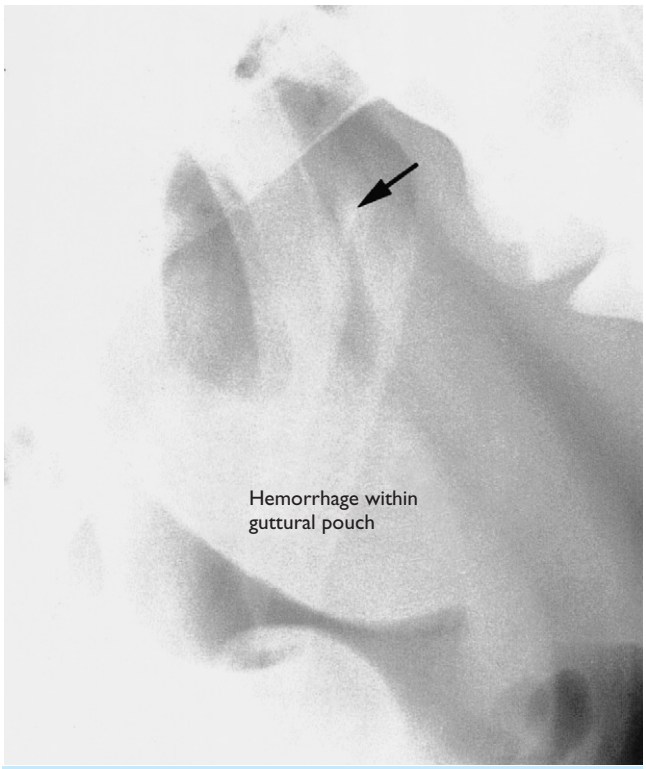


Fig. 27.35
Lateral radiograph of the guttural pouch region of a horse that avulsed the longus capitis and rectus capitis muscles from the basisphenoid and basioccipitus bones at the base of the skull. Notice the bone fragment (arrow) and the hemorrhage within the guttural pouch.

The history of trauma and the appearance of the hematoma within the medial wall of the guttural pouch are diagnostic for this condition.

Treatment and prognosis

Therapeutic aims

The goal of therapy is to provide supportive care if the horse has neurologic signs and confine the horse to minimize the risk of further hemorrhage.

Therapy

Two to three months of stall rest and broad-spectrum antimicrobial therapy are warranted due to the hematoma formation within the guttural pouch.[121] Judicious use of non-steroidal anti-inflammatory therapy for analgesia is recommended. If neurologic signs are severe and the horse is unable to rise, subdural hemorrhage involving the brainstem and cerebral cortex may be suspected and euthanasia is warranted.

Prognosis

The prognosis for return to function is good unless neurologic deficits are severe.[121]

Prevention

There is no known method of prevention.

Etiology and pathophysiology

Etiology

Avulsion of the rectus capitis muscles usually occurs following trauma.

Pathophysiology

Three muscles that flex the head and neck include the large longus capitis muscle and two small muscles, rectus capitis ventralis, and rectus capitis lateralis. These muscle course ventrally between the guttural pouches from their attachments on the basisphenoid and occipital bone, forming the cranial medial wall of the guttural pouches. Simultaneous contraction of these muscles as the horse falls over backwards would lead to avulsion fracture from the basisphenoid and occipital bones, resulting in hemorrhage from the guttural pouch and hematoma formation.

Epidemiology

Horses most commonly affected are young animals early in their training or breaking program. The disease is less common in older horses because they are less likely to fall over backwards or pull back violently when tied.

Temporohyoid osteoarthropathy

Recognition

History and presenting complaint

Most horses with temporohyoid ostreoarthropathy have clinical signs suggestive of facial nerve (cranial nerve VII), and/or vestibulocochlear nerve (cranial nerve VIII) deficits. Presenting complaints included facial nerve paralysis and lip droop, head tilt, ataxia or falling, difficulty eating, corneal ulceration/keratitis, nasal discharge, and head shaking/tossing.[124]

Physical examination

Physical examination findings include fever, facial and vestibulocochlear nerve deficits, including vestibular signs that may resemble ataxia, pain with manipulation of the jaw or opening the mouth, blepharospasm and corneal ulceration.[124]

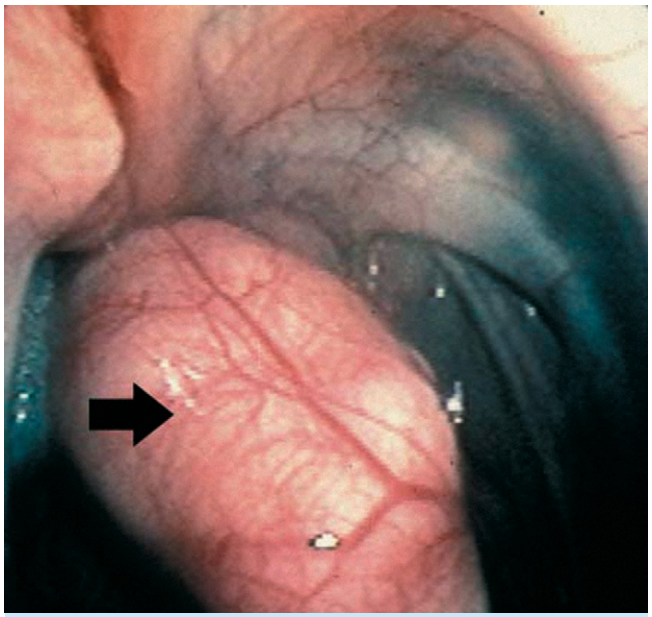


Fig. 27.36
Endoscopic image of the articulation of the stylohoid bone and the petrous portion of the temporal bone in a horse with temporohyoid osteoarthropathy. Notice the enlarged region (arrow) of the proximal aspect of the stylohyoid bone.

Special examination

The diagnosis of temporohyoid osteoarthropathy is made based on physical examination findings and endoscopic examination of the guttural pouches. Skull radiographs and computed tomography are sometimes used to help confirm the diagnosis or more fully describe the lesion at the temporohyoid articulation. Osseous proliferation at the proximal aspect of the stylohyoid bone is seen during endoscopic examination of the guttural pouch on the affected side (Fig. 27.36) Dorsoventral radiographic projections of the skull may show enlargement of the temporohyoid region. Computed tomographic scans may show fusion of the temporohyoid joint and osseous proliferation of the proximal portion of the stylohyoid bone. Occasionally, fracture of the stylohyoid bone can be seen. Schirmer tear test can be performed to assess tear production from the affected eye, especially if signs of facial neuropathy are present.

Laboratory examination

Most frequently, clinical laboratory examination is normal. Leukocytosis, lymphopenia, anemia, and hyperfibrinogenemia may occur.

Diagnostic confirmation

Endoscopic, radiographic, or computed tomographic evidence of temporohyoid fusion or enlargement are diagnostic for temporohyoid osteoarthropathy.

Treatment and prognosis

Therapeutic aims

The goals of therapy include resolution of the vestibular and facial nerve deficits, treatment or prevention of corneal ulceration, and protecting the horse from further trauma resulting from its vestibular disease. Most horses are treated with antibiotics and non-steroidal anti-inflammatory drugs, including trimethoprim sulfa, enrofloxacin, or penicillin and gentamicin for 30 days, and oral phenylbutazone or flunixin meglumine.[124] Surgical treatment or stylohyoidostectomy involves removing a piece of the stylohyoid bone to minimize motion at the temporohyoid articulation.[125] Corneal ulcers are treated with topical medication, and if the eyelid is not functional, a tarsorrhaphy may be performed to protect the cornea until facial neuropathy resolves or improves. Ocular lubricants can be applied to affected eyes several times daily if the cornea is healthy but eyelid function is abnormal.

Prognosis

Following temporohyoid osteoarthropathy, 63% of horses return to athletic activity and most horses return to their intended use. Rehabilitation time may be long, up to 2 years, though many clinical signs will abate within 30 to 60 days.[124]

Prevention

There are no known preventive measures.

Etiology and pathophysiology

Etiology

The etiology is unknown.

Pathophysiology

Temporohyoid osteoarthropathy is probably the result of primary osteoarthritis of the temporohyoid joint.[126] Alternatively, it may be the sequela to otitis media/interna that develops secondary to hematogenous spread of bacteria, ascending infection from the respiratory tract, otitis externa, or extension of guttural pouch empyema.[124,127] The infection and inflammatory reaction of the tympanic bulla, temporohyoid joint, and stylohyoid bone resolves, leaving bony proliferation of the proximal stylohyoid bone and fusion of the temporohyoid joint. Vestibular disease and facial nerve paralysis occur when osseous proliferation impinges on cranial nerves VII (facial) and VIII (vestibulocochlear) or if the petrous temporal bone fractures. The condition is usually unilateral but can be bilateral.

Epidemiology

Temporohyoid osteoarthropathy affects horses of all ages and sex and does not have a geographic predilection.

Tracheal obstructive disease

Primary obstructive tracheal disease in horses is rare, and includes tracheal collapse, fungal granulomas, chondritis, trauma, and foreign bodies. The equine trachea has an oval shape and measures approximately 5 by 7 cm, dorsoventrally to transversely, respectively. It is composed of 48 to 60 incomplete hyaline cartilage rings interspersed by fibroelastic annular ligaments. The dorsal area is made up of fibrous tissue and the trachealis muscle, which is attached to the concave surface of each cartilage ring. The trachealis muscle allows for changes in diameter of the trachea during inhalation and exhalation, while the fibroelastic annular ligaments permit unimpeded flexion and extension of the head and neck, important in running horses.

Recognition

History and presenting complaint

Horses with primary tracheal obstructive disease are exercise intolerant, make an abnormal respiratory noise during exercise or sometimes at rest, which is characterized as a honking sound, and have bilateral nasal discharge that may be mucopurulent or hemorrhagic.

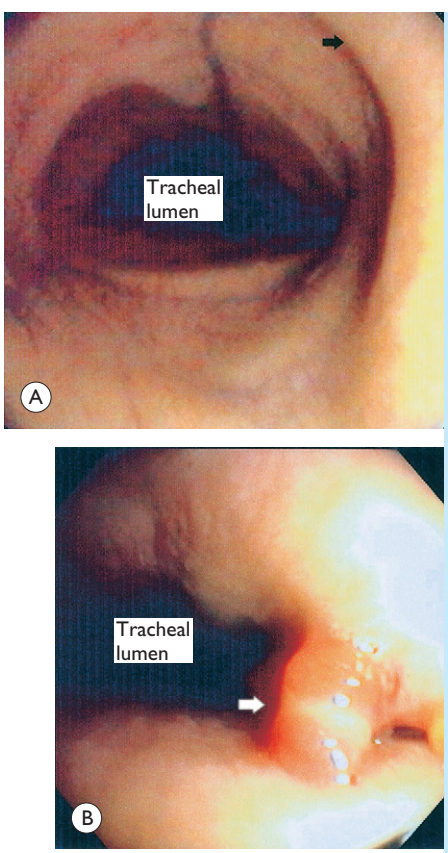


Fig. 27.37 (A) Endoscopic image of the lumen of the trachea of a horse with tracheal collapse. Notice the collapsed tracheal rings (arrow). (B) Endoscopic image of the lumen of the trachea of a horse that had tracheal trauma. Notice the granulation tissue (arrow) protruding into the collapsed lumen of the trachea.

Physical examination

Physical examination is usually normal. If tracheal trauma has occurred, palpation of the ventral cervical region may reveal a concavity in the area of previous trauma, swelling, or scar tissue. Thickened or abnormal tracheal rings may be palpable in the proximal to middle region of the cervical area if the rings have been traumatized or are chondritic. If the trachea is perforated, subcutaneous emphysema is noted along the neck, withers, and shoulders.

Special examination

Endoscopy, radiography, and ultrasonography can be useful to assess tracheal abnormalities. If the tracheal lesion is caused by a static mass, such as a fungal granuloma, chondritic cartilage, or persistently deformed trachea, endoscopic examination of the trachea at rest will be useful in assessing the tracheal lumen (Fig. 27.37A, B). If dynamic tracheal collapse occurs during exercise, endoscopic examination of the trachea during treadmill exercise is required to diagnose the dynamic collapse.[128] Lateral radiographs of the trachea are useful in assessing extraluminal masses that may cause intraluminal obstruction, as well as the position and extent of the tracheal lesion, if it is cranial to the thoracic inlet. Ultrasonography is also used to evaluate soft tissue densities external to the trachea that may impinge on the tracheal lumen such as abscesses, hematomas, or neoplastic lesions.

Laboratory examination

Complete blood count and serum chemistry values are usually normal.

Diagnostic confirmation

The diagnosis is confirmed based on endoscopic examination of the trachea at rest or during treadmill exercise and biopsy, histopathology, or culture of the mass. Endoscopic examination of the trachea at rest confirms intraluminal obstruction, which can occur as a result of trauma. Intraluminal masses, such as fungal granulomas, are biopsied and submitted for culture and cytology.[129] Granulomatous tracheitis caused by *Conidiobolus coronatus* can also be confirmed by agar gel immunodiffusion assay performed at the Centers for Disease Control and Prevention, Atlanta, GA.[129] Lesions of the tracheal rings, such as chondritis, are diagnosed based upon endoscopic examination, history of tracheal trauma or injection, and possibly localization of an abscess within the body of the tracheal cartilage. Dynamic tracheal collapse is diagnosed by endoscopic examination of the trachea during treadmill exercise if clinical signs are not apparent at rest and endoscopic examination of the upper airway and trachea is normal at rest.[128]

Treatment and prognosis

Therapeutic aims

The goal of treatment is to ameliorate the tracheal obstruction.

Therapy

Discrete intraluminal tracheal masses can be excised by use of transendoscopic contact Nd:YAG laser or sharply through a tracheotomy incision if the mass is within an accessible area of the trachea. Treatment of tracheal trauma includes systemic antimicrobial and non-steroidal anti-inflammatory therapy, if the tracheal lumen has been penetrated. Individual tracheal rings that have been traumatically damaged or are chondritic and cause airway obstruction can be resected.[130] Treatment of tracheal collapse is dependent upon the length and accessibility of the trachea involved. Some forms of tracheal collapse can be treated by stenting individual tracheal rings, tracheal prosthesis, or resection and anastomosis of the affected area.[130] Granulomatous tracheitis caused by *Conidiobolus coronatus* was successfully treated by intravenous sodium iodide 20%, 44 mg/kg, once daily for 7 days followed by 1.3 mg/kg organic iodide 4.57%, twice daily for 1 year.[129]

Prognosis

Prognosis for removal of discrete intraluminal masses within the trachea and return to function is excellent.[130] Horses with tracheal collapse have a good prognosis for life, but a guarded prognosis for athletic activity.

Prevention

There is no known method of prevention of tracheal obstruction.

Etiology and pathophysiology

Etiology

Chondritis of tracheal cartilages can occur following intratracheal injections or transtracheal aspiration, if a tracheal ring is perforated during the injection, trauma, or idiopathically.

Pathophysiology

The pathophysiology of tracheal obstruction is based upon the type of obstruction.

Epidemiology

Tracheal obstruction is rare in athletic horses.

References

1. Sisson S. Equine respiratory system. In: Getty R, ed. Sisson and Grossman's the anatomy of domestic animals. 5th edn. Philadelphia: WB Saunders; 1975; 498–499.
2. Nickels FA. Disease of the nasal cavity. Vet Clin North Am Equine Pract 1993; 9(1):111–122.
3. Hawkins JF, Tulleners EP, Evans LH, et al. Alar fold resection in horses: 24 cases (1979–1992). J Am Vet Med Assoc 1995; 206(12):1913–1916.
4. Greet T. Nasal aspergillosis in three horses. Vet Record 1982; 109(22):487–489.
5. Zamos DT, Schumacher J, Lay JK. Nasopharyngeal conidiobolomycosis in a horse. J Am Vet Med Assoc 1996; 208(1):100–101.
6. Korenek NL, Legendre AM, Andres FM, et al. Treatment of mycotic rhinitis with itraconazole in three horses. J Vet Intern Med 1994; 8(3):224–227.
7. Watt DA. A case of cryptococcal granuloma in the nasal cavity of a horse. Aust Vet J 1970; 46(10):493–495.
8. Nickels FA. Nasal Passages. In: Auer JA, Stick JA, eds. Equine surgery. 2nd edn. Philadelphia: WB Saunders; 1992; 326–336.
9. Rothaug PG, Tulleners EP. Neodymium:yttrium-aluminum-garnet laser-assisted excision of progressive ethmoid hematomas in horses: 20 cases (1986–1996). J Am Vet Med Assoc 1999; 214(7):1037–1041.
10. Gasser IS, Love NE, Tate LP. Radiographic diagnosis – ethmoid hematoma. Vet Radiol Ultrasound 2000; 41(3): 247–249.
11. Frees KE, Vaughan EM, Lillick JD. Severe complication after administration of formalin for treatment of progressive ethmoidal hematoma in a horse. J Am Vet Med Assoc 2001; 219(7):950–952.
12. Schumacher J, Yarborough T, Pasco J, et al. Transendoscopic chemical ablation of progressive ethmoidal hematoma in standing horses. Vet Surg 1998; 27:175–181.
13. Tremaine WH, Dixon PM. A long-term study of 277 cases of equine sinonasal disease. Part 1: details of horses, historical, clinical and ancillary diagnostic findings. Equine Vet J 2001; 33(3):274–282.
14. Trotter GW. Paranasal sinuses. Vet Clin North Am Equine Pract 1993; 9(1):153–170.
15. Ruggles AJ, Ross MW, Freeman DE. Endoscopic examination of normal paranasal sinuses in horses. Vet Surg 1991; 20:418–422.
16. Freeman DE, Orsini PG, Ross MW, et al. A large frontonasal bone flap for sinus surgery in the horse. Vet Surg 1990; 19(2):122–130.
17. Tremaine WH, Dixon PM. A long-term study of 277 cases of equine sinonasal disease. Part 2: treatments and results of treatments. Equine Vet J 2001; 33(3):283–289.
18. Boulton C. Equine nasal cavity and paranasal sinus disease: A review of 85 cases. Equine Vet Sci 1985; 5:268–271.
19. Ducharme N. Pharynx. In: Auer JA, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia: WB Saunders; 1992; 340–341.
20. Carr EA, Spier SJ, Kortz GD, et al. Laryngeal and pharyngeal dysfunction in horses homozygous for hyperkalemic periodic paralysis. J Am Vet Med Assoc 1996; 209(4):798–803.
21. Rehder RS. Equine upper airway and guttural pouch pressures during exercise. MS thesis, Cornell University, 1992.
22. Golland LC, Hodgson DR, Davis RE. Retropharyngeal lymph node infection in horses: 46 cases (1977–1992). Aust Vet J 1995 May; 72(5):161–164.
23. Franklin SH, Lane JG, Burn JF. Spectral analysis of respiratory noise in horses with upper-airway obstructions. In: Proceedings World Equine Airways Society 2001, CD.
24. Derksen FJ. Spectrum analysis of respiratory sounds in exercising horses with experimentally induced laryngeal

hemiplegia or dorsal displacement of the soft palate. Am J Vet Res 2001; 62:659–664.
25. Petsche VM, Derksen FJ, Berney CE, et al. Effect of head position on upper airway function in exercising horses. Equine Vet J Suppl 1995; 18:18–22.
26. Parente EJ, Martin BB, Tulleners EP, Ross MW. Upper respiratory dysfunctions in horses during high-speed exercise. Proc Am Assoc Equine Pract 1994; 40:81–82.
27. Hackett RP, Ducharme NG, Rehder RS. Use of the high-speed treadmill in management of horses with dorsal displacement of the soft palate. Proc Am Assoc Equine Pract 1992; 38:153–154.
28. Morris EA, Seeherman HJ. The dynamic evaluation of upper respiratory function in exercising horses. Proc Am Assoc Equine Pract 1988; 34:159–165.
29. Duggan VE, MacAllister CG, Davis MS. Xylazine-induced attenuation of dorsal displacement of the soft palate associated with epiglottic dysfunction in a horse. J Am Vet Med Assoc 2002; 221:399–401.
30. Cornelisse CJ, Holcombe SJ, Derksen FJ, et al. Effect of a tongue-tie on upper airway mechanics in horses during exercise. Am J Vet Res 2001; 62:775–778.
31. Beard WL, Holcombe SJ, Hinchcliff KW. Effect of a tongue-tie on upper airway mechanics during exercise following sternothyrohyoid myectomy in clinically normal horses. Am J Vet Res 2001; 62:779–782.
32. Franklin SH, Naylor JR, Lane JG. The effect of a tongue-tie in horses with dorsal displacement of the soft palate. Equine Vet J Suppl 2002; 34:430–433.
33. Holcombe SJ, Robinson NE, Jackson C, et al. Stabling is associated with airway inflammation in young Arabian horses. Equine Vet J 2001; 33(3):244–249.
34. Harrison IW, Raker CW. Sternothyrohyoideus myectomy in horses: 17 cases (1984–1985). J Am Vet Med Assoc 1988; 193(10):1299–1302.
35. Lewellyn HR. Sternothyroideus myotomy for the treatment of dorsal displacement of the soft palate. Proc Am Assoc Equine Pract 1997; 43:239–243.
36. Peloso JG, Stick JA, Nickels FA, et al. Epiglottic augmentation by use of polytetrafluoroethylene to correct dorsal displacement of the soft palate in a Standardbred horse. J Am Vet Med Assoc 1992; 201:1393–1395.
37. Ahern TJ. Oral palatopharyngoplasty; a survey of one hundred post-operative raced horses. Equine Vet Sci 1993; 13:670–672.
38. Ordidge RM. Thermal cautery of the equine soft palate as a treatment for displacement of the soft palate during exercise. Proceedings of the 7th World Congress, 2001; 287.
39. Hogan PM, Palmer SE. Transendoscopic laser cauterization of the soft palate as an adjunctive treatment for dorsal displacement of the soft palate. Proc Am Assoc Equine Pract 2002; 48:228–230.
40. Anderson JD, Tulleners EP, Johnston JK, et al. Sternothyrohyoideus myectomy or staphylectomy for treatment of intermittent dorsal displacement of the soft palate in race horses: 209 cases (1986–1991). J Am Vet Med Assoc 1995; 206:1909–1912.
41. Boulton EP, Seeherman HJ, Kirker-head CA, et al. Primary closure of equine laryngotomy incisions: a review of 42 cases. Vet Surg 1995; 24:226–230.
42. Holcombe SJ, Beard WL, Hinchcliff KW, Robertson JT. Effect of sternothyrohyoid myectomy on upper airway mechanics in normal horses. J Appl Physiol 1994; 77:2812–2816.
43. Tulleners E, Hamir A. Evaluation of epiglottic augmentation by use of polytetrafluoroethylene paste in horses. Am J Vet Res 1991; 52:1908–1916.
44. Holcombe SJ, Derksen FJ, Stick JA, Robinson NE. Effect of bilateral tenectomy of the tensor veli palatini muscle on soft palate function in horses. Am J Vet Res 1997; 58(3): 317–321.
45. Ducharme NG, Hackett RP, Woodie JB, et al. Investigation into the role of the thyrohyoid muscles in the pathogenesis of dorsal displacement of the soft palate in horses. Equine Vet J 2003; 35(3):258–263.
46. Tulleners EP, Stick JA, Leitch M, et al. Epiglottic augmentation for treatment of dorsal displacement of the soft palate in racehorses: 59 cases (1985–1994). J Am Vet Med Assoc 1997; 211(8):1022–1028.
47. Rehder R, Ducharme NG, Hackett RP, Nielan GJ. Measurement of upper airway pressures in exercising horses with dorsal displacement of the soft palate. Am J Vet Res 1995; 56:269–274.
48. Holcombe SJ, Derksen FJ, Stick JA, et al. Bilateral nerve blockade of the pharyngeal branch of the vagus nerve produces persistent soft palate dysfunction in horses. Am J Vet Res 1998; 59(4):504–508.
49. Linford RL, O'Brien TR, Wheat JD, et al. Radiographic assessment of epiglottic length and pharyngeal and laryngeal diameters in the Thoroughbred. Am J Vet Res 1983; 44:1660–1666.
50. Stick JA, Peloso JG, Morehead JP, et al. Endoscopic assessment of airway function as a predictor of racing performance in Thoroughbred yearlings: 427 cases (1997–2000). J Am Vet Med Assoc 2001; 219(7):962–966.
51. Hackett RP, Ducharme NG, Ainsworth DM, et al. Effects of extrathoracic airway obstruction on intrathoracic pressure and pulmonary artery pressure in exercising horses. Am J Vet Res 1999; 60:485–494.
52. Raphel C. Endoscopic findings in the upper respiratory tract of 479 horses. J Am Vet Med Assoc 1982; 56:470–474.
53. Lumsden JM, Stick JA, Caron JP, et al. Surgical treatment for epiglottic entrapment in horses: 51 cases (1981–1992). J Am Vet Med Assoc 1994; 205(5):729–735.
54. Honnas CM, Wheat JD. Epiglottic entrapment: a transnasal surgical approach to divide the aryepiglottic fold axially in the standing horse. Vet Surg 1988; 17:246–251.
55. Tulleners EP. Transendscopsic contact neodymium:yttrium aluminum garnet laser correction of epiglottic entrapment in standing horses. J Am Vet Med Assoc 1990; 196: 1971–1980.
56. Sweeney CF, Maxson AD, Soma LR. Endoscopic findings in the upper respiratory tract of 678 Thoroughbred racehorses. J Am Vet Med Assoc 1991; 198:1037–1038.
57. Morris EA, Seeherman HJ. Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. Equine Vet J 1991; 23:169–174.
58. Tulleners EP. Larynx. In: Auer JA, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia: WB Saunders, 1992; 355.
59. Parente EJ, Martin BV, Tulleners EP. Epiglottic retroversion as a cause of poor performance in two horses. Equine Vet J 1998; 30:270–272.
60. Holcombe SJ, Derksen FJ, Stick JA, Robinson NE. Effect of bilateral hypoglossal and glossopharyngeal nerve blocks on epiglottic and soft palate position in exercising horses. Am J Vet Res 1997; 58(9):1022–1026.
61. King DS, Tulleners EP, Martin BB, et al. Clinical experience with axial deviation of the aryepiglottic folds in 52 racehorses. Vet Surg 2001; 30:151–160.
62. Hawkins JF, Tulleners EP. Epiglottitis in horses: 20 cases (1988–1993). J Am Vet Med Assoc 1994; 205(11): 1577–1579.
63. Cardiot PJ. Roaring in horses: its pathology and treatment. Swan Sonnenschein; 1892; 7–78.

64. Tetens J, Derksen JF, Stick JA, et al. Efficacy of bilateral prosthetic laryngoplasty with and without bilateral ventriculocordectomy as treatments for laryngeal hemiplegia in horses. Am J Vet Res 1996; 57:1668–1673.
65. Ducharme NG, Hackett RP, Gleed RD, et al. Measurements of pulmonary capillary pressure in horses undergoing alteration of intrathoracic pressure by imposition of various upper airway resistive loads. Equine Vet J Suppl 1999;30:27–33.
66. Hawe C, Dixon PM, Mayhew IG. A study of an electrodiagnostic technique for the evaluation of equine recurrent laryngeal neuropathy. Equine Vet J 2001; 33(5):459–465.
67. Rakestraw PC, Hackett RP, Ducharme NG, et al. Arytenoid cartilage movement in resting and exercising horses. Vet Surg 1991; 20:122–127.
68. Hammer EJ, Tulleners E, Parente E, Martin BB. Videoendoscopic assessment of dynamic laryngeal function during exercise in horses with grade-III left laryngeal hemiparesis at rest: 26 cases (1992–1995). J Am Vet Med Assoc 1998; 2121:399–403.
69. Parente EJ, Martin BB, Tulleners EP, Ross MW. Upper respiratory dysfunctions in horses during high-speed exercise. Proc Am Assoc Equine Pract 1994; 40:81–82.
70. Dixon PM, McGorum BC, Railton DI, et al. A long-term survey of laryngoplasty in an older mixed-breed population of 200 horses. 1. Maintenance of surgical arytenoid abduction and complications of surgery. Abstract 62. In: Proceedings 2nd World Equine Airways Society 2001, CD.
71. Franklin SH, Land JG, Burn JF. Spectral analysis of respiratory noise in horses with upper-airway obstructions. In Proceedings World Equine Airway Symposium 2001, CD ROM.
72. Derksen JF, Stick JA, Scott EA, et al. Effects of laryngeal hemiplegia and laryngoplasty on airway flow mechanics in exercising horses. Am J Vet Res 1986; 47:16–26.
73. Hobday F. The surgical treatment of roaring in horses. North Am Vet Clin 1936; 17:17–21.
74. Quinlan D, Morton DD. Paralysis of the branches of the nervus vagus – N. Recurrens, N. Pharyngeus and N. Laryngeus cranialis as an etiological factor in whistling and roaring in horses: with some remarks on its heredity and surgical procedures in its treatment. J South Afr Vet Med Assoc 1957; 28:63–74.
75. Marks D, Mackay-Smith MP, Cushing LS, Leslie JA. Observations on laryngeal hemiplegia in the horse and treatment by abductor muscle prosthesis. Equine Vet J 1970; 2:158–166.
76. White NA, Blackwell RB. Partial arytenoidectomy in the horse. Vet Surg 1980; 9:5–12.
77. Ducharme NG, Hackett RP. What is the true value of laryngeal surgery. Comp Cont Educ 1991; 13:472–475.
78. Fulton IC, Derksen FJ, Stick JA, et al. Treatment of left laryngeal hemiplegia in Standardbreds using a nerve muscle pedicle graft. Am J Vet Res 1991; 52:1461–1466.
79. Ducharme NG, Viel L, Partlow GD, Hulland TJ. Attempts to restore abduction of the paralyzed equine arytenoid cartilage: Part III nerve anastomosis. Can J Vet Res 1989; 53:216–223.
80. Shappel KK, Derksen FJ, Stick JA, Robinson NE. Effects of ventriculectomy, prosthetic laryngoplasty, and exercise on upper airway function in horses with induced left laryngeal hemiplegia. Am J Vet Res 1988; 49:1760–1766.
81. Brown JA, Derksen FD, Stick JA, Holcombe SJ. Ventriculocordectomy reduces respiratory noise in horses with laryngeal hemiplegia. Abstract 62. In: Proceedings 2nd World Equine Airways Society 2001, CD.
82. Russel AP, Slone DE. Performance analysis after prosthetic laryngoplasty and bilateral ventriculectomy for laryngeal hemiplegia in horses: 70 cases (1986–1991). J Am Vet Med Assoc 1994; 204:1235–1241.
83. Kidd JA, Slone DE. Treatment of laryngeal hemiplegia in horses by prosthetic laryngoplasty, ventriculectomy and vocal cordectomy. Vet Rec 2002; 150:481–484.
84. Strand E, Martin GS, Haynes PF, et al. Career racing performance in Thoroughbreds treated with prosthetic laryngoplasty for laryngeal neuropathy: 52 cases (1981–1989). J Am Vet Med Assoc 2000; 217:1689–1696.
85. Hawkins JF, Tulleners EP, Ross MW, et al. Laryngoplasty with or without ventriculectomy for treatment of left laryngeal hemiplegia in 230 horses. Vet Surg 1997; 26:484–491.
86. Edwards RE, Ducharme NG, Hackett, RP, et al. The value of respiratory mechanics for detection of partial laryngeal obstruction in exercising horses. MS thesis. Cornell University, 1996.
87. Tulleners E, Harrison IW, Raker CW. Management of arytenoid chondropathy and failed laryngoplasty in horses: 75 cases (1979–1985). J Am Vet Med Assoc 1988; 192:670–675.
88. Lumsden JM, Derksen FJ, Stick JA, et al. Evaluation of partial arytenoidectomy as a treatment for equine laryngeal hemiplegia. Equine Vet J 1994; 24:125–129.
89. Hackett S. Clinical anatomy of the recurrent laryngeal nerve. Proceedings International Neurology Conference 1997; 106–107.
90. Duncan ID, Griffith IR. A light and electron microscopic study of the neuropathy of equine idiopathic laryngeal hemiplegia. Acta Neuropathol 1978; 4:483–501.
91. Duncan ID. The pathophysiology of equine idiopathic laryngeal hemiplegia. Proceedings International Neurology Conference 1997; 108–110.
92. Cole CR. Changes in the equine larynx associated with laryngeal hemiplegia. Am J Vet Res 1946; 7:69–77.
93. Duncan ID, Reifenrath P, Jackson KF, Clayton M. Preferential denervation of the adductor muscles of the equine larynx. II: Nerve pathology. Equine Vet J 1991; 23:99–103.
94. Duncan ID, Griffiths IR, Madrid RE. A light and electron microscopic study of the neuropathy of equine idiopathic laryngeal hemiplegia. Neuropathol Appl Neurobiol 1978; 4(6):483–501.
95. Baker GJ. Laryngeal asynchrony in the horses: Definition and significance. In: Snow DH, Persson SHB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta; 1983; 46–50.
96. Dixon PM, McGorum BC, Railton DI, et al. Clinical and endoscopic evidence of progression in 152 cases of equine recurrent neuropathy. Equine Vet J 2002; 34(1):29–34.
97. Ohnesorge B, Deegen E, Miesner K, Geldermann H. [Laryngeal hemiplegia in warm blood horses – a study of stallions, mares and their offspring]. Zentralbl Veterinarmed A 1993; 40:134–154.
98. Bohanon TC, Beard WL, Robertson JT. Laryngeal hemiplegia in draft horses. A review of 27 cases. Vet Surg 1990; 19(6):456–459.
99. Poncet PA, Montavon S. A preliminary report on the possible genetic basis of laryngeal hemiplegia. Equine Vet J 1989; 21:137–138.
100. Sullins K. Endoscopically guided laser debridement of arytenoid chondritis in five standing horses. Abstract 13. In: Proceeding World Equine Airways Society 2001, CD.
101. Haynes P, Snider T, McLure JR. Chronic chondritis of the arytenoid cartilage. J Am Vet Med Assoc 1980; 117: 1135–1142.

102. White NA, Blackwell RB. Partial arytenoidectomy in the horses. Vet Surg 1980; 9:5–12.
103. Tulleners E, Harrison IW, Raker CW. Management of arytenoid chondropathy and failed laryngoplasty in horses: 75 cases (1979–1985). J Am Vet Med Assoc 1988; 192:670–675.
104. Jensen R, Lauerman LH, Braddy PM, et al. Laryngeal contact ulcers in feedlot cattle. Vet Pathol 1980; 17:667–671.
105. Belknap JK, Derksen FJ, Nickels FA, et al. Failure of subtotal arytenoidectomy to improve upper airway flow mechanics in exercising Standardbreds with induced laryngeal hemiplegia. Am J Vet Res 1990; 51:1481–1486.
106. Lumsden JM, Derksen FJ, Stick JA, et al. Evaluation of partial arytenoidectomy as a treatment for laryngeal hemiplegia. Equine Vet J 1994; 26:125–129.
107. Harrison IW, Raker CW. Dorsal glottic stenosis after bilateral arytenoidectomy in two horses. J Am Vet Med Assoc 1988; 192:202–204.
108. Szmeja Z, Kopec T, Wojtowicz JG. Laser resection of the vocal cord growth of the arytenoid cartilage in the treatment of contact ulcer. Otolaryngol Pol 1995; 49:311–313.
109. McClure JJ, Koch C, Powell M, McClure JR. Association of arytenoid chondritis with equine lymphocyte antigens but no association with laryngeal hemiplegia, umbilical hernias and cryptorchidism. Anim Genet 1988; 19:427–433.
110. Lane GF. Fourth branchial arch defects in Thoroughbred horses: 60 cases. In: Proceeding of the World Equine Airways Symposium, CD Edinburgh, Scotland, 2001.
111. Zaw-Tun HA, Burdi AR. Reexamination of the origin and early development of the human larynx. Acta Anat (Basel) 1985; 122:163–184.
112. Hast MH. Early development of the human laryngeal muscles. Ann Otol Rhino Laryngol 1972; 81:524–530.
113. Goulden BE, Anderson LJ, Davies AS, Barnes GR. Rostral displacement of the palatopharyngeal arch: a case report. Equine Vet J 1976; 8:95–98.
114. Baxter GM, Allen D, Farrel RL. Paralaryngeal accessory bronchial cyst as a cause of laryngeal hemiplegia in a horse. Equine Vet J 1992; 24:67–69.
115. Blikslager AT, Tate LP, Tudor R. Transendoscopic laser treatment of rostral displacement of the palatopharyngeal arch in four horses. J Clin Laser Med Surg 1999; 17:49–52.
116. Wilson RG, Sutton RH, Groenendyk S. Rostral displacement of palatopharyngeal arch in a Thoroughbred Yearling. Aust Vet J 1986; 63:99–100.
117. Leveille R, Hardy J, Robertson JT, et al. Transarterial coli embolization of the internal and external carotid and maxillary arteries for prevention of hemorrhage from guttural pouch mycosis in horses. Vet Surg 2000; 29(5):389–397.
118. Greet TRC. Outcome of treatment in 35 cases of guttural pouch mycosis. Equine Vet J 1987; 19(5):483–487.
119. Freeman DE, Ross MW, Dona wick WJ, et al. Occlusion of the external carotid and maxillary arteries in the horse to prevent hemorrhage from guttural pouch mycosis. Vet Surg 1989; 18(1):39–47.
120. Kipper A, Frees K. Hypoglossal neuritis with associated lingual hemiplegia secondary to guttural pouch mycosis. Vet Pathol 1993; 30(6):547–556.
121. Sweeney CR, Freeman DE, Sweeney RW, et al. Hemorrhage into the guttural pouch (auditory tube diverticulum's) associated with rupture of the longus capitis muscle in three horses. J Am Vet Med Assoc 1993; 202(7):1129–1132.
122. Davis EW, Legendre AM. Successful treatment of guttural pouch mycosis with itraconazole and topical enilconazole in a horse. J Vet Intern Med 1994; 8(4):304–305.
123. Freeman DE, Ross MW, Dona wick WJ. 'Steal phenomenon' proposed as the cause of blindness after arterial occlusion for treatment of guttural pouch mycosis in horses. J Am Vet Med Assoc 1990; 197(7):811–812.
124. Walker AM, Sellon DC, Cornellisse CJ, et al. Temporohyoid osteoarthropathy in horses: 33 cases (1993–2000). J Vet Intern Med 2002; 16(6):697–703.
125. Blythe LL, Watrous BJ, Shire MH. Prophylactic partial stylohyoidostectomy for horses with osteoarthropathy of the temporohyoid joint. J Equine Vet Sci 1994; 14:32–37.
126. Blythe LL. Otitis media and interna and temporohyoid osteoarthropathy. Vet Clin North Am Equine Pract 1997; 13:21–42.
127. Power HT, Watrous BJ, de Lahunta A. Facial and vestibulocochlear nerve disease in six horses. J Am Vet Med Assoc 1983; 183:1076–1080.
128. Tetens J, Hubert JD, Eddy AL, et al. Dynamic tracheal collapse as a cause of exercise intolerance in a Thoroughbred. J Am Vet Med Assoc 2000; 216(5):722–724.
129. Steiger RR, Williams MA. Granulomatous tracheitis caused by *Conidiobolus coronatus* in a horse. J Vet Intern Med 2000; 14(3):311–314.
130. Tate LP, Koch DB, Sembrat RF, et al. Tracheal reconstruction by resection and end-to-end anastomosis in the horse. J Am Vet Med Assoc 1981; 178(3):253–258.
131. Holcombe SJ, Derksen FJ, Berney C, et al. Effect of topical anesthesia of the laryngeal mucosa on upper airway mechanics in exercising horses. Am J Vet Res 2001; 62(11):1706–1710.
132. Belknap JK, Derksen FJ, Nickels FA, et al. Failure of subtotal arytenoidectomy to improve upper airway flow mechanics in exercising Standardbreds with induced laryngeal hemiplegia. Am J Vet Res 1990; 51(9):1481–1486.

CHAPTER 28

Lower airway function: responses to exercise and training

Dorothy M. Ainsworth

Physiologic responses to exercise

Overview

During high intensity exercise, the metabolic demands of the horse – oxygen consumption and carbon dioxide production – increase more than 30-fold relative to resting conditions. As a consequence, the ventilatory output must increase in order to meet gas exchange requirements and to aid in heat dissipation. Despite the recruitment of respiratory muscles that produce large inspiratory and expiratory pressures, complemented by the generation of locomotory-associated intrathoracic and intra-abdominal pressures, the ventilatory response of the horse during high intensity exercise is inadequate. This finding, along with the lack of training-induced improvements in respiratory system output, has led many physiologists to conclude that the respiratory system of the horse is the major limiting factor to athletic performance.

Structure and function of the lower respiratory tract

The intrathoracic trachea bifurcates into the right and left mainstem bronchi at the level of the fifth or sixth intercostal space and enters the hilum of each lung. At its division from the trachea, the right bronchus assumes a straighter, more horizontal position relative to the left bronchus. Each bronchus subsequently divides into lobar, segmental, and subsegmental bronchi with the eventual formation of bronchioles. In the distal part of the bronchial tree, the terminal bronchioles lead into poorly developed respiratory bronchioles or open directly into alveolar ducts.[1] The tracheobronchial lining consists of tall columnar, pseudostratified epithelium interspersed with serous and goblet cells.[2] This is supplanted by short ciliated cells and non-ciliated Clara cells of the bronchioles, and then by type I and type II pneumocytes at the level of the alveoli.[3] Type I pneumocytes, with thin cytoplasmic extensions 0.2 to 0.5 μm thick, cover the majority of the alveolar surface.[3] The cuboidal type II cells, with their characteristic lamellar cytoplasmic inclusions that form surfactant, are also considered to be 'stem cells', replacing the type I cells in lung injury. Also scattered throughout the lower respiratory tract are lymphocytes, macrophages, mast cells and occasional eosinophils, cell types that are critical for the development of pulmonary immune responses.[4]

The pulmonary structures are subserved by two vascular beds. The major source of blood is via the pulmonary circulation, a low-pressure, low-resistance system (during resting conditions), which participates in gas and heat exchange at the alveolar level and provides nutrients to the alveolar constituents. The distribution of the pulmonary arterial flow to the various lung regions in the resting horse does not appear simply to reflect the effects of gravitational forces or the effects of pressure gradients between the pulmonary arteries, veins and alveoli as originally proposed.[5] Using microspheres to examine the distribution of pulmonary blood in resting Thoroughbreds, Hlastala and colleagues (1996) found that blood flow to the cranial most portions of the lungs was uniformly low (in three of the four horses) and that blood flow increased linearly with the vertical height of the lung (opposite to gravity).[6] Hlastala also found a great deal of heterogeneity of blood flow within a single isogravitational plane, suggesting that pulmonary blood flow is not simply related to pressure gradients between pulmonary arteries, veins and the alveoli. Otherwise, at a given vertical height, the distribution of blood flow would have been homogeneous. The investigators suggested that the reduction of pulmonary blood flow to the ventral lung regions might reflect the greater

length and resistance of the vessels bringing blood to these areas.

With just mild exercise (trotting), there is a redistribution of blood flow to the dorsal lung region but no improvement in the heterogeneity of blood flow at a given isogravitational plane.[7] The increased flow to the dorsal lung regions may simply reflect regional differences in vascular reactivity,[8] regional differences in structure (volume density of capillaries), and/or changes in pulmonary vascular pressures.[7]

The bronchial circulation, a high-pressure circulatory bed, is the second source of blood flow to the lungs. At its origin from the aorta, it is a single vessel that subsequently divides into a right and left bronchial artery at the hilar region of the lung. The artery courses along the bronchi and provides nutrients to the lymphatic, vascular and airway components and supplies arterial blood to the pleural surface.[1] In ponies exercising at 6 m/s (7% incline) for nearly 30 min, the bronchial blood flow was found to increase 16-fold relative to resting levels.[9] The increase in blood flow, attributed to a decrease in vascular resistance, was highly correlated with the exercise-induced increases in the pulmonary artery temperature.

The pulmonary structures are innervated by parasympathetic, sympathetic, and non-adrenergic non-cholinergic (NANC) pathways.[10] The relative contributions of these pathways to the airway tone in healthy resting and exercising horses have been examined. Neither muscarinic blockade of the parasympathetic system (the vasoconstrictor system) nor β_2-adrenergic activation of the sympathetic system (the vasodilator system) alters resting airway diameter.

The major function of the lung is gas exchange – uptake of oxygen and elimination of carbon dioxide. During resting conditions, the horse, utilizing a breathing frequency of 12–15 breaths per minute and a tidal volume of nearly 6 liters, produces a total minute ventilation of approximately 72–80 liters per minute.[11] During this same period, the horse consumes approximately 2.1 L/min of oxygen (3000 L/day) and produces approximately 1.7 L/min of carbon dioxide (2400 L/day). Thus the lung provides an important means by which normal arterial oxygen and carbon dioxide tensions and arterial pH are maintained. As discussed below, impairment of this pulmonary function becomes evident in horses exercising at intensities exceeding 60–65% of maximum oxygen consumption.[12]

Additional functions of the lung include metabolism of bioactive amines (pulmonary circulation), production of surfactant and the maintenance of pulmonary defense mechanisms. The lower respiratory tract also aids in thermoregulation through evaporative heat losses. It has been estimated that approximately 25% of the heat load generated during low intensity exercise is dissipated through the respiratory tract.[13]

Pulmonary function testing

In resting horses, respiratory mechanics (tidal and minute volume, breathing frequency, dynamic lung compliance and total pulmonary resistance) have been routinely measured using flow meters and esophageal balloon catheters (Table 28.1) or using the technique of forced oscillation.[18] Measurement of lung volumes other than tidal and minute volume requires the use of the inert gas dilution technique (end-expiratory lung volume, EELV) and the construction of quasistatic pressure–volume curves obtained in anesthetized or heavily sedated horses (total lung capacity (TLC), residual volume (RV)).[19,20] Estimates of TLC range from 45 to 55 liters while those of RV range from 9 to 10 liters (Fig. 28.1). The variability in the lung volume measurements may be due, in part, to positional and anesthetic effects.[19,21] End-expiratory lung volume measurements in awake horses using helium dilution or nitrogen washout techniques yield values ranging from 20 liters to 35 liters.[15,17,22] Note that in horses the term EELV rather than functional residual capacity (FRC) is used to describe the volume of gas remaining in the respiratory system at the end of expiration. As expiration in humans is a passive process, FRC represents the volume resulting from the outward recoil of the chest wall and inward recoil of the lungs. Thus horses, in contrast to humans, breathe below rather than from the FRC of the respiratory system.[23] Vital capacity of the horse, the amount of air that could be inhaled

Table 28.1 Range of ventilatory parameters in horses during eupneic breathing

V_T (L)	4.9	5	4.1	5.7
fb (per min)	15.5	14.5	14.7	9.6
$\dot{V}_E$ (L/min)	75	68	60	55
C_{dyn} (L/cmH_2O)	2.3	1.3	–	3.2
R_L (cmH_2O/L/s)	–	0.36	0.61	0.43
Reference	14	15	16	17

V_T, tidal volume; fb, breathing frequency; $\dot{V}_E$, expired minute ventilation; C_{dyn}, dynamic compliance; R_L pulmonary resistance.
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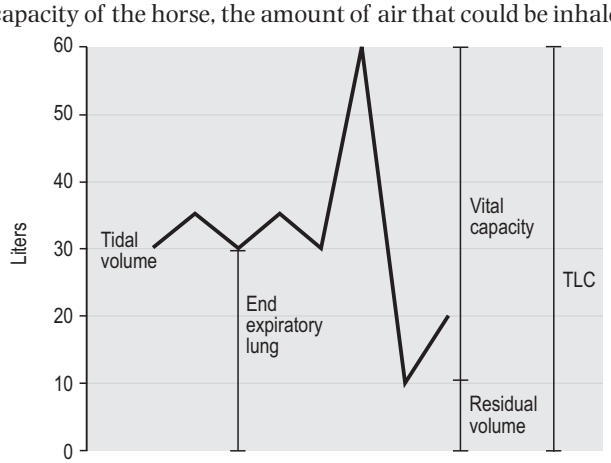
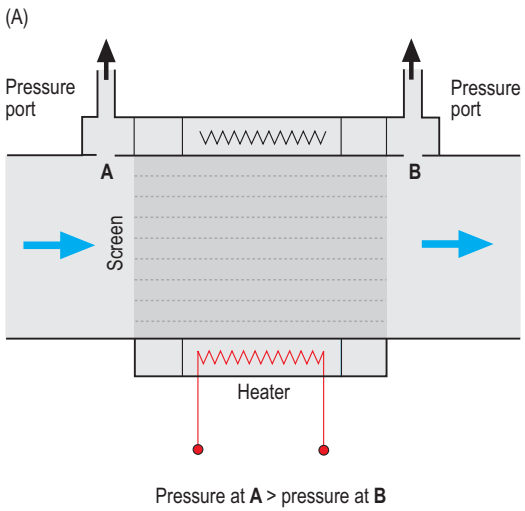


Fig. 28.1
Equine lung volumes. The total lung capacity (TLC) of the horse is approximately 60 liters. During eupneic breathing, the horse uses a tidal volume of 5 liters that may increase to 18 liters during strenuous exercise. End-expiratory lung volume during eupneic breathing is 30 liters but has not been measured during exercise.



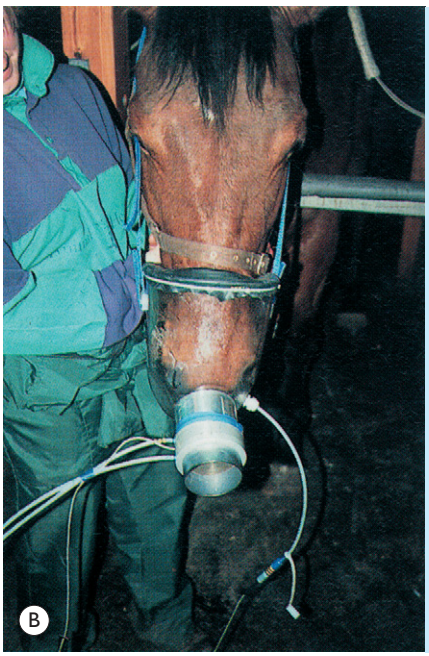


Fig. 28.2
Flow meter. Diagram (A) and photograph (B) of a pneumotach attached to a breathing mask. This device is used to measure airflow in resting and exercising horses. The pressure difference across a heated screen is detected during breathing and transduced to a flow signal. Pneumotachs may become coated with airway secretions. (Reproduced with permission from Marlin and Roberts.[27])

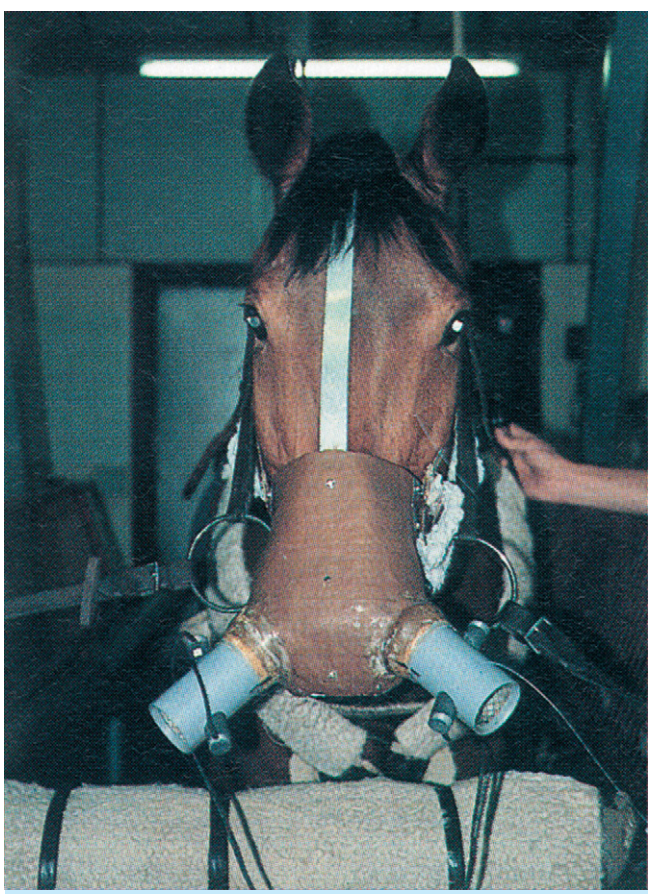


Fig. 28.3
Ultrasonic flow meter. Photograph of a horse wearing a breathing mask with two ultrasonic flow meters centered over each nostril. This may offer less resistance to breathing than the pneumotach, but may suffer from baseline drift. (Reproduced with permission from Marlin and Roberts.[27])

following a forced expiration, ranges from 35 to 45 liters (Fig. 28.1).

Accurately measuring exercise-associated ventilatory parameters such as V_T, fb, C_{dyn}, R_L in the horse has proven to be challenging for several reasons. Breathing masks increase the respiratory tract dead space and cause rebreathing of carbon dioxide.[24] The breathing mask may also alter the horse's respiratory pattern such that locomotory:respiratory coupling during high intensity exercise does not occur.[25,26] Flow meters that are attached to the breathing mask – either pneumotachs (Fig. 28.2A, B) or ultrasonic flow devices (Fig. 28.3) – also may be problematic.[27] Pneumotachs offer a resistance to breathing and when they become coated with airway secretions, overestimate actual airflow.[24] Open flow systems,[28] traditionally used to measure metabolic rates during exercise (Fig. 28.4), have been intermittently converted to closed ventilatory systems, using pneumotach-like devices. The respiratory parameters of 5–10 breaths are obtained before gas exchange impairment occurs (rebreathing CO_2) or before respiratory secretions accumulate on the pneumotachograph.[24] Ultrasonic flow detectors have also been used in place of pneumotachs. These devices may exhibit baseline drift due to moisture buildup and, because they are sensitive to gas densities, are unable to be used in studies examining the effects of various gases (heliox) on respiratory mechanics.[27]

Because of technical difficulties, exercise-associated changes in lung volumes (TLC, EELV) have not been measured in the horse, confounding the interpretation of flow:volume loops. (See 'Mechanical factors limiting ventilation', below.) It is not known if TLC remains unchanged in the horse as it does in the human as the determinants of TLC – respiratory muscle strength, lung and chest wall

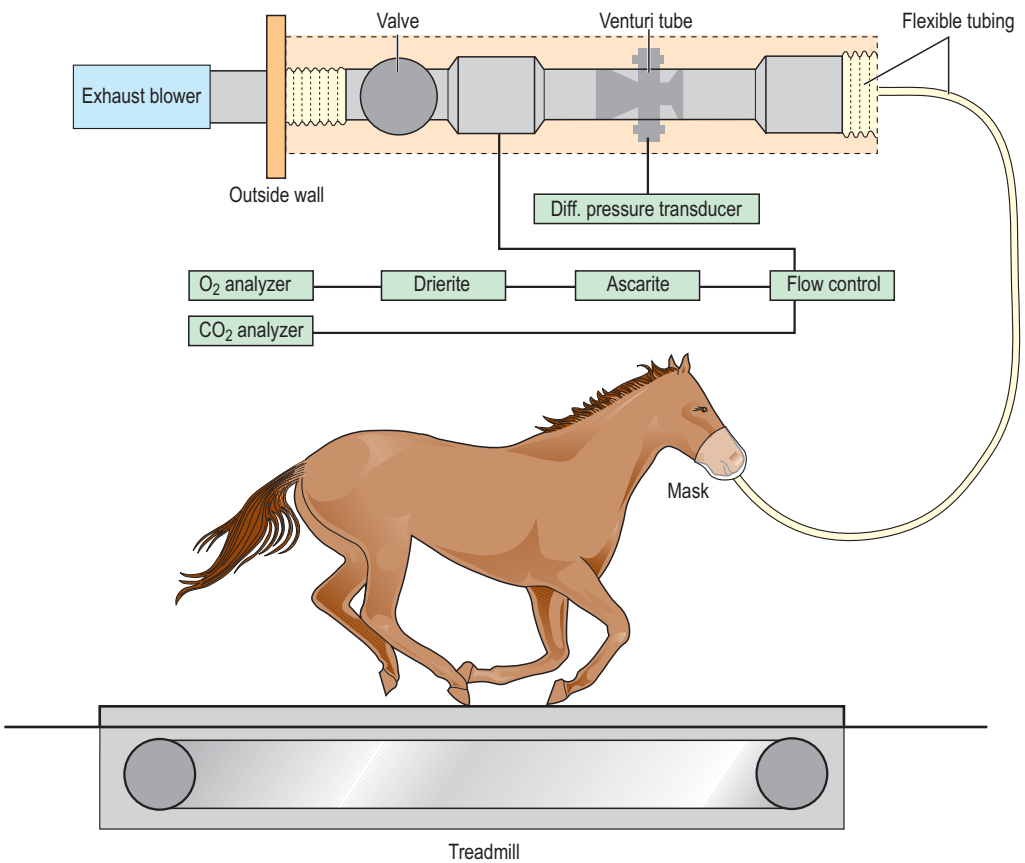


Fig. 28.4
Diagram of an open flow system used to measure expired carbon dioxide and consumed oxygen during exercise. (Reproduced with permission from Seeherman and Morris.[28])

recoil – have not been measured in exercising horses.[29] In humans, FRC decreases with exercise but when high workloads are imposed, EELV may then increase towards or above normal due to expiratory flow limitations.[30] Although EELV has not been measured in the horse, exercise-induced increases in the end-expiratory costal diaphragmatic length (i.e. lengthening of the diaphragm prior to initiation of inspiration) detected by sonomicrometry techniques, suggest that EELV decreases.[31] The actual volume change in EELV is unknown.

Response of the respiratory system to exercise

Metabolic demand

The exceedingly high metabolic demands of strenuous exercise in the horse must be met by corresponding increases in the output of the respiratory and cardiovascular systems. The magnitude of exercise-induced changes in mean oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$) and in heart rate (HR), as a function of running speed are depicted in Fig. 28.5. Note that $\dot{V}O_2$ and $\dot{V}CO_2$ increase linearly up to speeds of 10 m/s and thereafter change little, as evidenced by the plateau.[32] Exercise speeds required to produce 115% $\dot{V}O_{2\,max}$ would thus be extrapolated by extending the linear portion of the exercise speed–VO_2 relationship. The average maximum oxygen consumption in horses performing incremental exercise tests has been reported to be 138 mL/kg/min in Standardbreds[33] and 142 mL/kg/min in Thoroughbreds.[34] Values as high as 190 mL/kg/min for individual horses have been recorded. Relative to the resting value of 4–5 mL/kg/min,

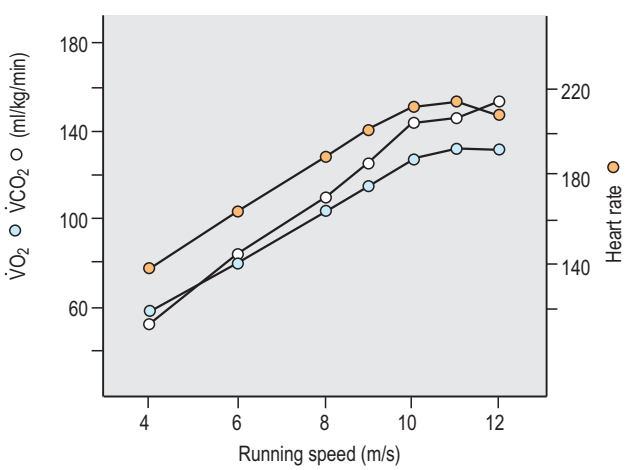


Fig. 28.5
Metabolic demands of exercise. The mean exercise-associated increases in carbon dioxide production ($\dot{V}CO_2$), oxygen consumption ($\dot{V}O_2$) and heart rate (HR) in Thoroughbred horses performing an incremental exercise test. (Reproduced with permission from Rose et al.[32])

Table 28.2 Blood gas data from Thoroughbreds performing an incremental exercise test on a treadmill

	Rest	6 m/s	8 m/s	14 m/s, 3.5° incline	Recovery 5 min walk
pHa (mmHg)	7.42	7.44	7.41	7.21	7.13
$Paco_2$ (mmHg)	43.9	36.5	39.6	50.0	23.8
Pao_2 (mmHg)	101.2	104.2	100.9	73.5	96.9
Cao_2 (mL/dL)	20.6	26.4	27.1	26.5	27.5
Sao_2 (%)	99.0	99.0	98.2	89.3	96.9
Pvo_2 (mmHg)	40.3	27.7	23.1	14.0	49.6
Cvo_2 (mL/dL)	16.4	14.3	9.4	2.3	17.4

pHa, arterial pH; $Paco_2$, arterial carbon dioxide tensions; Pao_2: arterial oxygen tensions; Cao_2, arterial oxygen content; Sao_2, arterial oxygen saturation; Pvo_2, mixed venous oxygen tensions; Cvo_2, mixed venous oxygen content. Reproduced with permission, from Manohar et al.[37]

this represents a 30-fold increase in oxygen consumption during strenuous exercise!

Exercise-associated increases in $\dot{V}o_2$ are mediated by increases in both oxygen delivery and tissue extraction. Delivery of oxygen is enhanced not only by increases in cardiac output, but also by increases in hemoglobin (red cell numbers) that result from splenic contraction. The spleen, which stores approximately one-third to one-half of the horse's total red blood cells, is the source of the 1.7-fold increase in hemoglobin at the onset of exercise.[35] Indeed, splenectomy[36] reduces maximum oxygen consumption by approximately 31%. As each gram of hemoglobin is capable of binding 1.3 mL of oxygen, the total arterial oxygen content (Cao_2), the sum of dissolved and bound oxygen, increases from a resting value of approximately 21 mL/dL to a value of 27 mL/dL in strenuously exercising horses (Table 28.2).[37]

Extraction of oxygen at the tissue level is enhanced by a right shift of the oxyhemoglobin dissociation curve (Fig. 28.6), responding to increases in carbon dioxide tensions, hydrogen ion concentrations or elevations in tissue temperatures. The net result is that the amount of dissolved oxygen (Po_2) is increased as oxygen is 'unloaded' from the hemoglobin. This improves the oxygen gradient between the tissue capillary and the cell mitochondria, enhancing diffusion into the cell. In the horse, the primary mediator of the Bohr effect, the rightward shift of the oxyhemoglobin dissociation curve, appears to be the metabolic acidosis of exercise.[38]

The magnitude of tissue oxygen extraction during exercise, the difference between the arterial (Cao_2) and venous oxygen content (Cvo_2), can be appreciated from the data presented in Table 28.2. At rest, the horse utilizes approximately 4 mL/dL of oxygen as opposed to the nearly 25 mL/dL consumed when the horse gallops at 14.5 m/s on a grade. Understandably, venous oxygen tensions are reduced from 40 torr at rest to 12 torr during maximal exercise. Although, as anticipated, ventilation increases during exercise, the response is insufficient to prevent the development of arterial hypoxemia (Pao_2 < 85 mmHg) and hypercapnia ($Paco_2$ > 45 mmHg). (See 'Gas exchange during exercise', below.)

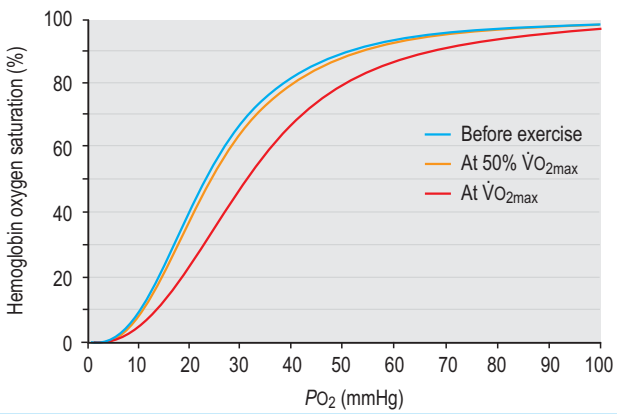


Fig. 28.6
Oxyhemoglobin dissociation curve. With exercise, there is an increase in tissue temperature, carbon dioxide production, hydrogen ion concentration which facilitates unloading of oxygen (right shift of oxyhemoglobin dissociation curve) at the tissue capillary. (Reproduced with permission from Fenger et al.[38])

Ventilatory output

During exercise, the magnitude of the increase in ventilatory output will be a function of the intensity and of the duration of exercise. Representative changes in ventilatory parameters are shown in Table 28.3 for Thoroughbreds[11] and in Table 28.4 for Standardbreds[39] performing an incremental exercise test.

As shown in Table 28.3, tidal volume (V_T) and minute ventilation ($\dot{V}_E$) increase linearly with treadmill speed and correlate with increases in inspiratory muscle activity.[40] Breathing frequency (fb) increases linearly with speed from rest to 8 m/s but, at faster speeds, only slight increases in breathing frequency occur. In Thoroughbreds, breathing frequency is entrained or linked to stride frequency during the canter and gallop, a phenomenon termed locomotory:respiratory coupling (LRC).[41] Breathing frequency may or may not be coupled to stride frequency during trotting and is usually not linked to stride frequency during walking.[42] Interestingly,

Table 28.3 Ventilatory parameters of Thoroughbred horses during an incremental exercise test and during recovery

	Rest	Walk 1.6 m/s	Trot 3.4 m/s	Canter 8 m/s	Gallop 10 m/s	Gallop 12 m/s	Gallop 10 m/s, 2°	Gallop 10 m/s, 4°	Recovery 10 min walk
V_T (L)	4.8	5.8	6.4	9.2	11.5	12.4	12.3	13.2	6.5
fb (per min)	16	65	91	113	122	126	118	121	126
$\dot{V}_E$ (L/min)	77	361	564	1042	1335	1562	1453	1585	777
Peak $\dot{V}_E$ (L/s)	5.1	14.3	27.6	45.3	55	65.2	60.2	63.9	39.2
Peak $\dot{V}_I$ (L/s)	5.1	17.9	30.5	52.5	66.6	77.9	68.5	78.8	31.6
Δmax Ppl (cmH_2O)	4.4	15.6	24.2	56.1	73.4	84.2	77.5	83.9	22.0
Wrm (J/L)	0.41	1.20	2.41	3.82	5.16	6.07	5.37	6.22	2.1
R_L (cmH_2O s/L)	0.20	0.25	0.30	0.49	0.53	0.52	0.53	0.55	0.25
$\dot{V}O_2$ (mL/kg/min)	4.6	20.2	25.3	85.4	114.3	124.2	124.4	139.3	27.7
$\dot{V}CO_2$ (mL/kg/min)	3.8	15.9	23.1	80.6	113.5	136.2	123.9	142	29.8
PaO_2 (mmHg)	92	102	99	83	77	69	72	70	116
$PaCO_2$ (mmHg)	47	46	43	46	49	53	49	49	33

V_T, tidal volume; fb, breathing frequency; $\dot{V}_E$, expired minute ventilation; peak $\dot{V}_E$, peak expiratory flow; peak $\dot{V}_I$, peak inspiratory flow; $\Delta P_{Pl\ max}$, difference between peak inspiratory and peak expiratory pressure; Wrm, work of breathing; $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production.
Note during the last two exercise levels, the treadmill was inclined 2 and 4 degrees respectively.
Reproduced with permission, from Art et al.[11]

despite the development of LRC, stride length and V_T are not tightly coupled during the canter or gallop. This enables V_T to be increased independently in response to metabolic need or demand.[43] That is, in horses galloping at a constant speed on a treadmill, increases in the treadmill incline (and in $\dot{V}O_2$) induce increases in minute ventilation and in V_T without altering stride length.

In contrast to the exercising Thoroughbred, the trotting Standardbred utilizes a slightly different breathing pattern.[39] At submaximal exercise, trotters entrain breathing frequency with stride frequency 1:1 but this ratio changes to 1:1.5, 1:2 or 1:3 at maximum exercise.[44] This increases inspiratory and expiratory times and generates a greater tidal volume. At comparable metabolic workloads ($\dot{V}O_2$ of Thoroughbreds = 140 mL/kg/min, $\dot{V}O_2$ of Standardbreds = 133 mL/kg/min), trotters exhibit a slower breathing frequency and a slightly greater V_T than Thoroughbreds (Tables 28.3, 28.4). At comparable speeds (10 m/s, 0 degrees incline), the ventilatory output of the Standardbreds exceeds that of the Thoroughbred horses but the greater response is commensurate with the increased metabolic workload (166 mL/kg/min versus 114 mL/kg/min).

Exercise-associated alterations in alveolar ventilation ($\dot{V}_A$) have also been measured in horses. In a study of Thoroughbreds performing an incremental exercise test, Butler and colleagues reported a 20-fold increase in $\dot{V}_A$ from the resting value (38 L/min) when horses galloped 12 m/s for 2 minutes.[43] The physiologic dead space to tidal volume ratio (V_D/V_T) initially increased from the resting value of 0.41 when horses trotted, but then returned to the resting value as exercise intensity increased. Although V_T, $\dot{V}_A$ and V_D increase proportionately with exercise, the increase in alveolar ventilation, relative to the increase in $\dot{V}CO_2$, is insufficient to prevent hypercapnia from developing (Tables 28.2, 28.3, 28.4). (See 'Gas exchange during exercise', below.)

During exercise, total pulmonary resistance (R_L) and the work of breathing increase exponentially with ventilatory

Table 28.4 Ventilatory parameters of Standardbred horses during an incremental exercise test

	Rest	Walk 1.7 m/s	Trot 4 m/s	Trot 7 m/s	Trot 8 m/s	Trot 9 m/s	Trot 10 m/s
V_T (L)	5	5	9	13	15	17	20
fb (per min)	19	79	79	79	90	90	90
$\dot{V}_E$ (L/min)	95	395	711	1027	1350	1530	1800
pHa (mmHg)	7.37	7.42	7.41	7.37	7.32	7.24	7.22
$PaCO_2$ (mmHg)	44	45	43	46	47	48	51
PaO_2 (mmHg)	99	110	99	88	84	80	75
BE (mmol/L)	1.2	1.9	1.9	0.9	–1.4	–4.1	–7.1
$\dot{V}O_2$ (mL/kg/min)	11	29	55	104	133	157	166
$\dot{V}CO_2$ (mL/kg/min)	9	23	53	95	134	168	185

V_T, tidal volume; fb, breathing frequency; $\dot{V}_E$, expired minute ventilation; pHa, arterial pH; $PaCO_2$, arterial carbon dioxide tensions; PaO_2, arterial oxygen tensions; BE, base excess. After an 8-minute warm-up period horses exercised for 1 minute at each of the speeds.
Reproduced with permission from Art and Lekeux.[39]

output (Table 28.3). The exercise-associated increase in R_L is attributed to the generation of turbulent flow in the upper respiratory tract during inspiration and the narrowing of intrapulmonary airways during expiration.[11,45,46] Understandably, pretreatment of healthy exercising horses with bronchodilators – clenbuterol, albuterol, or ipratropium – fails to reduce total pulmonary resistance or the work of breathing.[46,47] Note also in Table 28.3 that the work of breathing increases 15-fold from the resting value when the horse gallops at 12 m/s. Minimizing the work of breathing during high intensity exercise has been suggested as a contributing cause to gas exchange failure in the athletic horse.[48]

Control of breathing during rest and during exercise

Rhythmic breathing during eupnea has been attributed to the workings of a central pattern generator that, through its effects on the intermediary bulbospinal neurons of the medulla, ultimately activates inspiratory and expiratory motoneuron pools of the spinal cord. In the resting horse both inspiration and expiration are active processes reflecting the electromechanical activation of the diaphragm (inspiratory muscle) and of the transverse abdominal and external oblique muscles (expiratory muscles).[22,23] The role of the rib cage muscles in generating the breath has not been well studied in the horse.

During eupneic breathing, the initial generation of inspiratory flow precedes electrical activation of the diaphragm and is attributed to outward recoil of the chest wall and relaxation of abdominal expiratory muscles (Fig. 28.7). With diaphragmatic activation, inspiratory airflow again increases, causing the biphasic flow pattern. During expiration, relaxation of the diaphragm contributes to the initial generation of expiratory flow. Once expiratory muscles are activated, there is a further increase in expiratory flow.

When horses are exercised, linear increases in the diaphragmatic electromyogram (EMG) are associated with linear increases in the transdiaphragmatic pressure (Fig. 28.8).[40] Abdominal muscles are also recruited during the exercise hyperpnea. In ponies walking on the treadmill, there is a temporal correlation between the development of peak transverse abdominal EMGs and peak positive esophageal pressure, suggesting an expiratory function for this muscle.[49] In contrast, the EMGs of the rectus abdominis and abdominal oblique muscles in horses during mild to high intensity exercise exhibit a locomotory-associated modulation.[50]

The generation of a breath during eupnea or during the exercise hyperpnea is shaped by inputs from: (i) central and peripheral chemoreceptors; (ii) mechanoreceptors of the intra- and extrathoracic airways and lung parenchyma; (iii) phrenic afferents; (iv) locomotory-associated stimuli; and (v) higher central nervous system (CNS) centers.

Chemoreceptors Chemoreceptors are sensors that detect changes in CO_2, O_2 and pH and have been classified, based upon anatomical location, as either central or peripheral. At a given pH, the ventilatory response of the central chemoreceptors, presumed to be located in the medulla, is greater during a respiratory acidosis than during a metabolic acidosis. The augmented response is attributed to the more soluble CO_2 that easily permeates the blood–brain barrier, activating the central chemoreceptors. In awake chronically instrumented horses, activation of central chemoreceptors by hypercapnic challenge augments both inspiratory and expiratory muscle activation

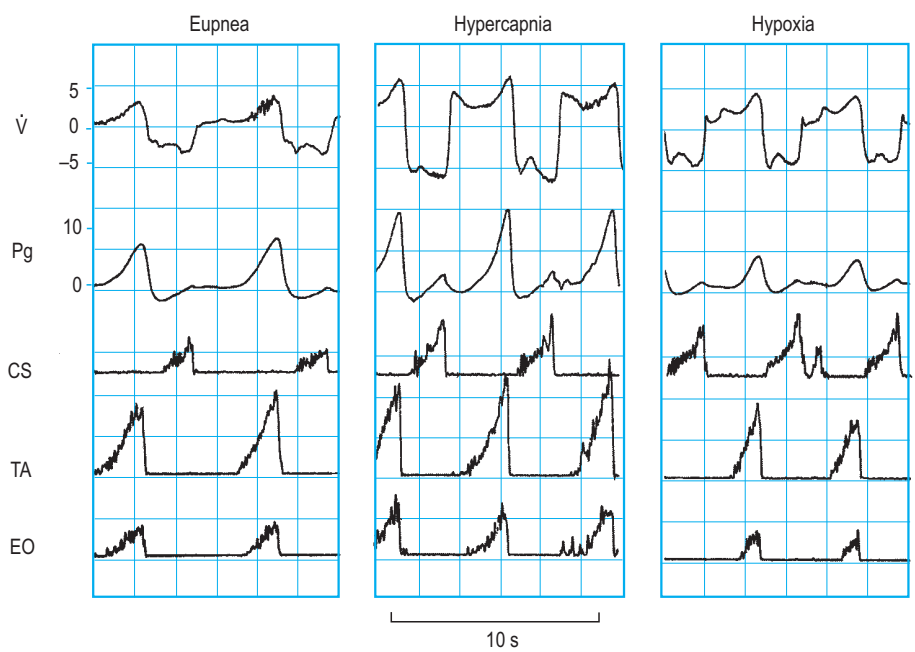


Fig. 28.7
Relationship between respiratory flow ($\dot{V}$), gastric pressure changes (Pg) and respiratory muscle (costal diaphragm (CS), transverse abdominal (TA) and external abdominal oblique (EO)) EMGs during eupneic, hypercapnic and hypoxic breathing. At rest, initial inspiratory flow precedes activation of the diaphragm and is attributed to relaxation of expiratory muscles (decrease in Pg). Similarly, the initial generation of expiratory flow precedes abdominal expiratory muscle activation and is attributed to relaxation of inspiratory muscles. With hypercapnic challenge, inspiratory and expiratory muscles are recruited to increase tidal volume and minute ventilation. Hypoxia causes an increase in inspiratory muscles but less of an increase in abdominal expiratory muscles. (Reproduced with permission from Ainsworth et al.[22])

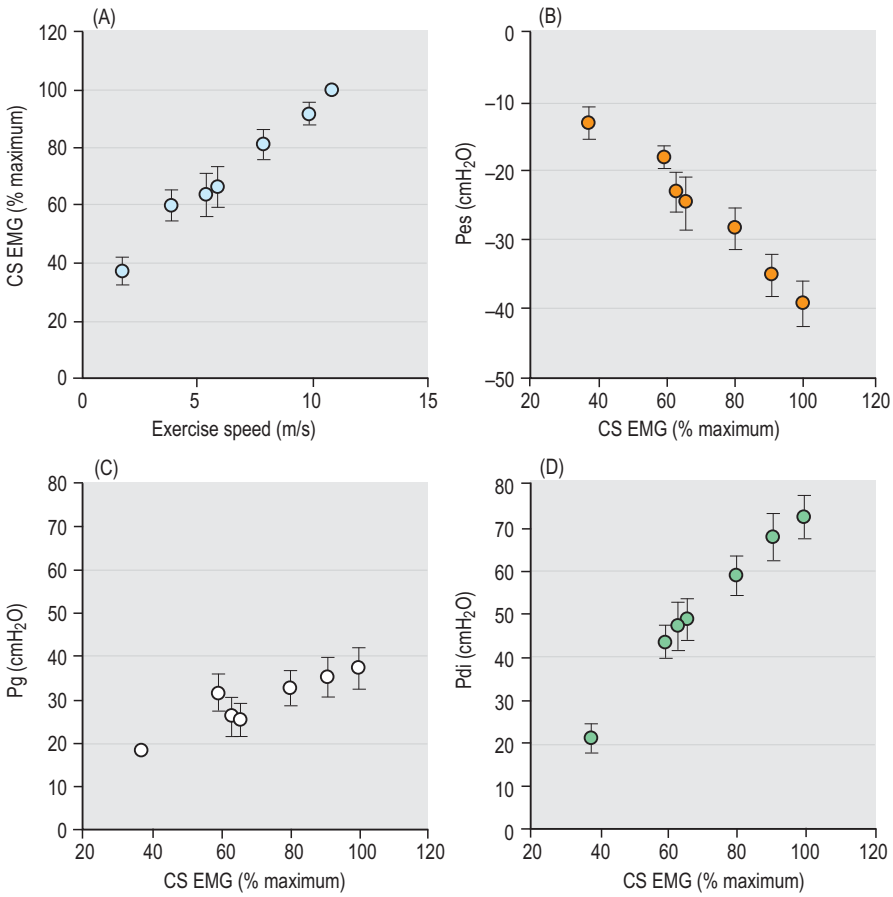


Fig. 28.8
Relationship between diaphragmatic activation and mechanical output during incremental exercise in horses. In panel A, the linear increase in the diaphragm (CS) EMG that occurs as horses exercise at faster treadmill speeds is demonstrated. The increase in electrical activity of this inspiratory muscle is associated with a progressive decrease in peak esophageal pressure (panel B), a progressive increase in peak inspiratory gastric pressure as the diaphragm descends into the abdominal cavity during inspiration (panel C) and a linear increase in the mechanical output of the diaphragm, the transdiaphragmatic pressure (Pdi) during exercise. (Reproduced with permission from Ainsworth et al.[50])

(Fig. 28.7), leading predominantly to a V_T response with little change in breathing frequency.[22]

Peripheral chemoreceptors are located at the bifurcation of the carotid arteries and predominantly detect changes in oxygen tensions. Activation of peripheral chemoreceptors via hypoxic challenge increases the magnitude and frequency of inspiratory muscle activation with little change in abdominal expiratory muscle activity (Fig. 28.7).[22]

Although arterial hypoxia and hypercapnia develop during exercise,[12,51] it does not appear to be the result of impaired chemoreception. When horses breathe a hyperoxic mixture (inspired fraction (F_IO_2) = 0.3) while galloping at 14 m/s, there is a reduction in $\dot{V}_A$ relative to normoxic trials – an expected response. When the F_IO_2 is reduced from 0.21 to 0.16 in those horses galloping at 14 m/s (causing a corresponding decrease in Pao_2 from 56 to 38 torr), tidal volume and minute ventilation increase 20%, confirming that an intact hypoxic drive exists.[48] Interestingly, when exercising horses (14 m/s) breathe a hypercapnic gas mixture (F_ICO_2 = 0.06) causing $Paco_2$ to increase from 50 to 80 torr, ventilation fails to increase in the majority of horses studied.[52] The occasional horse will uncouple breathing with limb movement to increase tidal volume.

The question of why the horse does not increase ventilation in response to the decrease in Pao_2 (65% $\dot{V}O_{2\,max}$) – when mechanical flow limitations do not exist – is unknown. Some investigators have suggested that this breathing strategy simply reflects that of a 'smart' ventilatory controller that 'chooses' to minimize the mechanical cost of breathing rather than to optimize blood gas tension and acid–base balance.[48]

The question of why the horse develops hypercapnia at near maximal exercise is discussed below in the section on 'Mechanical factors limiting ventilation'.

Mechanoreceptors Breathing pattern is also influenced by mechanoreceptive input from receptors within the airways of the respiratory system, within the costovertebral articulations and within the rib cage and abdominal musculature (spindles, Golgi tendon organs). Within the lung, three types of pulmonary mechanoreceptors have been identified: the slowly adapting receptors (SARs), the rapidly adapting receptors (RARs) and the non-myelinated C fibers.[53] Vagally mediated inputs from the SARs, responding to increases in lung inflation, feed back onto the central respiratory controller to terminate inspiration and to activate expiratory muscles. The RARs are mechanoreceptors with a primary function of mediating augmented breaths or sighs. Changes in lung compliance during eupneic breathing are thought to be sensed by RARs which then initiate sighs. Pulmonary and bronchial C fibers, vagally mediated non-myelinated fibers, are activated by substances produced, released and catabolized in the lungs (bronchial C fibers) or by mechanical alterations in the lung parenchyma that occur with congestion and edema (pulmonary C fibers). Their contribution to the

control of breathing in the horse has not been investigated but in other species, activation results in a tachypneic pattern.[53]

In resting ponies, elimination of mechanoreceptor input, either by vagal cooling or by local anesthesia, prolongs inspiratory time, decreases breathing frequency and R_L, increases V_T but has no effect on arterial blood gas tension, minute ventilation and dynamic compliance.[54] In ponies performing mild treadmill exercise (walking, trotting), removal of vagally mediated afferent inputs via hilar denervation produces similar effects. There is an increase in V_T, a decrease in breathing frequency and a preservation of minute ventilation and arterial blood gases.[55] Thus, during low intensity exercise, mechanoreceptor inputs are not critical for the exercise hyperpnea to develop. However, the effects of vagal deafferentation on the pattern of breathing (locomotory:respiratory coupling) or on gas exchange in horses performing high intensity exercise remains to be determined.

Phrenic afferents The diaphragm and the non-respiratory muscles are innervated by small afferents (types III and IV) that respond to mechanical and chemical stimuli.[56] Although the majority of studies examining the effects of phrenic afferents on the control of breathing have been obtained in studies of anesthetized cats and dogs, the data confirm muscle afferents to be powerful stimuli to ventilation. In lightly anesthetized dogs, electrical stimulation of phrenic afferents causes a 500% increase in ventilation – a response equivalent to that induced with breathing 10% CO_2![57] Nevertheless, it does not appear that diaphragmatic afferents are the primary drive for the exercise hyperpnea as diaphragmatic deafferentation does not affect ventilation or arterial carbon dioxide tensions in ponies that are mildly exercised.[58,59]

Locomotory-associated stimuli Thoroughbred horses routinely entrain or couple breathing frequency with limb movement.[41,42] The mechanism of this coupling has not been established but it has been postulated to involve spinal afferents. Evidence for this comes from a study in ponies with partial spinal cord ablation. The net effect of the intervention is to attenuate the exercise-induced increases in breathing frequency, suggesting that feedback from limb movement modifies the exercise hyperpnea.[60]

In addition to neural inputs that would affect the pattern of breathing during exercise, locomotory-associated forces have also been suggested to significantly contribute to the exercise hyperpnea. A number of benefits could possibly derive from integration of locomotion and respiration since locomotion might affect the mechanical characteristics of the respiratory system by stiffening the chest wall, by reducing respiratory system compliance and by increasing the work of breathing.

Three exercise-associated forces postulated to generate airflow in horses during locomotion include: (i) the to and fro movements of the liver and intestines (visceral piston) effecting diaphragmatic movement; (ii) the concussive forces resulting from limb impact that are transmitted to the thoracic cavity to produce pressure and volume changes; and (iii) the compressive forces developing within the abdominal cavity during lumbosacral flexion and extension that ultimately produce pressure and volume changes within the thoracic cavity. Although this biomechanical model of ventilation fits well with the observed locomotory movements and respiratory airflow patterns in galloping horses, little conclusive evidence exists to support their relative contributions to the exercise hyperpnea. Young and colleagues have estimated that the visceral displacements are 230 degrees out of phase with ventilation.[61] They suggested that lumbosacral flexion and extension exerted a more significant biomechanical effect on ventilation. Frevert and colleagues also studied the breathing pattern of galloping horses that occasionally departed from the 1:1 LRC ratio.[62] By ensemble averaging the horse's respiratory flow signals using limb frequency as a trigger, they were able to calculate the contribution of limb concussive forces to ventilation. They found that stride-related volume excursions averaged 10–20% of the tidal volume. Finally, EMG recordings of respiratory muscles obtained in chronically instrumented exercising horses have clearly demonstrated that increases in phasic electrical activity of the diaphgram correlate with increases in transdiaphragmatic pressure generation independent of LRC (Fig. 28.8).[40]

CNS inputs Behavioral and thermal inputs from higher CNS centers influence the pattern of breathing during eupnea and may also exert modifying influences on ventilation during prolonged exercise in the horse.[13,63] For example, when Thoroughbreds exercise at 40% $\dot{V}O_{2\,max}$ for 60 minutes, arterial carbon dioxide tensions decrease 10 torr further from 'steady-state' levels occurring 10 minutes into exercise. During this time, the pulmonary artery temperatures increase 2.6°C and the work of breathing nearly doubles, suggesting to the investigators that the stimulus for the ventilatory increase is a thermoregulatory one.[63]

Other CNS inputs, specifically those radiating from locomotory-associated areas in the CNS, have also been suggested to exert a major role in the development of the exercise hyperpnea. This idea, called the central command concept, was first proposed by Johansson and later refined in 1913 by Krogh and Lindhard.[64] Increases in ventilation during exercise are hypothesized to arise secondary to neural impulses emanating from suprapontine structures which 'command' muscles to exercise. These impulses radiate to respiratory and cardiovascular centers and thus stimulate neuronal activity, driving ventilation and respiratory muscles concurrently. The hypothesis was based primarily on the rapidity of the ventilatory and circulatory responses, which could not be accounted for by humoral mechanisms.[65] Support for the central command theory comes from studies of decorticate cats that walk on a treadmill spontaneously or during electrical or chemical stimulation of the hypothalamic locomotor regions.[66,67] In these studies: (i) the respiratory and cardiovascular responses preceded spontaneous locomotion – suggesting that the 'hyperpnea' was not dependent upon afferent feedback – and (ii) the ventilatory response was proportional to the locomotory response. While appealing, the data have two major limitations. The decorticate cat might not duplicate physiological exercise and the metabolic rate was only minimally increased during the locomotion.[65]

Gas exchange during exercise

When Thoroughbreds or Standardbreds exercise at intensities exceeding 65% of the maximum oxygen consumption ($\dot{V}O_{2\,max}$), arterial hypoxemia occurs and the alveolar–arterial oxygen difference widens.[12,44] As exercise intensity exceeds 85% of $\dot{V}O_{2\,max}$, arterial hypercapnia ensues.[12,44,51,68] This is evident in the data presented in Tables 28.2, 28.3, and 28.4. Gas exchange failure occurs in horses performing treadmill incremental tests, treadmill sprint tests[69] as well as in horses exercising on a racetrack.[12,68,70]

In contrast to the horse, strenuously exercised ponies do not develop hypoxemia and hypercapnia, but rather develop an 'appropriate' ventilatory response characterized by normoxemia and hypocapnia[71] (Table 28.5). The ventilatory equivalent – the volume of expired (or inspired) gas per volume of oxygen consumed – is 1.6-fold greater for the pony as compared to a Thoroughbred! Why the horse fails to develop an appropriate ventilatory response at submaximal exercise (i.e. hypoxemia) is unknown and does not appear to be due to a failure of chemoreception. The inadequate ventilatory response may simply reflect a breathing strategy that minimizes the exponential increase in work of breathing during exercise.[48]

The mechanisms causing the arterial hypoxemia have been extensively investigated in exercising horses using a variety of approaches such as increasing the F_IO_2 or replacing inspired nitrogen with helium.[72,73] It was not until the multiple inert gas elimination technique was adapted for use in the exercising horse that the mechanisms causing the reduced Pao_2 and the widened alveolar–arterial oxygen difference (A–aDo_2) could be partitioned out.[44,74] In this technique, the airway elimination of inert gases that are dissolved in saline and infused into the venous blood is measured. The rate of elimination is dependent upon the ventilation: perfusion ratio and upon the solubility of that inert gas in the blood.[75]

Hypoventilation Although the increase in arterial (and alveolar) carbon dioxide tensions would contribute to the development of hypoxemia during exercise by reducing alveolar oxygen tensions, hypoventilation is not the major cause of hypoxemia.[51] In fact, it only accounts for a 6–7 torr reduction in arterial oxygen tensions at the highest exercise levels. The possible causes of the hypercapnia are discussed in the section on 'Mechanical factors limiting flow', below.

Shunts and ventilation:perfusion inequalities Relative to the resting condition, exercise does not cause an increase in intrapulmonary shunts. Thus, these do not contribute to the development of arterial hypoxemia.[44,45] There is, however, a small but significant increase in the degree of ventilation:perfusion mismatch that develops with exercise. In Standardbred trotters working at 96% of maximum $\dot{V}O_2$, ventilation:perfusion mismatch accounts for 36–41% of the observed arterial hypoxemia.[44,76] In Thoroughbreds galloping at 80% of $\dot{V}O_{2\,max}$, approximately 25% of the arterial hypoxemia is attributed to ventilation:perfusion inequalities.[74,77] The cause of the ventilation:perfusion mismatch is unknown but has been hypothesized to be due to the development of low-grade interstitial edema, pulmonary hemorrhage, regional differences in pulmonary blood flow, reduced gas mixing in the large airways or airway obstruction.[44] Overtrained horses that exhibit red cell hypervolemia also have a worsening of exercise-associated ventilation:perfusion inequalities.[76] Typically such horses develop pulmonary arterial pressures during exercise that are significantly greater than normovolemic cohorts and have an increased incidence of exercise-induced pulmonary hemorrhage.[76]

Diffusion limitation The major cause of the exercise-induced hypoxemia in the horse is a diffusion limitation.[12,44,72,74] During exercise, the combination of rapid pulmonary blood flows coupled with a much reduced venous oxygen content have been hypothesized to cause insufficient time to achieve complete equilibration of gas exchange across the capillary–alveolar interface. Interestingly, the mean capillary transit time has been estimated using the relationship Vc/Qt, where Vc is the total capillary blood volume (calculated from morphometric data)[78] and Qt is the cardiac output. Estimates of capillary transit time range from 386 to 404 milliseconds in the horse[72,76] and exceed transit times of 0.29 seconds for the dog or 0.35 seconds for the pony.[79] However, in contrast to the horse, the dog and pony do not exhibit diffusion limitation despite markedly shortened capillary transit times. Some investigators have suggested that the horse may exhibit a greater degree of heterogeneity in the transit time or in the diffusion:perfusion that is not accounted for by simply calculating the mean capillary transit time.[74]

Table 28.5 Comparison of ventilatory responses of ponies and horses at comparable metabolic work rates after 2 min of exercise

Exercise intensity	Group	Pao_2 (mmHg)	$PaCO_2$ (mmHg)	pHa	HCO_3 (mmol/L)	$\dot{V}_E/\dot{V}O_2$
60% $\dot{V}O_{2\,max}$	Thoroughbreds	81	40	7.47	29	27.6
60% $\dot{V}O_{2\,max}$	Ponies	89	32	7.44	22	43.7
115% $\dot{V}O_{2\,max}$	Thoroughbreds	68	50	7.26	21	26.3
115% $\dot{V}O_{2\,max}$	Ponies	95	35	7.30	17	41.9

PaO_2, arterial oxygen tensions; $PaCO_2$, arterial carbon dioxide tensions; pHa, arterial pH; HCO_3, bicarbonate; $\dot{V}_E/\dot{V}O_2$, ventilatory equivalent.

Reproduced with permission from Katz et al.[71]

Mechanical factors limiting ventilation

The cause of the hypoventilation (hypercapnia) during high intensity exercise is unknown but has been postulated to be due to: (i) an increase in dead space ventilation secondary to the high breathing frequency; (ii) a mechanical flow limitation that results from the very short inspiratory and expiratory times; and/or (iii) locomotory:respiratory coupling.

If metabolic workload is held constant and the horse's breathing frequency is manipulated by changing the treadmill incline and speed, there is no effect on arterial carbon dioxide tensions.[80] This suggests that dead space ventilation is not the cause of hypercapnia. The data of Butler and colleagues also demonstrated that the ratio of dead space to tidal volume does not increase with strenuous exercise.[43]

Interestingly, when fb is manipulated by altering treadmill speed and incline while preserving metabolic demand, peak expiratory flow rates change very little (85–95 L/s). This suggests the development of an expiratory flow limitation. As large expiratory pulmonary pressures are generated during exercise, dynamic compression of the non-cartilaginous airways is hypothesized to limit expiratory flow.[80] This hypothesis is supported by data obtained from horses performing strenuous exercise while breathing heliox – a gas mixture consisting of 15% oxygen and 85% helium.[81] By replacing nitrogen with helium, there is a decrease in the gas density of the respired mixtures and a reduction in the turbulent flow. Thus, horses galloping at 8 m/s on a 7% incline while breathing the heliox mixture demonstrate a significant increase in $\dot{V}O_2$, $\dot{V}CO_2$, V_T, $\dot{V}_E$, and fb relative to the normoxic trials. Furthermore, despite an increase in metabolic workload which occurred with the heliox trials, horses were still able to increase alveolar ventilation sufficiently to reduce the severity of the arterial hypercapnia by 4 torr!

Definitive proof of an expiratory flow limitation in exercising horses requires the measurement of flow volume loops relative to changes in end-expiratory lung volume.[41] In human athletes, expiratory flow limitations (Fig. 28.9) occur but may also be reduced or minimized during exercise if EELV is increased.[30,82] However, as the athlete breathes from a higher EELV, the work of breathing is also increased. Although flow:volume loops have been measured in exercising horses (Fig. 28.10), it is not known whether limitation truly occurs and whether the horse can 'adjust' EELV to minimize the limitations to flow.

The question of whether LRC causes hypercapnia during high intensity exercise was addressed in a novel study by Evans and colleagues.[83] They measured arterial blood gases, fb and fs in Standardbred horses that were studied at comparable metabolic workloads either pacing (LRC ratio ≠ 1) or galloping (LRC ratio = 1). At 100% $\dot{V}O_{2\ max}$, the $PaCO_2$ of the galloping horses with strict entrainment was no different from that of the pacing horses that did not entrain breathing with ventilation. This suggested that in Standardbred horses, LRC does not impede alveolar ventilation.[83]

In summary, expiratory flow limitation may be a plausible explanation for the development of hypercapnia during near maximal exercise. However, one cannot discount the possibility that the pattern of breathings elected by the horse during strenuous exercise is also one chosen to minimize the work of breathing, one designed to prevent the development of diaphragmatic fatigue and one that prevents 'steal' of blood flow from the locomotory muscles.

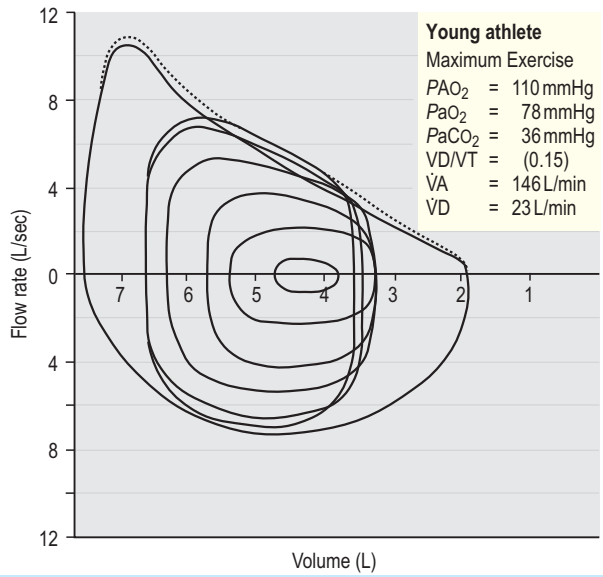


Fig. 28.9
Flow:volume loop from a human athlete performing incremental exercise. Inspiratory flow is below and expiratory flow is shown above the lung volume axis. The dashed line indicates the maximum expiratory flow obtainable in that individual. Eupneic breathing is indicated by the small loop centered near 4.25l. With the onset of exercise, end-expiratory lung volume decreases, but as expiratory flow limitations are reached, end expiratory lung volume increases (loop moves to the left). (Reproduced with permission from Johnson et al.[82])

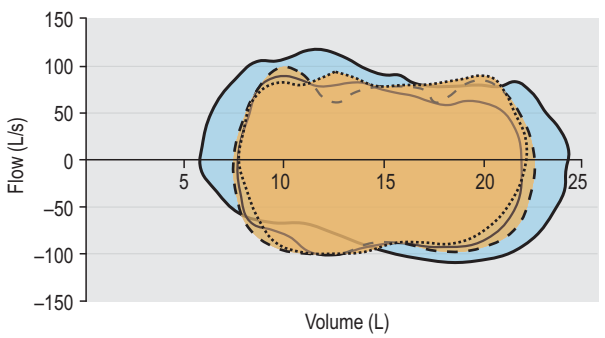


Fig. 28.10
Flow:volume loop from a Thoroughbred horse performing exercise at 115% $\dot{V}O_{2\ max}$. Loops were not placed relative to EELV. The four different loops were obtained while the horse exercised at 0% incline (thin solid line); 5% incline (thick dashed line); 10% incline (thin dashed line) and 20% incline (thick solid line). (Reproduced with permission from Bayly et al.[80])

Physiologic responses to training

Responses and mechanisms

As training is associated with increases in aerobic power, it is logical to assume that the respiratory system would undergo training-induced adaptations to increase its ventilatory output. Evans and Rose (1988) examined the effects of a 7-week submaximal training program on respiratory responses of Thoroughbred horses.[84] Although maximal oxygen consumption increased by approximately 23% (attributed to increases in cardiac output and stroke volume), minute ventilation remained unchanged. Evans and Rose also found a 6 torr reduction in Pao_2 tensions following training in horses exercising at 100% $\dot{V}o_{2\ max}$, but this difference was not statistically significant.[84] Art and Lekeux (1993) also examined the effects of a five-step training program on cardiopulmonary and respiratory parameters in Thoroughbred horses.[85] Each step of the program lasted 3 weeks and consisted of a treadmill acclimatization period, a light exercise period (20 min of turnout), an aerobic training period (walk, trot, canter 3 days/week), an interval training period and a detraining period. A standardized exercise test was performed after each step of the program. Although peak $\dot{V}o_2$ increased from approximately 117 mL/kg/min to 145 mL/kg/min at the end of the training program, training-induced changes in V_T, fb, and $\dot{V}_E$ were not found. The investigators did not measure concomitant changes in arterial blood gases. Christley and colleagues (1997) examined the effects of a 16-week training program on blood gases in Thoroughbreds.[86] The program consisted of an 8-week endurance phase followed by an 8-week sprint phase. They found that training significantly increased $\dot{V}o_{2\ max}$ by 19%, decreased Pao_2 by 5 torr and increased $Paco_2$ by 4 torr. The lack of a significant increase in alveolar ventilation as metabolic workload increased led to the deterioration in blood gas values. Roberts et al[87] measured both ventilatory and blood gas parameters in Thoroughbred horses that underwent a 16-week training session that closely mimicked the one used for race horses in Great Britain. They also found a worsening of the arterial hypoxemia and hypercapnia after training (Table 28.6),[87] confirming the findings of previous investigators. Training does not lead to an improvement in the ventilatory parameters, and because maximum oxygen consumption and carbon dioxide production increase, there is a worsening of the blood gases relative to the pre-training values.

In contrast to the studies that have been conducted in Thoroughbreds, there are few data evaluating the effects of training on ventilatory parameters in Standardbreds.

In summary, although training-induced modifications of the cardiac and musculoskeletal systems occur in the horse, there is a lack of pulmonary adaptations to training. This, combined with the high metabolic demands placed upon the horse during high intensity exercise, leads one to conclude that the respiratory system is a major limitation to the athletic performance of the equine athlete.

Table 28.6 Effects of a 16-week training program on ventilatory parameters in Thoroughbred horses galloping at 12 m/s

	Pre-training	Post-training
V_T (L)	14.6	15
fb (per min)	125	125
$\dot{V}_E$ (L/min)	1550	1800
Peak $\dot{V}_I$ (L/s)	79	80
Peak $\dot{V}_E$(L/s)	60	60
pHa	7.25	7.30
$Paco_2$ (mmHg)	53.6	56.5
Pao_2 (mmHg)	81	65

V_T, tidal volume; fb, breathing frequency; $\dot{V}_E$, expired minute ventilation; $\dot{V}_I$, peak inspiratory flow; $\dot{V}_E$, peak expiratory flow; pHa, arterial pH; $Paco_2$, arterial carbon dioxide tension; Pao_2, arterial oxygen tension. Reproduced with permission from Roberts et al.[87]

References

1. McLaughlin RF, Tyler WS, Canada RO. A study of the subgross pulmonary anatomy in various mammals. Am J Anat 1961; 109:149–161.
2. Breeze R, Turk M. Cellular structure, function and organization in the lower respiratory tract. Environ Health Perspect 1984; 55:3–24.
3. Pirie M, Pirie HM, Cranston S, et al. An ultrastructural study of the equine lower respiratory tract. Equine Vet J 1990; 22:338–342.
4. Mair TS, Batten EH, Stokes CR, et al. The histological features of the immune system of the equine respiratory tract. J Comp Pathol 1987; 97:575–586.
5. Amis TC, Pascoe JR, Hornof W. Topographic distribution of pulmonary ventilation and perfusion in the horse. Am J Vet Res 1984; 45:1597–1601.
6. Hlastala MP, Bernard SL, Erickson HH, et al. Pulmonary blood flow distribution in standing horses is not dominated by gravity. J Appl Physiol 1996; 81:1051–1061.
7. Bernard SL, Glenny RW, Erickson HH, et al. Minimal redistribution of pulmonary blood flow with exercise in racehorses. J Appl Physiol 1996; 81:1062–1070.
8. Pelletier N, Robinson NE, Kaiser L, et al. Regional differences in endothelial function in horse lungs: possible role in blood flow distribution? J Appl Physiol 1998; 85:537–542.
9. Manohar M, Duren SE, Sikkes BP, et al. Bronchial circulation during prolonged exercise in ponies. Am J Vet Res 1992; 53:925–929.
10. Robinson NE. Bronchodilators in equine medicine. Proc Am Coll Vet Intern Med 1992; 10:287–291.
11. Art T, Anderson L, Woakes AJ, et al. Mechanics of breathing during strenuous exercise in thoroughbred horses. Resp Physiol 1990; 82:279–294.
12. Bayly WM, Grant BD, Breeze RG, et al. The effects of maximal exercise on acid–base balance and arterial blood gas tension in thoroughbred horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta; 1983; 400–407.

13. Hodgson DR, Davis RE, McConaghy FF. Thermoregulation in the horse in response to exercise. Br Vet J 1994; 150:219–235.
14. Willoughby RA, McDonell WN. Pulmonary function testing in horses. Vet Clin North Am: Large Anim Pract 1979; 1:171–196.
15. Gallivan GJ, McDonell WN, Forrest JB. Comparative pulmonary mechanics in the horse and the cow. Res Vet Sci 1989; 46:322–330.
16. Lavoie JP, Pascoe JR, Kupershoek CJ. Partitioning of total pulmonary resistance in horses. Am J Vet Res 1995; 56:924–929.
17. Aguilera-Tejero E, Pascoe JR, Amis TC, et al. Measurement of pulmonary diffusing capacity for carbon monoxide and functional residual capacity during rebreathing in conscious thoroughbreds. Am J Vet Res 1993; 54:1752–1757.
18. Young SS, Tesarowski D. Respiratory mechanics of horses measured by conventional and forced oscillation techniques. J Appl Physiol 1994; 76:2467–2472.
19. Leith DE, Gillespie JR. Respiratory mechanics of normal horses and one with chronic obstructive lung disease. Fed Proc 1971; 30:556.
20. Couëtil LL, Rosenthal FS, Simpson CM. Forced expiration: a test for airflow obstruction in horses. J Appl Physiol 2000; 88:1870–1879.
21. Sorenson PR, Robinson NE. Postural effects on lung volumes and asynchronous ventilation in anesthetized horses. J Appl Physiol 1980; 48:97–103.
22. Ainsworth DM, Ducharme NG, Hackett RP, et al. Regulation of respiratory muscle activities during chemoreceptor stimulation in the adult horse (*Equus caballus*). Am J Vet Res 1995; 56:366–373.
23. Koterba AM, Kosch PC, Beech J, Whitlock T. Breathing strategy of the adult horse (*Equus caballus*) at rest. J Appl Physiol 1988; 64:337–346.
24. Bayly WM, Schulz DA, Hodgson DR, et al. Ventilatory responses of the horse to exercise: effect of gas collection systems. J Appl Physiol 1987; 63:1210–1217.
25. Holcombe SJ, Beard WL, Hinchcliff KW. Effect of a mask and pneumotachograph on tracheal and nasopharyngeal pressures, respiratory frequency and ventilation in horses. Am J Vet Res 1996; 57:250–253.
26. Geor RJ, Staempfli HR, McCutcheon LJ, et al. Effect of gas collection system on respiratory and stride frequency and stride length. Equine Vet J Suppl 1995; 18:53–57.
27. Marlin DJ, Roberts CA. Qualitative and quantitative assessment of respiratory airflow and pattern of breathing in exercising horses. Equine Vet Educ 1998; 10:178–186.
28. Seeherman JH, Morris EA. Methodology and repeatability of a standardized treadmill exercise test for clinical evaluation of fitness in horses. Equine Vet J Suppl 1990; 9:20–25.
29. Stubbing DG, Pengelley LD, Morse J, et al. Pulmonary mechanics during exercise in normal males. J Appl Physiol 1980; 49:506–510.
30. Henke KG, Sharratt M, Pegelow D, et al. Regulation of end-expiratory lung volume during exercise. J Appl Physiol 1988; 64:135–146.
31. Ainsworth DM, Eicker SW, Ducharme NG, et al. Costal diaphragmatic length changes during exercise. Am Rev Resp Crit Care 1996; 153:A297.
32. Rose RJ, Hodgson DR, Bayly WM, Gollnick PD. Kinetics of VO_2 and VCO_2 in the horse and comparison of five methods for determination of maximum oxygen uptake. Equine Vet J Suppl 1990; 39–42.
33. Evans DL, Rose RJ. Determination and repeatability of maximum oxygen uptake and other cardiorespiratory measurements in the exercising horse. Equine Vet J 1988; 20:94–98.
34. Rose RJ, Hodgson DR, Kelso TB, et al. Maximum O_2 uptake, O_2 debt and deficit, and muscle metabolites in Thoroughbred horses. J Appl Physiol 1988; 64:781–788.
35. Landgren GL, Gillespie JR, Fedde MR, et al. O_2 transport in the horse during rest and exercise. Adv Exp Med Biol 1988; 227:333–336.
36. Wagner P, Erickson BK, Kubo K, et al. Maximum oxygen transport and utilization before and after splenectomy. Equine Vet J Suppl 1995; 18:82–89.
37. Manohar M, Goetz TE, Hassan AS. Effect of prior high-intensity exercise on exercise-induced arterial hypoxemia in Thoroughbred horses. J Appl Physiol 2001; 90:2371–2377.
38. Fenger CK, McKeever KH, Hinchcliff KW, et al. Determinants of oxygen delivery and hemoglobin saturation during incremental exercise in horses. Am J Vet Res 2000; 61:1325–1332.
39. Art T, Lekeux P. Ventilatory and arterial blood gas tension adjustments to strenuous exercise in Standardbreds. Am J Vet Res 1995; 56:1332–1337.
40. Ainsworth DM, Eicker SW, Nalevanko ME, et al. The effect of exercise on diaphragmatic activation in exercising horses. Respir Physiol 1996; 106:35–46.
41. Attenburrow DP, Goss VA. The mechanical coupling of lung ventilation to locomotion in the horse. Med Eng Phys 1994; 15:188–192.
42. Lafortuna CL, Reinach E, Saibene F. The effects of locomotor-respiratory coupling on the pattern of breathing in horses. J Physiol 1996; 492:587–596.
43. Butler PJ, Woakes AJ, Anderson LS, et al. Stride length and respiratory tidal volume in exercising thoroughbred horses. Respir Physiol 1993; 93:51–56.
44. Nyman G, Bjork M, Funkquist P, et al. Ventilation–perfusion relationships during graded exercise in the Standarbred trotter. Equine Vet J Suppl 1995; 18:63–69.
45. Art T, Serteyn D, Lekeux P. Effect of exercise on the partitioning of equine respiratory resistance. Equine Vet J 1988; 20:268–273.
46. Slocombe RF, Covelli G, Bayly WM. Respiratory mechanism of horses during stepwise treadmill exercise tests, and the effect of clenbuterol pretreatment on them. Aust Vet J 1992; 69:221–225.
47. Bayly WM, Slocombe RF, Schott HC 2nd, et al. Effects of inhalation of albuterol sulphate, ipratropium bromide and frusemide on breathing mechanics and gas exchange in healthy exercising horses. Equine Vet J 2001; 33:302–310.
48. Pelletier N, Leith DE. Ventilation and carbon dioxide exchange in exercising horses: effect of inspired oxygen fraction. J Appl Physiol 1995; 78:654–662.
49. Gutting SM, Forster HV, Lowry TR, et al. Respiratory muscle recruitment in awake ponies during exercise and CO_2 inhalation. Respir Physiol 1991; 86:315–332.
50. Ainsworth DM, Smith CA, Eicker SW, et al. Pulmonary–locomotory interactions in exercising dogs and horses. Respir Physiol 1997; 110:287–294.
51. Bayly WM, Hodgson DR, Schulz DA, et al. Exercise-induced hypercapnia in the horse. J Appl Physiol 1989; 67: 1958–1966.
52. Landgren GL, Gillespie JR, Leith DE. No ventilatory response to CO_2 in Thoroughbreds galloping at 14 m/s. In: Persson SBD, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP; 1991; 59–65.
53. Coleridge HM, Coleridge JCG. Reflexes evoked from the tracheobronchial tree and lungs. In: Fishman AP, Cherniack NS, Widdicombe JG, Geiger SR, eds. The respiratory system. Part 1, Volume II. Baltimore: Williams and Wilkins; 1986; 395–429.

54. Derksen FJ, Robinson NE, Slocombe RF, et al. Pulmonary function tests in standing ponies: reproducibility and effect of vagal blockade. Am J Vet Res 1982; 43:598–602.
55. Flynn C, Forster HV, Pan LG, et al. Role of hilar nerve afferents in hyperpnea of exercise. J Appl Physiol 1985; 59:798–806.
56. Frazier DT, Revelette WR. Role of phrenic nerve afferents in the control of breathing. J Appl Physiol 1991; 70:491–496.
57. Yu J, Younes M. Powerful respiratory stimulation by thin muscle afferents. Respir Physiol 1999; 117:1–12.
58. Forster HV, Lowry TF, Pan LG, et al. Diaphragm and lung afferents contribute to inspiratory load compensation in awake ponies. J Appl Physiol 1994; 76:1330–1339.
59. Forster HV, Erickson BK, Lowry TF, et al. Effect of helium-induced ventilatory unloading on breathing and diaphragm EMG in awake ponies. J Appl Physiol 1994; 77:452–462.
60. Pan LG, Forster HV, Wurster RD, et al. Effect of partial spinal cord ablation on exercise hyperpnea in awake ponies. J Appl Physiol 1990; 69:1821–1827.
61. Young IS, Alexander McNR, Woakes PJ, et al. The synchronization of ventilation and locomotion in horses (*Equus caballus*). J Exp Biol 1992; 166:19–31.
62. Frevert CS, Nations CS, Seeherman HJ, et al. Airflow associated with stride in the horse. Physiologist 1990; 33:A83.
63. Bayly W, Schott H, Slocombe R. Ventilatory responses of horses to prolonged submaximal exercise. Equine Vet J Suppl 1995; 18:23–28.
64. Krogh A, Lindhard J. A comparison between voluntary and electrically induced muscular work in man. J Physiol (Lond) 1917; 51:182–201.
65. Dempsey JA, Forster HV, Ainsworth DM. Regulation of hyperpnea, hyperventilation and respiratory muscle recruitment during exercise. In: Dempsey JA, Pack AI, eds. Regulation of breathing. New York: Marcel Dekker; 1995; 1065–1134.
66. Eldridge FL, Milhorn DE, Kiley JP, et al. Stimulation by central command of locomotion, respiration and circulation during exercise. Respir Physiol 1985; 59:313–337.
67. DiMarco AF, Ramaniuk JR, von Euler C, et al. Immediate changes in ventilation and respiratory pattern associated with onset and cessation of locomotion in the cat. J Physiol (Lond) 1983; 343:1–16.
68. Thornton J, Essen-Gustavsson B, Lindholm A, et al. Effects of training and detraining on oxygen uptake, cardiac output, blood gas tensions, pH and lactate concentrations during and after exercise in the horse. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta; 1983; 470–486.
69. Christely RM, Evans DL, Hodgson DR et al. Blood gas changes during incremental and sprint exercise. Equine Vet J Suppl 1999; 30:24–26.
70. Littlejohn A, Snow DH. Circulatory, respiratory and metabolic responses in Thoroughbred horses during the first 400 meters of exercise. Eur J Appl Physiol 1988; 58:307–314.
71. Katz LM, Bayly WM, Hines MT, et al. Differences in the ventilatory responses of horses and ponies to exercise of varying intensities. Equine Vet J Suppl 1999; 30:49–51.
72. Bayly WM, Schulz DA, Hodgson DR, et al. Ventilatory response to exercise in horses with exercise-induced hypoxemia. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP; 1987; 172–182.
73. Erickson BK, Peischl RL, Erickson HH. Alleviation of exercise-induced hypoxemia utilizing inspired 79% helium 20.95% oxygen. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Uppsala, Sweden: ICEEP Publications; 1991; 54–58.
74. Wagner PD, Gillespie JR, Landgren GL, et al. Mechanism of exercise-induced hypoxemia in horses. J Appl Physiol 1989; 66:1227–1233.
75. Hedenstierna G, Nyman G, Dvart C, et al. Ventilation–perfusion relationships in the standing horse: An inert gas elimination study. Equine Vet J 1987; 19:514–519.
76. Funkquist P, Wagner PD, Hedenstierna G, et al. Ventilation-perfusion relationships during exercise in Standardbred trotters with red cell hypervolaemia. Equine Vet J Suppl 1999; 30:107–113.
77. Seaman J, Erickson BK, Kubo K, et al. Exercise induced ventilation/perfusion inequality in the horse. Equine Vet J 1995; 27:104–109.
78. Constantinopol M, Jones JH, Weiber ER, et al. Oxygen transport during exercise in large mammals II. Oxygen uptake by the pulmonary gas exchanger. J Appl Physiol 1989; 67:871–878.
79. Karas RH, Taylor CR, Jones JH, et al. Adaptive variation in the mammalian respiratory system in relation to energetic demand. VII. Flow of oxygen across the pulmonary gas exchanger. Respir Physiol 1987; 69:101–115.
80. Bayly WM, Redman MJ, Sides RH. Effect of breathing frequency and airflow on pulmonary function in high-intensity equine exercise. Equine Vet J Suppl 1999; 30:19–23.
81. Erickson BK, Seaman J, Kubo K, et al. Hypoxic helium breathing does not reduce alveolar-arterial PO_2 difference in the horse. Respir Physiol 1995; 100:253–260.
82. Johnson BD, Saupe KW, Dempsey JA. Mechanical constraints on exercise hyperpnea in endurance athletes. J Appl Physiol 1992; 73:874–886.
83. Evans DL, Silverman EB, Hodgson DR, et al. Gait and respiration in standardbred horses when pacing and galloping. Res Vet Sci 1994; 57:233–239.
84. Evans DL, Rose RJ. Cardiovascular and respiratory responses to submaximal exercise training in the thoroughbred horse. Eur J Physiol 1988; 411:316–321.
85. Art T, Lekeux P. Training-induced modifications in cardiorespiratory and ventilatory measurements in Thoroughbred horses. Equine Vet J 1993; 25:532–536.
86. Christley RM, Hodgson DR, Evan DL, et al. Effects of training on the development of exercise-induced arterial hypoxemia in horses. Am J Vet Res 1997; 58:653–657.
87. Roberts CA, Marlin DJ, Lekeux P. The effects of training on ventilation and blood gases in exercising Thoroughbreds. Equine Vet J Suppl 1999; 30:57–61.

CHAPTER 29

Non-infectious diseases of the lower respiratory tract

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Inflammatory airway disease (IAD, small airway disease, small airway inflammatory disease, lower airway disease, bronchiolitis)

- IAD is associated with exercise intolerance, cough, and increased respiratory secretions.
- Young athletic horses are commonly affected and up to 65% of race horses have IAD.
- Bronchoalveolar lavage fluid cytology and exercise testing are valuable diagnostic tools for IAD.
- Horses with IAD exhibit various degrees of airflow obstruction and airway hyperresponsiveness.
- Etiology of IAD appears to be multifactorial with environmental dusts playing an important role.
- Therapy is aimed at decreasing environmental dusts and controlling airway inflammation.
- Aerosol therapy with corticosteroids and bronchodilators is effective.

Recognition of the disease

History and presenting complaint

A mild form of lower airway inflammatory disease commonly encountered in young athletic horses has been recognized recently as a separate entity from recurrent airway obstruction (RAO) and termed 'inflammatory airway disease' (IAD).[1–3] In the majority of cases, RAO and IAD may be differentiated on clinical grounds (Table 29.1). However, some have argued that, over time, horses with IAD may progress to RAO.[4] The incidence of IAD in race horses may vary between 11% and 65% depending on the diagnostic criteria used (endoscopy, cytology) and the conditions of examination (i.e. before versus after exercise).[5–7] Horses with IAD usually have a history of decreased performance, mild exercise intolerance, cough, and increased respiratory secretions.[1,8] Foals and older horses may also suffer from IAD.[9,10] In these cases, the diagnosis is often reached by excluding infectious and other non-infectious causes of lower airway inflammation. The possibility of IAD should be considered in horses with signs of respiratory disease including tracheobronchial mucopurulent exudate that do not respond, or relapse, after antimicrobial therapy and further diagnostic tests should be pursued (e.g. bronchoalveolar lavage).

Duration of IAD is 7 weeks on average with a range from 4 to 22 weeks, which is longer than most infectious respiratory diseases.[8,11] In a study involving 170 Thoroughbred horses in training over a 2-year period, it was estimated that during 8 of the 24 months, horses had some degree of IAD.[8] IAD appears to be more common in young athletic horses with the incidence decreasing with increasing age.[6,12] IAD is particularly common in Thoroughbred and Standardbred race horses, but has been also reported in a variety of other breeds such as Quarter Horse, Warmblood, Appaloosa, and American Saddlebred.[7,8,10,13,14] In fact, horses of any breed may be affected but race horses are over-represented because

Table 29.1 Comparison between recurrent airway obstruction (RAO) and inflammatory airway disease (IAD) in horses

		RAO	IAD
Signalment	Age	> 6 years	> 1 year
	Activity level	+/++	++/+++
Clinical signs	Duration	Months to years Recurrent	1–6 months Not recurrent
	Cough	Chronic intermittent	38% of cases
	Exudate in airways	Mucopurulent (++/+++)	Mucoid to mucopurulent (+/++)
	Lung sounds	Breath sounds (++/+++), wheezes, crackles	Normal
	Increased respiratory efforts	++/+++	0/+
	Exercise intolerance	++/+++	+/++
Etiology		Allergy to molds	Multifactorial
Pathophysiology	Lower airway obstruction	++/+++	0/+
	BALF cytology	Neutrophilia (> 25%)	Neutrophilia (5–20%) Eosinophilia (> 1%) Mastocytosis (> 2%)
	Airway hyper-responsiveness	+/+++	+/+++
Histopathology	Bronchiolitis	++/+++	+/++

Low/mild: +; medium/moderate: ++; high/severe: +++.

of several factors. First, the major limiting factor to performance in a race horse is pulmonary gas exchanges.[15] Therefore even a mild degree of respiratory disease may have a profound negative impact on performance whereas the same problem in a dressage horse would be considered clinically insignificant. Second, most race horses are kept in an environment that is particularly challenging for the respiratory tract. They are often confined in stables with suboptimal ventilation 24 hours/day (except for the training session), exposed to high levels of respirable irritants (e.g. dust and endotoxins from straw and hay), and mingle with a large population of horses originating from various locations.[16,17] Third, race-horse training and racing schedule and frequent traveling are often stressful, impairing the body's immune response and commonly resulting in lower airway disease.

The most common complaints reported by owners of athletic horses with IAD, other than race horses, are chronic cough, exercise intolerance, and prolonged recovery after exercise. These horses may be involved in a variety of activities such as barrel racing, three-day event, dressage, or simply trail riding. Owners often report a history of infectious respiratory disease in the months preceding the diagnosis of IAD with several horses in the barn being affected. The typical history is that all horses recovered except for the one with IAD, which continued to cough intermittently while in the stall and/or being ridden.

Physical examination

The most common clinical signs associated with IAD are increased respiratory secretions, cough, and decreased performance.[1,7,18] Estimation of the quantity of mucus present in the trachea by endoscopy reveals that horses free of respiratory disease have either no mucus or a few isolated flecks and horses with IAD have a pool of mucus at the thoracic inlet or a continuous stream of variable width (Fig. 29.1).[5,6] In addition, the severity of IAD is related to the amount of mucopus and the

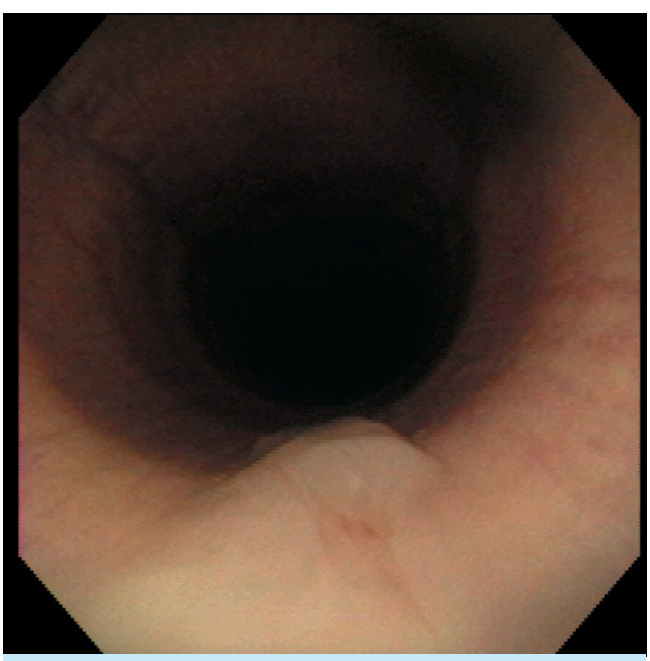


Fig. 29.1
Increased mucopurulent secretions visualized by endoscopy of the trachea in a horse with inflammatory airway disease.

percentage of neutrophils in tracheal wash or in bronchoalveolar lavage (BAL) fluid.[6,10] The incidence of tracheal exudate has been found to increase after strenuous exercise by some investigators[5] but not by others.[19] In healthy horses, the amount of tracheal mucus is not affected by age.[20]

Cough is present in only 38% of horses with IAD. However, 85% of coughing horses have IAD.[8,21] Daily observation of horses in training showed that coughing is not noted 62% of the time during which they have IAD.[8] Epidemiologic studies of Thoroughbred race horses in training found a strong association between coughing, the amount of mucus present in the upper airways, and pharyngeal lymphoid hyperplasia.[12,21] Also, a strong association exists between coughing, isolation of bacteria, and the degree of inflammation in tracheal wash fluid.[6,21] Nevertheless, bacteriologic examination of tracheal wash samples reveals that 35–58% of horses with IAD do not have significant amounts of bacteria in their tracheal wash fluid.

Other clinical signs of respiratory disease such as nasal discharge and fever do not appear to be associated with the disease.[8] Nevertheless, an increased amount of seromucoid nasal discharge post-exercise is commonly observed in horses with IAD. Thoracic auscultation is usually normal; however, some horses may exhibit increased breath sounds or wheezes. Horses with severe IAD may have a slightly increased respiratory rate and abdominal contraction on expiration. For the most part, IAD is subclinical and may go undetected unless coughing is present or tracheal exudate is detected by endoscopy.[10]

Effects of IAD on performance The negative impact of IAD on performance is suggested by several studies. A field study of Standardbred race horses (n = 965) revealed that mucopurulent exudate is visible by post-race endoscopy of the trachea in 39% of horses finishing in the last two positions compared with only 10% of horses finishing first or second.[7] In other words, horses finishing in the last two positions were 5.8 times more likely to have mucopurulent exudate during post-race endoscopy of the trachea than horses finishing first or second ($P < 0.0001$). Another study found that Thoroughbred race horses exhibiting marked decrease in performance had a significantly higher percentage of neutrophils in BAL fluid.[18] Subsequent return to previous level of performance was reported in 41% of horses with IAD after implementation of environmental changes aimed at decreasing the amount of airborne dust in the horses' stall.[18] However, no controlled studies have yet demonstrated a cause and effect relationship between IAD and decreased performance. Other signs associated with exercise intolerance are delayed recovery of normal respiratory rate after exercise and abnormally increased respiratory efforts compared with the level of work. These latter signs are more likely to be recognized in athletic horses other than race horses because most of their activities do not require exercising at or above maximal aerobic capacity.

The effect of IAD on performance is dependent on the level of exercise and the severity of the disease. Pulmonary gas exchange is the limiting factor to performance in fit horses as illustrated by the marked exercise-induced arterial hypoxemia and hypercapnia developed by healthy race horses exercising strenuously.[22,23] During a race, horses exercise at or above maximum aerobic capacity ($\dot{V}O_{2max}$). In this situation, a relatively mild degree of IAD may significantly impair gas exchange and result in decreased performance. IAD is not likely to cause exercise intolerance in a trail riding horse exercising at less than 50% of $\dot{V}O_{2max}$ until the disease causes marked airflow obstruction or frequent coughing. Therefore, the clinician needs to select diagnostic tools and interpret test results based on the horse's fitness level and type of activity.

Mechanisms responsible for decreased performance in horses with IAD are mainly speculative at this point in time. A study of Standardbred race horses performing submaximal exercise tests on a treadmill found that horses with IAD exhibited increased pulmonary artery pressure and red cell volume (RCV/kg bodyweight (BW)) in comparison to healthy controls.[24] These findings suggested a compensatory response to exercise-induced hypoxemia[25,26] even though significant differences in Pa_{O_2} between IAD and control horses were not found. The elevated pulmonary artery pressure was thought to result from increased vascular resistance. Elevation in RCV/kg BW or packed cell volume has been shown to correlate with increase in pulmonary blood pressure and vascular resistance.[27,28] Also, horses with more severe airway disease such as heaves have significantly elevated pulmonary artery pressure.[29,30] Another investigation evaluating gas exchanges and lung biopsy parameters in Standardbred race horses showed that horses with IAD had lower tidal volume and minute ventilation at a speed corresponding to a heart rate of 200 beats/min ($\dot{V}_{E\text{-}200}$/kg BW), and increased RCV/kg BW.[31] In addition, the severity of lung biopsy score was negatively correlated with $\dot{V}_{E\text{-}200}$/kg BW, suggesting that bronchial epithelial hyperplasia of the small airways was probably causing airflow obstruction. Indeed, small airway obstruction may be detected in horses with IAD using sensitive methods such as forced expiration or forced oscillatory mechanics (Fig. 29.2).[10,32,33] One study showed that race horses with IAD exhibited more pronounced exercise-induced hypoxemia than did healthy controls during a standardized run to fatigue treadmill test (Fig. 29.3).[34] Both groups of horses had comparable Pa_{CO_2}, suggesting that impaired gas exchange was likely to be a result of ventilation–perfusion mismatching and not hypoventilation. Exercise-induced hypoxemia is a physiologic phenomenon in horses[22] and the degree of arterial hypoxemia is more pronounced as the level of training increases.[35] Therefore, assessment of the significance of exercise-induced hypoxemia is dependent on control data matched for horses' age and fitness level.

Poor performance may result from a variety of causes such as lameness, exertional rhabdomyolysis, and cardiac and neurologic diseases. More importantly, it is common to diagnose several problems in the same horse.[36] In a retrospective study of 275 horses evaluated because of a complaint of poor performance Morris and Seeherman reported that 84% of cases were diagnosed with a combination of problems involving one or more body system.[36] These findings underscore the importance of performing a comprehensive evaluation of poorly performing horses.

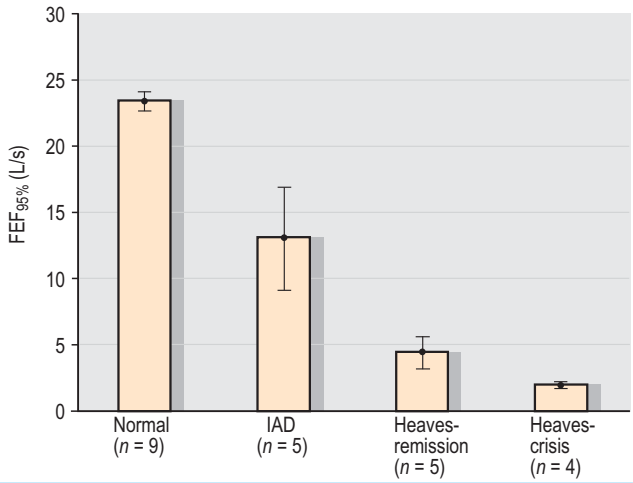


Fig. 29.2
Forced expiratory flow at 95% of exhaled vital capacity ($FEF_{95\%}$) measured during forced expiration in healthy horses and horses with inflammatory airway disease, and recurrent airway obstruction (heaves) during disease remission and exacerbation (crisis).

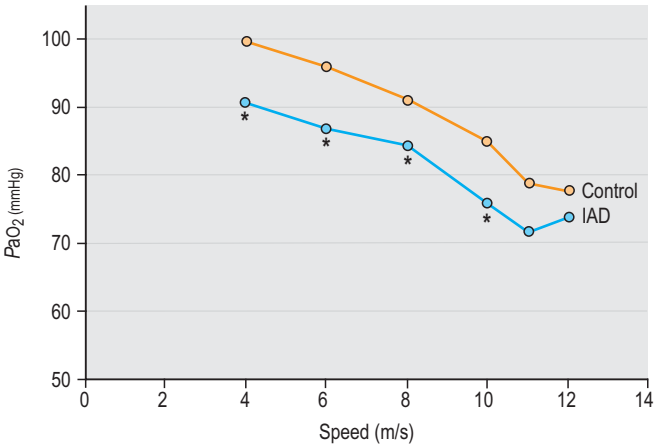


Fig. 29.3
Partial pressure of oxygen in arterial blood of race horses subjected to a standardized treadmill test. * Values are significantly different from control horses ($P < 0.05$).

Special examination

Endoscopic examination of the respiratory tract is a simple and valuable diagnostic tool for IAD. Horses with normal respiratory tract have at most a few flecks of mucus visible in the trachea by endoscopy.[20,37] Increased mucopurulent exudate in the tracheobronchial tree is detected in the majority of horses with IAD (Fig. 29.1). Also, endoscopic examination and BAL procedure tend to induce more coughing in horses with IAD.[18] However, increased tracheal exudate is present in the majority of pulmonary diseases other than IAD.[37]

Cytologic examination of respiratory secretions is important when trying to confirm a diagnosis of pulmonary disease. Tracheal secretions may be collected by direct aspiration or wash of tracheal lumen via transcutaneous catheterization or through an endoscope.[38–41] Several studies have shown an association between IAD and neutrophilia in tracheal secretions.[21,42] However, cytologic examination of tracheal mucus in horses free of respiratory disease is highly variable, as illustrated by the fact that neutrophils may range from 3 to 83% of cells.[43,44] In addition, tracheal wash cytology has been found to correlate poorly with pulmonary histopathology.[43,45] Tracheal wash cytology is a useful tool for investigation of IAD in horse populations for research purposes but may not be as valuable for the diagnosis of IAD in individual animals. In contrast, variability in BAL fluid cytology is limited, with most studies reporting neutrophils < 5% of cells (Table 29.2).[46,47] Furthermore, BAL cytology reportedly correlates well with histopathology of the lungs[48] and does not correlate with tracheal wash cytology.[44]

A BAL may be easily performed in field conditions using either a flexible endoscope (≥ 2 m long) or an equine BAL catheter at least 2.5 m long and 10 mm diameter with an inflatable cuff at the end (Bivona, Gary, IN; Cook, Bloomington, IN; Jorgensen Laboratories, Loveland, CO). The technique has been described in detail previously.[49,50] The horse has to be sedated with xylazine hydrochloride (0.4–0.8 mg/kg, i.v.) or detomidine hydrochloride (0.01–0.02 mg/kg, i.v.) and restrained with a nose twitch. The flexible endoscope or BAL tube is then passed through the nasal passages and advanced until wedged into the distal airways. Coughing may be prevented by spraying airways with a 0.2–0.5% lidocaine (lignocaine) solution (5–10 mL at a time) as the instrument is advanced into the respiratory tract, particularly focusing on the glottis and carina. Horses with IAD may cough excessively during the procedure and routine premedication with inhaled albuterol sulfate (1–2 μg/kg) 5–10 minutes prior to the BAL is beneficial. A 100–300 mL bolus of warm sterile saline solution is infused under pressure followed by immediate but gentle aspiration of the fluid using 60 mL syringes or a suction pump. It is important always to use the same technique during a BAL because the volume of fluid used as well as the number of boluses administered have a significant effect on cell count and differential (see Table 29.2). Fluid samples should be processed within 1 to 2 hours or stored on ice or at 4°C if sample shipping to the laboratory is to be delayed. Normal BAL fluid should appear slightly turbid with a layer of white foam on the surface (surfactant). Between 50 and 90% of the volume infused is expected to be retrieved.

Lung function can be measured in a variety of ways including assessment of gas exchanges, determination of lung volumes (spirometry), and evaluation of the movement of air in and out the respiratory tract (lung mechanics). Evaluation of gas exchange was discussed above in the section on effects of IAD on performance. Spirometry is useful in severe obstructive diseases such as RAO but not in milder diseases like IAD. Lung mechanics allows quantification of the degree of airflow obstruction present in horses' airways. Airflow obstruction is the basic mechanism responsible, at least in part, for some of the manifestations of IAD such as exercise intolerance and cough. The advantage of lung mechanics is quantification of airflow obstruction,

Table 29.2 Bronchoalveolar lavage fluid cytology in control horses and in horses with inflammatory airway disease (IAD)

BAL technique	Horse type/ number	Leukocytes (cells/mL)	Alveolar macrophages (%)	Lymphocytes (%)	Neutrophils (%)	Eosinophils (%)	Mast cells(%)	Reference
Control horses								
5 × 50 mL saline-syringe-endoscope	Training (no racing)/40	133.5 ± 8.2	56.9 ± 1.9	38.2 ± 1.8	4.1 ± 0.5	0.3 ± 0.2	0.4 ± 0.2	Clark et al[328]
50 mL saline-pump-endoscope	Pasture/9	782.2 ± 272.0	54.3 ± 16.4	28.8 ± 16.2	14.4 ± 10.1	0.4 ± 1.0	2.0 ± 1.1	Sweeney et al[329]
300 mL saline-pump-endoscope	Pasture/8	175.9 ± 110.7	49.5 ± 13.0	40.4 ± 14.6	2.5 ± 1.5	0.1 ± 0.4	7.4 ± 2.7	Sweeney et al.[329]
3 × 100 mL saline-pump-endoscope	Pasture/6	378.3 ± 141.3	59.2 ± 7.4	33.0 ± 8.1	1.2 ± 1.2	0.2 ± 0.4	6.5 ± 2.1	Sweeney et al.[329]
4 × 60 mL saline-syringe-tube	Racing/11		65 ± 6.2	28 ± 5.8	7 ± 3.3	0 ± 0	0.2 ± 0.3	Forgarty and Buckley[18]
1 × 250 mL saline-pump-endoscope	Racing/12	530 ± 170	60.1 ± 4.8	36.7 ± 5.4	2.2 ± 1.4	0.03 ± 0.1	0.4 ± 0.4	Hare et al[2]
300 mL LRS-BAL tube	Racing/6	153.2 ± 17.1	64.8 ± 4.6	28.3 ± 2.9	3.8 ± 0.3	1.2 ± 0.8	0.3 ± 0.3	Rush et al[1]
2 × 250 mL saline-pump-endoscope	Racing/6	360 (260–540)	67.7 (61–78.8)	31.5 (19–35)	0.4 (0.2–1.4)	0.3(0–1)	1(0–2.8)	Hare and Viel[60]
1 × 250 mL saline-pump-endoscope	Racing/10	445 ± 142	68.8 ± 8.8	22.9 ± 7.4	3.8 ± 5.5	2.0 ± 1.0	1.5 ± 0.3	Couëtil and DeNicola[34]
IAD horses								
4 × 60 mL saline-syringe-tube	Racing/65		64 ± 15.2	23 ± 11.4	**13 ± 12***	0.1 ± 0.3	0.3 ± 0.7	Forgarty and Buckley[18]
1 × 250 mL saline-pump-endoscope	Racing/12	590 ± 290	56 ± 13	37 ± 16	4.1 ± 3.5	0.2 ± 0.2	**3.1 ± 1.0***	Hare et al[2]
300 mL LRS-BAL tube	Racing/32	366.0 ± 16.8	**48.4 ± 1.9***	**36.0 ± 1.9***	**10.4 ± 1.1***	3.8 ± 1.5	1.8 ± 1.5	Rush et al[1]
2 × 250 mL saline-pump-endoscope	Racing/5	650 (320–1100)	58.6 (40.6–62.4)	25.8 (22.6–31.4)	0.8 (0–1.8)	**11.8 (6.4–26.4)***	1.4 (0.4–2.4)	Hare and Viel[60]
1 × 250 mL saline-pump-endoscope	Racing/13	582 ± 122	**54.8 ± 10.8***	33.6 ± 10.7	**12.0 ± 7.7***	0.4 ± 1.4	1.4 ± 0.4	Couëtil and DeNicola[34]

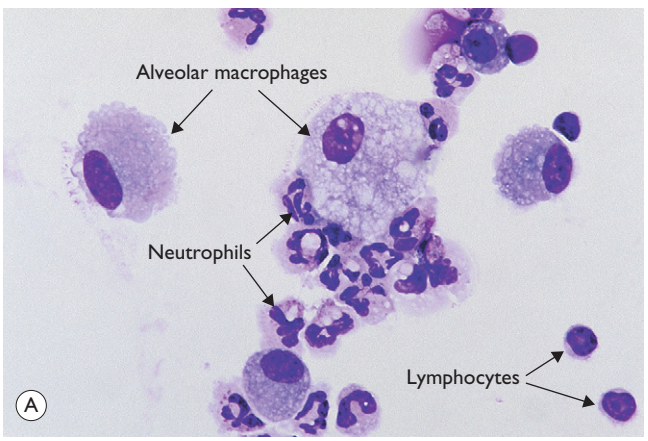
* Significantly different from controls ($P < 0.05$).
LRS, lactated Ringer's solution; BAL, bronchoalveolar fluid.

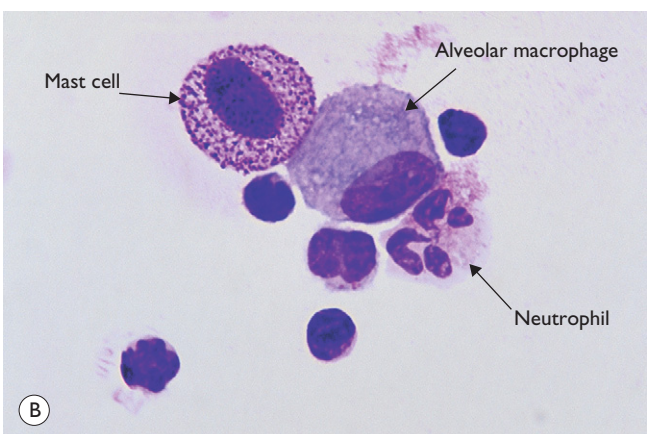
which is often subclinical in horses with IAD, enabling the clinician to determine the severity of the disease process and providing objective means of assessing response to therapy. The disadvantage is that sophisticated equipment and a sound understanding of respiratory physiology are required. Therefore, tests of lung mechanics are currently used mainly in the research arena and in some referral clinics.

There are four main methods used in the horse to evaluate lung mechanics. First, measurement of pleural pressure changes in relation to airflow at the nose during normal (tidal) breathing or 'conventional lung mechanics'. Second, measurement of airflow during forceful exhalation or 'forced expiration'. Third, evaluation of the pressure–flow relationship while an oscillating source of flow is applied to the respiratory system during tidal breathing ('forced oscillometry'). Fourth, measurement of thoracic and abdominal volume changes by inductance plethysmography in relation to airflow at the nose during tidal breathing ('flowmetrics'). Conventional lung mechanics was the first test of lung mechanics adapted to the horse[51] and is still commonly used in research.[52–54] However, this test has not been used extensively in clinical settings because it does not permit detection of airway obstruction until it is severe and clinical signs are then evident.[10,55] Forced expiration (FE) was initially performed in the horse by Gillespie and Leith in anesthetized animals.[56] More recently, the technique was adapted to conscious but sedated horses.[57] In people, FE requires the patient to inhale maximally to total lung capacity (TLC) and immediately exhale as hard and completely as possible to residual volume while expiratory flow, volume, and time are recorded. Expiratory flow is not limited during the first 20% of the FE when lung volume is close to TLC and is only dependent on the level of effort. During the rest of the maneuver expiratory flow reaches a maximum. Increasing effort will not increase expiratory flow further; therefore, this later part of the flow–volume curve is called 'effort independent' and reflects the degree of small airway patency. Similar findings have been reported in horses where forced expiratory flow during late FE (i.e. $FEF_{95\%}$) has been shown to be a sensitive parameter for the detection of mild airway obstruction such as in IAD (Fig. 29.2).[10] Forced oscillometry has the advantage of being non-invasive and has been used both in research and clinical cases. Horses with IAD often show frequency dependence of resistance with higher values obtained at the lower frequencies (1–3 Hz) suggestive of heterogeneous airway obstruction.[32]

Finally, flowmetrics has the greatest potential for use in the field because it is easily portable and also non-invasive.[58]

Another means of detecting airway obstruction is by testing airway reactivity in response to an inhaled irritant such as histamine. Exaggerated airway narrowing in response to an irritant is called airway hyper-responsiveness. Airway reactivity may be quantified using the four tests of lung mechanics described above.[33,57–59] Airway hyper-responsiveness is a prominent feature of IAD in horses with increased BAL fluid eosinophil and mast cell counts.[33,60] The sensitivity of forced oscillometry and flowmetrics is enhanced when used to detect airway hyper-responsiveness. This increased bronchoconstriction in response to inhaled irritants plays an important role in the pathogenesis of the cough and presumably exercise intolerance.





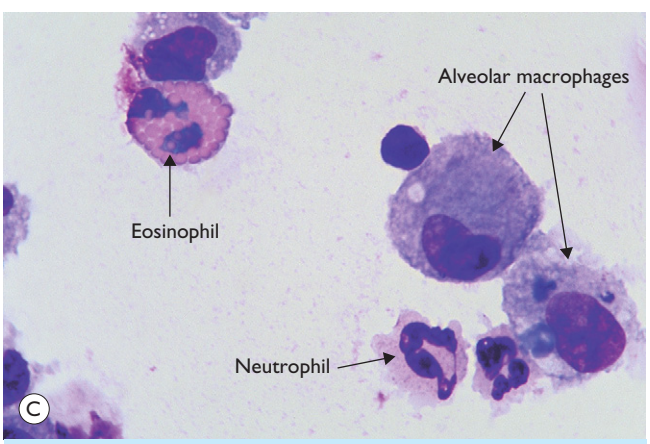


Fig. 29.4
Bronchoalveolar lavage fluid cytology in horses with IAD characterized by increased percentage of neutrophils (A), mast cells (B), and eosinophils (C). ×100.

Laboratory examination

Hemogram and serum biochemistry of horses with IAD are usually within normal limits.

Cytologic specimens of BAL fluid are prepared by centrifugation and processed with Wright's stain. Differential cell counts should be determined by examination of at least 200 cells per slide and preferably 500. Cytologic analysis of BAL fluid allows recognition of three types of inflammatory profiles in IAD (Table 29.2).[50] The most commonly encountered profile is characterized by an increased total nucleated cell count with mild neutrophilia (5–20% cells), lymphocytosis, and monocytosis (Fig. 29.4A).[1,10,18] Two other cytologic profiles characterized by increased percentages of mast cells (> 2%, Fig. 29.4B) and eosinophils (> 1%, Fig. 29.4C) are also observed in some horses with IAD.[2,60] In contrast, BAL of horses with RAO shows moderate to severe neutrophilia (> 20% cells), lymphopenia, and decreased alveolar macrophages.[10,61,62] Cytology of BAL fluid collected from horses with RAO in clinical remission may be normal if sufficient time away from offending allergens has been allowed. Some RAO cases may be clinically normal but still exhibit some degree of pulmonary neutrophilia and, therefore, may be difficult to differentiate from IAD. A practical way to discriminate RAO from IAD is by performing a hay challenge and monitoring clinical signs of respiratory disease, which should develop within a few hours to a few days in RAO affected horses.[53,63] Horses with IAD exposed to moldy hay may exhibit a worsening of coughing and pulmonary neutrophilia. However, they do not develop increased respiratory efforts or nostril flaring like RAO affected horses do.

Necropsy examination

Histopathologic examination of the lungs may be conducted ante-mortem using transcutaneous lung biopsy needles or post-mortem. Horses with IAD present similar histopathologic findings to horses with RAO but with less severe and chronic changes.[48] Typical morphologic findings include peribronchiolitis, bronchiolitis, bronchiolar epithelial hyperplasia, goblet cell metaplasia, luminal mucus, and in some cases alveolitis.[24,31] Severity of histopathologic changes assessed by a scoring system appears to be negatively correlated to various indices of respiratory and cardiovascular function in horses with IAD.[31] Consequently, as pulmonary lesions become more severe, horses become more exercise intolerant.

Diagnostic confirmation

In horses presenting with clinical signs including cough, increased respiratory secretions, and poor performance

detailed history, physical examination, and diagnostic tests should help eliminate differential diagnoses. Horses with IAD are not febrile; therefore, presence of a fever suggests infectious respiratory diseases such as viral diseases, bronchopneumonia, pleuropneumonia, and pulmonary abscess. Hematology findings may be helpful. However, they are often non-specific. Leukocytosis with neutrophilia is commonly found with bacterial respiratory infections and during the acute phase of a bacterial infection, increased numbers of immature neutrophils ('left shift') may be observed. Neutrophilia may also accompany non-infectious inflammatory diseases (e.g. toxins), neoplasia, mycotic, and parasitic infections. Hematologic changes during the early phase of a viral respiratory infection (e.g. influenza) are often characterized by normocytic, normochromic anemia, lymphopenia or lymphocytosis, and sometimes neutropenia.[64,65] Neutrophilia may follow within a week of initial clinical signs, particularly in cases of secondary bacterial infection. Monocytosis

Table 29.3 Therapeutic aerosols used for the treatment of inflammatory airway disease (IAD) and recurrent airway obstruction (RAO)

Drug	Trade name (Laboratory)	Dose delivered per actuation	Number of doses per canister	Device	Dose	Duration of action
Bronchodilators						
Albuterol	Torpex (Boehringer and 3M)	120 μg	200	3M ED	1–2 μg/kg[a]	1 hour
	Combivent (Boehringer)	120 μg (+ 21 μg ipratropium)	200	AeroMask	2–3 μg/kg	1 hour
	Proventil (Schering)	120 μg	200			
Ipratropium bromide	Atrovent (Boehringer)	18 μg	200	AeroMask	0.5–1 μg/kg	4–6 hours
	Atrovent (Boehringer)	0.02% solution for nebulization	2.5 mL vial	Ultrasonic nebilizer	2–3 μg/kg	4–6 hours
	Combivent (Boehringer)	21 μg (+ 120 μg albuterol)	200			
Fenoterol	Only in Canada			AeroMask	2–4 μg/kg	
Pirbuterol	Maxair inhaler (3M)	200 μg	300	3M ED	1–2 μg/kg	1 hour
Salmeterol	Serevent (Glaxo Wellcome)	25 μg	120 (13 g canister)	3M ED	0.5–1 μg	6–8 hours
Corticosteroids						
Beclomethasone	Beclovent (Glaxo Wellcome)	42 μg	200 (16.8 g canister)	3M ED AeroMask	1–3 μg/kg, q 12 hours 2–6 μg/kg, q 12 hours	
Fluticasone	Flovent (Glaxo Wellcome)	220 μg	120 (13 g canister)	AeroMask	2–4 μg/kg, q 12 hours	
Other						
Sodium cromoglycate	Generic	0.02% solution for nebulization	2 mL vials	Jet nebulizer Ultrasonic nebulizer	200 mg, q 12 hours 80 mg, q 24 hours	

3M ED: Aerosol delivery device for equine developed by 3M Animal Care Products; AeroMask: Aerosol delivery device for equine developed by Trudell Medical International.

[a] Approved for use in horses at a dose of 360–720 μg per horse no more than four times per day.

q, every.

may develop during the recovery phase of a viral infection.

Coughing is often chronic intermittent (> 3 weeks) in horses with IAD. Main differential diagnoses are mild cases of RAO and summer pasture-associated obstructive pulmonary disease (SPAOPD), and parasitic pneumonitis. Horses with RAO and SPAOPD typically display severe exercise intolerance and increased respiratory efforts during periods of disease exacerbation. However, these signs may be subtle during periods of disease remission. In those cases, pulmonary function testing or more simply, moldy hay challenge will help reaching a definitive diagnosis. Neutrophilia is commonly observed in BAL fluid from horses with RAO, SPAOPD, and IAD.[1,61,66] The neutrophilia is usually more pronounced with RAO and SPAOPD than with IAD. However, there is significant overlap between diseases.[10] Eosinophilic inflammation may be associated with IAD,[67] parasitic pneumonitis (*Parascaris equorum*, *Dictyocaulus arnfieldi*), hypersensitivity pneumonitis, fungal pneumonia, and cutaneous habronemiasis.[2,68,69] Clinical signs of parasitic pneumonitis are non-specific. Fecal flotation (Baermann technique) is often not diagnostic of *P. equorum* infection because migration through the lungs occurs during the prepatent period.[70] *D. arnfieldi* follows a complete cycle in donkeys, mules, and asses. However, the infection is usually not patent in horses. Therefore, the Baermann fecal flotation is not useful either. *P. equorum* pneumonitis is more commonly detected in foals less than 6 month of age. *D. arnfieldi* usually occurs in horses in contact with infected donkeys and rarely by ingesting larvae excreted by infected horses.[71] A presumptive diagnosis may be reached when respiratory secretions reveal eosinophilic inflammation with sometime evidence of parasite eggs or larvae, exposure to donkeys exists, and anthelmintic therapy results in clinical improvement.[70] Increased metachromatic cells (mast cells, basophils) have been described in horses with IAD but this has not been associated with other types of respiratory disease.[2,4]

Treatment

Therapeutic aims

Treatment of IAD should combine environmental changes and medical therapy. The goals of medical therapy are to control airway inflammation and relieve airflow obstruction using mainly corticosteroids and bronchodilators. Most of the drugs and dosages recommended are based on studies performed on horses with RAO. However, good clinical response of IAD has been observed using those guidelines (Table 29.3). Both systemic and aerosolized drugs are effective, but the potential for adverse effects and prolonged elimination times is greater with systemic administration. The advantages of aerosol therapy are ease of administration, high efficacy, and safety. The disadvantages are cost and environmental effects of certain types of propellants (i.e. CFCs). Non-steroidal anti-inflammatory and antihistamine drugs are ineffective for the treatment of IAD.

Therapy

Environmental changes Inhaled dust particles play an important role in the pathophysiology of IAD and treatment of IAD should always include recommendation to decrease environmental irritants to airways. Several measures may help reduce exposure of the horse's airways to respirable particles and are discussed in detail in the section on RAO, below.

Systemic medical therapy Systemic corticosteroids are effective for the treatment of non-infectious respiratory inflammation. Nevertheless a good understanding of the relationship between potency, duration of action, and adrenal suppression is needed in order to minimize potential undesirable side effects. The same corticosteroids used for RAO may be used to treat IAD (see RAO section for complete discussion).

Oral administration of low-dose (50–150 U every 24 hours) interferon alpha (IFNα) for 5 days has been shown to reduce neutrophil, macrophage, lymphocyte, and total nucleated cell counts in the BAL fluid of race horses with IAD followed over 2 weeks.[72] A parallel reduction in BAL fluid immunoglobulins and inflammatory mediators concentrations was demonstrated, which suggested plasma exudation as a result of airway inflammation.[73] Higher doses of IFNα (450 U) appeared to be less effective. Endoscopic scores based on respiratory exudate, cough, and pharyngeal lymphoid hyperplasia were significantly reduced after 1 week of therapy but were not different from placebo at 2 weeks. Mast cell and eosinophil counts did not change after IFNα therapy. Until the pathophysiology of IAD is established, pulmonary anti-inflammatory effects of IFNα may be attributed to antiviral activity or immunomodulatory properties.[73]

Non-specific immunostimulants such as *Propionobacterium acnes* are recommended as an adjunct treatment for a variety of chronic respiratory diseases and as prophylactic agents for stress-associated (e.g. long-distance transport, weaning) respiratory diseases.[74,75] However, the efficacy of such therapy has not been demonstrated conclusively for IAD.

Aerosol therapy This topic is discussed in detail in the RAO section. Drugs used in the treatment of IAD are listed in Table 29.3.

Corticosteroids No clinical trials have been reported concerning the use of inhaled corticosteroids for IAD. However, the same drugs used to treat RAO are beneficial for IAD and as a general rule the low end of the range recommended for RAO is appropriate for IAD cases. Beclomethasone dipropionate (2–4 μg/kg, every 12 hours) and fluticasone propionate (1–3 μg/kg, every 12 hours) are recommended to treat IAD using commercially available metered dose inhaler (MDI) delivery devices (AeroMask, Equine Haler). Improved clinical signs, decreased airway hyper-responsiveness, and reduced pulmonary inflammation are detectable within 2 weeks of therapy.

Bronchodilators Bronchodilators are indicated to relax airway smooth muscle and relieve airflow obstruction. Two main classes of inhaled bronchodilators have been used in the horse: β_2-agonists (e.g. albuterol) and anticholinergics. Bronchodilators should not be used as only therapy for IAD because they do not suppress airway inflammation and do not reduce airway hyper-responsiveness.[76] In addition, prolonged use of β_2-agonists without corticosteroids induces receptor downregulation, which renders the drug less effective. In horses with significant airway obstruction, bron-

chodilators should be administered prior to corticosteroids in order to optimize lung deposition.

As for corticosteroids, the choice of inhaled bronchodilator and dosages recommended to treat IAD are the same as for RAO.

Cromones Sodium cromoglycate (cromolyn) has been shown to improve clinical signs and to decrease bronchial hyper-responsiveness when administered to horses with IAD characterized by a high mast cell count in BAL fluid (Table 29.3).[2] However, it is ineffective for the treatment of IAD with other inflammatory profiles.

Prognosis

Horses with IAD have a good prognosis for return to previous level of performance. In some cases the disease may recur but in the majority of cases implementation of environmental changes combined with medical therapy results in long-lasting resolution of the clinical signs.

Etiology and pathophysiology

Putative causes of IAD include bacteria, viruses, and inhaled environmental pollutants with a modulatory role played by factors such as the horse's immune response and genetic make-up.

The likelihood of isolating bacteria from tracheal wash samples collected from race horses in training is strongly associated with the cytologic degree of inflammation.[6,8,21] Isolation of more than 10^3 colony-forming units of pathogenic *Streptococcus* spp. is also strongly associated with coughing.[21] Bacterial species most frequently isolated are *Streptococcus* spp., *Pasteurella/Actinobacillus* spp., and *Bordetella* spp. *Mycoplasma* have not been reported in horses with IAD. Reportedly, race horses diagnosed with lower airway infection based on BAL cytology respond to antibiotic therapy in 31% of the cases.[18] The marked increase in the risk of coughing in horses with high numbers of bacteria in tracheal secretions, the common isolation of bacteria with potential to cause pulmonary disease, and the association between IAD and detection of intracellular bacteria in tracheal secretions argue for a causative role of bacteria in the pathogenesis of IAD (see page 683).

However, several factors suggest that bacteria may in fact be present in the trachea because of contamination during sampling or transient colonization of the proximal airways. First, no bacteria are cultured in 27–54% of horses with IAD.[6,77] Second, the trachea is not a sterile environment and potentially pathogenic bacteria may be isolated by tracheal wash in 8–25% of healthy horses with isolation of non-pathogenic organisms in as many as 75% of those horses.[78,79] Third, the presence of bacteria in the airways may result from decreased mucociliary clearance and not from primary infection. Fourth, successful treatment of IAD with oral IFNα or inhaled glucocorticoids suggests that infectious agents are not causative agents but rather opportunistic invaders of the tracheobronchial tree.[4,50,72]

Contrary to common belief, respiratory viruses do not appear to play an important role in IAD. Several reports have shown no evidence of viral infections in horses with IAD based on serology or virus isolation aimed at detecting equine herpes, influenza, adenovirus, and rhinoviruses.[5,8,21] These findings are consistent with the fact that no relationship has been found between presence of fever and IAD.[8]

The role of exposure to dust in the pathogenesis of IAD is suggested by several studies. Healthy yearlings fed hay demonstrate a significant increase in BAL fluid neutrophil count and percentage, and a higher airway inflammation score when housed in a stable than when kept on pasture.[80] Natural exposure of healthy horses to moldy hay or controlled exposure to organic molds and endotoxins to levels encountered during natural exposure results in BAL fluid neutrophilia[62,82,83] and airway hyper-responsiveness.[81] Also, horses in training kept on straw bedding experience episodes of IAD that last longer than in horses bedded on paper.[8] These findings are consistent with data showing that conventional horse management consisting of indoor housing with straw bedding and feeding of hay results in much larger dust exposure levels than housing of horses on wood shavings and pelleted feed or keeping them on pasture.[16,84] Some horses with IAD demonstrate increased eosinophil or metachromatic cell counts in BAL fluid, suggesting hypersensitivity response of the lower airways to inhaled allergens.[1,2,4,60]

Atmospheric oxidants such as ozone have the potential to cause lower airway inflammation in horses, but levels encountered during natural exposure are unlikely to induce IAD in otherwise healthy animals.[85] Nevertheless, horses exercising strenuously while exposed to ozone levels comparable to atmospheric concentrations develop histologic evidence of airway damage and horses with IAD have elevated indices of oxidant injury[86] in BAL fluid, suggesting that oxidant injury may play a role in the pathophysiology if IAD.[85,87]

Several additional factors commonly encountered in athletic horses may contribute to the pathogenesis of IAD. Transportation of horses over long distances may induce airway inflammation and colonization of the tracheobronchial tree by bacteria.[88,89] Strenuous exercise results in colonization of the lower airways by large numbers of bacteria (10- to 100-fold compared with pre-exercise levels).[90] Both heaves in horses and asthma in people have a significant heritable component.[91,92] Therefore, airway response to environmental challenges is probably modulated by certain genes, and study of linkage between respiratory diseases such as heaves and IAD and certain immunomodulator genes will help identify animals at risk and in designing better ways of treating and preventing respiratory diseases.

Epidemiology

Several epidemiologic studies concerning IAD have been conducted on Standardbred and Thoroughbred race horses. However, only anecdotal reports are available for other breeds. The incidence of IAD is 22% in Standardbreds based on endoscopic evidence of mucopurulent exudate in the tracheobronchial tree within 30–90 minutes after a race.[7] In Thoroughbreds in training, the incidence is 50% on average

using similar endoscopic criteria as in Standardbreds. However, the incidence ranged from 13% in horses examined at rest to 65% in horses evaluated after strenuous exercise.[5] A few isolated specks of exudate were observed in 58% of the horses examined and a continuous stream was present in 42%. Similar results have been reported when the definition of IAD is based on an inflammation scoring system including detection of exudate during tracheal endoscopy and proportion of neutrophils and nucleated cell count in tracheal wash fluid. Only 38% of horses with IAD have a cough. However, horses that cough are four times more likely to have IAD.[8] Monthly fluctuation in the incidence of IAD based on inflammation score in Thoroughbreds in training may vary between 0 and 45%.[8] Age appears to be a significant factor, with 2-year old horses being two to seven times more likely to be affected by IAD than older horses.[8,12,42]

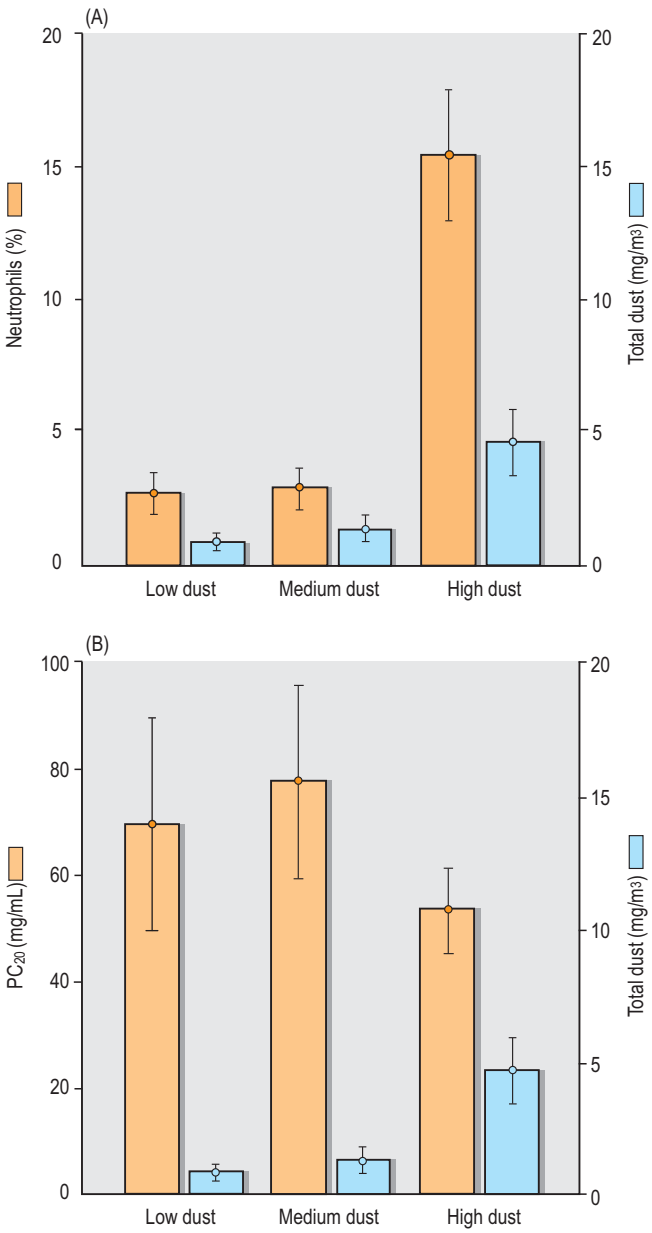


Fig. 29.5
Effect of dust exposure on (A) bronchoalveolar lavage fluid cytology and (B) airway responsiveness to histamine challenge. Low dust: horse in stall fed pellets and bedded on wood shavings; Medium dust: horse in stall fed pellets and bedded on straw; High dust: horse in stall fed moldy hay and bedded on straw. Total dust was measured in the breathing zone of the horse. PC_{20}: provocative concentration of histamine required to decrease $FEV_{1.5}$ by 20%.

Prevention

The risk of IAD is significantly lower in older horses, suggesting that development of an appropriate immune response may protect horses from IAD.[12,42] Even though viral diseases do not appear to play a major role in IAD, proper vaccination against respiratory pathogens prior to introduction of young horses into the stable is recommended.

Air quality, in particular low dust level, is an important part of preventive measures (see discussion of environmental changes in the RAO section, below). Horses kept in well-ventilated stalls and bedded on shredded paper are four times less likely to develop IAD than horses housed in closed stalls and bedded on straw.[8] Also, a study showed that young healthy horses fed hay while being maintained on pasture for a 3-month period did not exhibit signs of respiratory disease. However, they developed pulmonary neutrophilic inflammation within a month of being housed inside a barn on the same diet and bedded on straw.[80] Another study found that adult horses free of respiratory disease initially and exposed to incremental amounts of dust for 2 weeks at a time showed an increased percentage of neutrophils in BAL fluid and an increase in airway responsiveness to histamine challenge (Fig. 29.5).[81] These studies suggest that exposure of horses to dust levels commonly encountered in standard housing systems is sufficient to cause airway inflammation and pulmonary dysfunction in otherwise healthy horses.

Recurrent airway obstruction (RAO, SPAOPD, heaves, chronic obstructive pulmonary disease (COPD), broken wind)

- RAO is associated with exercise intolerance, increased tracheobronchial exudate, mild to severely increased respiratory efforts, and occasionally cough.
- Mature and older horses housed in stables for extended periods and fed hay are commonly affected.
- Horses suffering from summer pasture-associated obstructive pulmonary disease (SPAOPD) are clinically indistinguishable from RAO except that they develop clinical signs while at pasture during the summer.

- Bronchoalveolar lavage fluid cytology and response to bronchodilators are valuable diagnostic tools for RAO.
- Horses with RAO exhibit severe airflow obstruction and airway hyper-responsiveness.
- RAO appears to be hypersensitivity to inhaled organic molds with additional role played by inhaled endotoxins.
- Therapy is aimed at decreasing exposure to environmental allergens, decreasing airway inflammation with glucocorticoids, and relieving airway obstruction with bronchodilators.

Recognition of the disease

History and presenting complaint

Recurrent airway obstruction (RAO) or heaves is an allergic disease characterized by cough, accumulations of mucopurulent secretions in the tracheobronchial tree, abnormal breath sounds, increased respiratory efforts, and exercise intolerance.[93] Coughing and nasal discharge are frequently reported in horses with RAO (84% and 54% respectively). However, they are non-specific signs of respiratory disease.[11] Similarly, presence of tracheal exudate is common (96%) yet it is also found in a variety of pulmonary diseases. Exercise intolerance is usually marked but highly dependent on the level of exertion required of the horse as well as disease severity. Frequent bouts of coughing may be the main perceived cause of exercise intolerance. Horses with RAO exhibiting mild respiratory signs at rest may only show abnormally increased respiratory efforts for a given exercise intensity or prolonged recovery post-exercise. Because of a lack of objective data on 'normal' cardiopulmonary variables during exercise and recovery period in healthy horses, most of the assessment concerning exercise intolerance is based on the owner's or trainer's perception.

Clinical signs of RAO usually resolve within a few days after placing the horse on pasture or improving the environment by reducing organic dusts and increasing ventilation in the stall. Conversely, susceptible horses housed indoors and exposed to moldy hay develop clinical signs within a few hours to a few days.[53,59] Summer pasture-associated obstructive pulmonary disease (SPAOPD) is clinically indistinguishable from RAO except that historical findings reveal disease flare-ups while horses are kept at pasture during summer months and clinical improvement during winter or after horses are housed indoor.[66,94] Horses with RAO and SPAOPD tend to be mature (> 7 years) to old animals and there is no apparent breed or sex predilection.[11,94] Duration of the disease varies from months to years with periods of disease exacerbation (crisis) alternating with periods of clinical remission of variable duration. Hence, clinical signs are recurrent but the disease is permanent.[3]

Effects of RAO on performance RAO is widely accepted as a cause of exercise intolerance. However, few studies have attempted to understand the mechanisms responsible for this impaired performance. Horses with severe clinical signs are markedly hypoxemic and sometimes hypercapnic at rest, but values are not different from healthy controls during periods of disease remission.[53,95,96] Pronounced ventilation–perfusion mismatching appears to be responsible for these gas exchange abnormalities.[29,97,98] During submaximal exercise, horses with RAO in crisis become significantly more hypoxemic and hypercapnic and these abnormalities are associated with decreased expired minute ventilation and increased work of breathing.[99] Interestingly, alveolar ventilation and oxygen consumption may be maintained because of compensatory mechanisms such as decreased dead space ventilation, increased cardiac output and hemoglobin concentration. However, these compensatory mechanisms are likely to increase oxygen consumption by respiratory and cardiac muscles and to reduce the amount of oxygen available for exercising muscles, the net result being exercise intolerance as demonstrated by Art et al.[99] This phenomenon has been demonstrated in humans where respiratory muscles consume 10–15% of maximum oxygen consumption in trained athletes and up to 50% in chronic obstructive pulmonary disease (COPD) patients.[100] Decreasing the workload on respiratory muscles by mechanical ventilation during exercise has been shown to improve oxygen supply to locomotor muscles.[101] Consequently, locomotor muscle fatigue may in fact limit exercise capacity in humans with COPD exercising beyond the anaerobic threshold. On the other hand, COPD patients exercising below the anaerobic threshold may be more limited by ventilation. Whether these findings apply to exercising horses with RAO remains to be proven.

Physical examination

Horses with RAO may present with a wide spectrum of clinical signs depending on disease severity. Horses with mild RAO may exhibit little to no clinical signs of respiratory disease

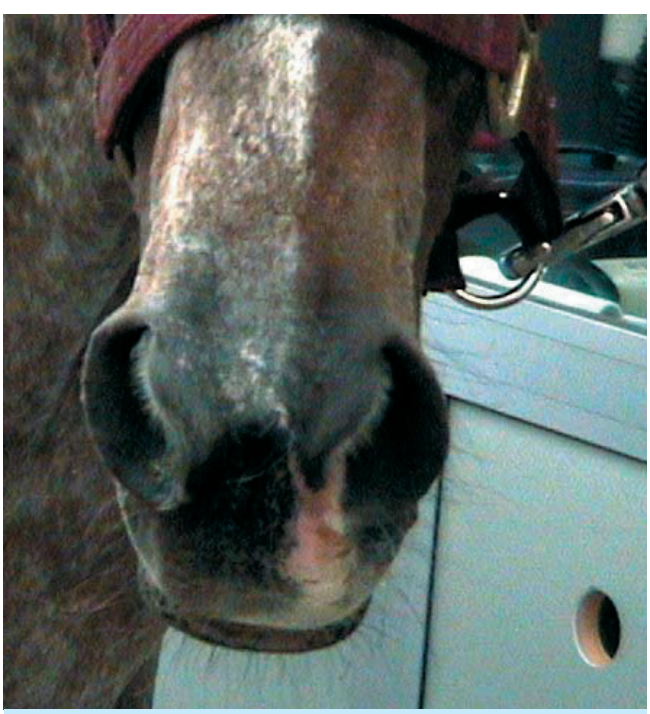


Fig. 29.6
Horse with RAO exhibiting increased respiratory efforts (nostril flaring).

except for exercise intolerance and may be difficult to differentiate from horses with IAD (Table 29.1). On the other end of the spectrum, horses with severe RAO show markedly increased respiratory efforts manifested by nostril flaring, head and neck extension, pronounced abdominal muscle contraction during expiration (heaving), and exaggerated rib excursion during inspiration (Fig. 29.6). Over time, horses develop hypertrophy of the external abdominal oblique muscles resulting in the characteristic 'heave line'. Respiratory rate is quite variable but is usually elevated. These clinical signs result from small airway obstruction secondary to airway inflammation, bronchospasm, mucus plugging of airways, and thickening of the airway wall.

Bilateral mucoid to mucopurulent nasal discharge may be present. A deep cough may be heard intermittently or in bouts of paroxysmal coughing. Thoracic auscultation may reveal increased breath sounds bilaterally, an extended area of auscultation, and abnormal breath sounds (i.e. crackles, wheezes). Horses' thick chest wall renders auscultation an insensitive indicator of pulmonary disease with abnormal findings obtained in less than 50% of horses with RAO.[11]

Special examination

Horses with normal respiratory tract have either no or just a few flecks of mucus visible upon endoscopy of the airways.[20,37] The presence of variable amounts of respiratory secretions in the tracheobronchial tree is found in the majority of RAO horses. However, it is also common in horses with IAD and infectious pulmonary diseases.[5,7,37] Horses with severe pulmonary disease, including heaves, often exhibit marked airway erythema and bronchial edema illustrated by blunting of the carina and 'bumpiness' of the airway surface (Fig. 29.7). Nevertheless, many horses with severe heaves and large amounts of tracheal exudate do not have visible signs of tracheobronchial inflammation.[37]

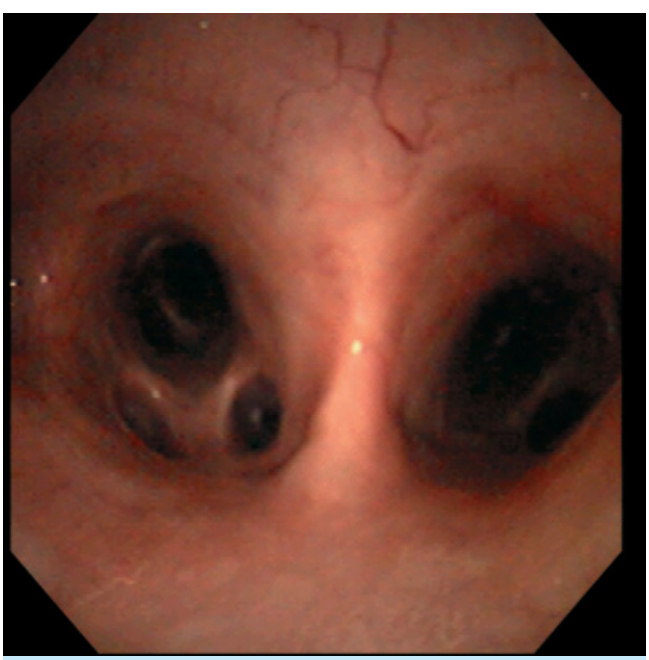


Fig. 29.7
Endoscopic view of the carina in a horse with RAO and marked bronchial edema.

Collection of respiratory secretions using tracheal wash (TW) or BAL techniques is important for diagnostic purposes and monitoring response to therapy. Description of the techniques and indications have been discussed in the IAD special examination section of this chapter. Sedation of the horse prior to BAL collection is mandatory and sometimes needed as well for TW. Administration of α_2-agonist sedatives (e.g. xylazine, detomidine) to horses with RAO results in significant decrease in respiratory rate, minute ventilation, and variable effects on pulmonary resistance (R_L) and dynamic lung compliance (C_{dyn}).[102–104] Pao_2 in affected horses is either maintained or only mildly decreased after administration of sedatives. Similar effects of sedatives on lung function are reported in healthy horses. Therefore, administration of sedatives to horses with RAO prior to diagnostic procedures is considered safe. The volume of fluid retrieved during the BAL procedure may be decreased in RAO horses due to small airway collapse as fluid is aspirated back. However, as long as the volume of fluid infused is sufficient (250–500 mL) there is no significant difference in absolute or differential cell counts between aliquots retrieved sequentially.[105] Therefore, interpretation of BAL fluid cytology in horses with RAO has diagnostic value even if the procedure only yielded a small amount of fluid.

Thoracic radiographs may be useful to rule out pulmonary diseases other than RAO. However, interpretation of radiographs is considered insensitive because radiographic findings correlate poorly with histopathology of the lungs and interpretation of images is highly variable between examiners.[106] Also, no radiographic findings are specific for a particular inflammatory lung disease, which renders chest radiography of limited value for the diagnosis of RAO.

Pulmonary function tests allow quantification of lung dysfunction using various techniques (see discussion in 'IAD/special examination'). During episodes of disease exacerbation, bronchoconstriction, edema of airway wall, and accumulation of secretions in the airways result in airflow obstruction and stiffening of the lungs. These structural changes translate into functional changes such as increased maximal changes in transpulmonary pressure (ΔP_{plmax}) R_L and decreased C_{dyn} (Table 29.4).[6,18] Values return within the normal range when horses are in disease remission. However, measurement of lung mechanics during tidal breathing is not sensitive and test results usually become abnormal when horses display obvious clinical signs of heaves. These tests are still useful in clinical practice to evaluate reversibility of airway obstruction after administration of a bronchodilator or to assess response to therapy because clinical signs alone are poor predictors of lung function, i.e. a significant degree of airway obstruction may still be present after the course of therapy even though clinical signs have resolved.[107] Another test of lung function called forced expiration has the advantage of being more sensitive than standard lung mechanics, allowing detection of airway obstruction in RAO horses in the absence of clinical signs (i.e. disease remission; Fig. 29.2).[108] Unfortunately, this test is technically

Table 29.4 Ranges of standard lung mechanics in healthy horses and horses with RAO during disease remission or crisis

Variable	Healthy	Healthy	RAO			RAO			
			Remission	Remission	Remission	Crisis	Crisis	Crisis	Crisis
n	9 horses	6 ponies	5 horses	9 horses	6 ponies	9 horses	6 horses	4 horses	6 ponies
ΔP_{plmax} (cmH_2O)	5.5 ± 1.6		5.7 ± 1.7	8.6 ± 0.5		58.4 ± 4.3	36 ± 18	19.8 ± 9.8	
R_L (cmH_2O/L/s)	0.49 ± 0.30	0.95 ± 0.15	0.61 ± 0.17	0.56 ± 0.06	0.84 ± 0.25	2.85 ± 0.23	3.4 ± 1.1	1.39 ± 0.89	5.0 ± 0.62
C_{dyn} (L/cmH_2O)	2.26 ± 0.60	0.73 ± 0.10	2.16 ± 1.00	1.11 ± 0.19	0.96 ± 0.29	0.15 ± 0.04	0.2 ± 0.22	0.96 ± 0.45	0.21 ± 0.06
V_T (L)	6.26 ± 1.51	1.91 ± 0.2	5.64 ± 0.94		1.55 ± 0.23		4.9 ± 1.4	4.48 ± 0.72	1.77 ± 0.3
f (breaths/min)	11.7 ± 2.6	15.5 ± 1.3	17.3 ± 2.8		21.9 ± 3.6		17 ± 9	21.1 ± 6.2	27.1 ± 4.2
Reference	Couetil et al[10]	Broadstone et al[102]	Couetil et al[10]	Robinson et al[330]	Broadstone et al[102]	Robinson et al[330]	Ammann et al[170]	Couetil et al[10]	Broadstone et al[102]

ΔP_{plmax}, maximum change in transpulmonary pressure; R_L, pulmonary resistance; C_{dyn}, dynamic lung compliance; V_T, tidal volume; f, breathing frequency.

demanding and currently restricted for laboratory use. Lung function may be assessed using forced oscillatory mechanics (FOM), which requires only placement of a face mask on the horse. Horses with RAO in crisis exhibit frequency dependence of resistance. However, horses with mild clinical signs or in disease remission usually have values within normal limits.[32,109] Another non-invasive method that is well suited for field-testing combines the use of respiratory inductance plethysmography and pneumotachography during normal breathing at rest.[58] Airflow measured at the nostril opening by a pneumotachograph is compared with the flow signal derived from bands placed around chest and abdomen. Several indices derived from this lung function test correlate with conventional lung mechanics (ΔP_{plmax}, R_L) and allow quantification of airway obstruction in horses with RAO as well as response to bronchodilators or histamine challenge.[58]

A unique feature of horses with airway obstruction (RAO, SPAOPD, IAD) is their increased airway narrowing in response to challenge with irritants such as histamine or methacholine (hyper-responsiveness). Response to challenge (bronchoprovocation) may be assessed using different types of lung function test such as standard lung mechanics,[59,110–113] forced oscillatory mechanics,[114] respiratory inductance plethysmography,[33,58] and forced expiration.[57] In general, the greater the airway obstruction, the more pronounced the bronchoconstriction for a given concentration of irritant. Bronchoprovocation may prove to be a useful method for the detection of mild to moderate RAO in horses that do not display overt clinical signs.

Lung volume measurements, in particular functional residual capacity (FRC), are increased in horses with RAO compared with healthy controls.[115,116] However, as disease severity increases, the amount of air trapped behind obstructed airways rises and may lead to decreased FRC when measured by gas dilution techniques (helium or nitrogen),[117] when in fact FRC measured by plethysmography would show an increased volume.[118] The maximum volume of air that can be exhaled after a deep inspiration (FVC) is not smaller in horses with RAO, but the time needed to exhale FVC is significantly longer.[10] As a result, horses with airway obstruction have decreased forced expiratory volume in a given time (e.g. FEV_1 for volume exhaled in 1 second) and decreased forced expiratory flow during end expiration (Fig. 29.2). These findings suggest that expiratory flow limitation would be likely to occur during strenuous exercise when horses complete 1.5–2 respiratory cycles per second and contribute to the exercise intolerance manifested by RAO horses.

In addition to alteration in lung mechanics, RAO horses exhibit abnormal gas exchanges at rest during periods of disease exacerbation leading to hypoxemia and sometimes hypercapnia.[117,119] These blood gas abnormalities are mainly the result of ventilation–perfusion mismatch and increased dead-space ventilation.[29] Horses with mild clinical signs usually have normal blood gases. During exercise, the degree of exercise-induced hypoxemia and hypercapnia is markedly worse in RAO horses in crisis compared with those in remission.[99] Deterioration in gas exchanges appears to be mainly due to further deterioration in the ventilation–perfusion relationship.

Few studies have examined the relationship between lung histopathology, clinical signs, and lung function in horses with chronic airway disease. Significant correlation between percutaneous lung biopsy scores and clinical signs ($r = 0.58$) has been reported in RAO horses[120] and between mucus score in lung biopsies and clinical signs ($r = 0.78$) in horses with SPAOPD.[121] Also, clinical signs are correlated with indices of lung function such as ΔP_{plmax} in both RAO and SPAOPD.[10,121] Another investigation evaluating gas exchanges and lung biopsy parameters in Standardbred race horses with IAD showed that the severity of lung biopsy score was negatively correlated with lower minute ventilation at a speed corresponding to a heart rate of 200 beats/min, suggesting that bronchial epithelial hyperplasia of the small airways was probably causing airflow obstruction.[31] However, a similar relationship was not found in horses with RAO.

Laboratory examination

Hemogram and serum biochemistry are usually within the normal range,[61] although some horses with acute severe RAO may exhibit a mild hyperfibrinogenemia.

Cytologic examination of TW or BAL fluid is often useful to reach a final diagnosis. TW fluid obtained from horses with RAO and SPAOPD usually reveals a marked increased in neutrophil percentages (> 50%; range, 7–96%).[37,39,45,79] Neutrophils are non-degenerate and even if bacteria are isolated in some cases, they do not play a role in the pathogenesis of the disease. Increased amounts of mucus containing casts of inspissated mucus originating from the bronchioles (Curschmann's spirals) are often present in long-standing cases.[38] Several reports also found a wide range of neutrophil ratios in TW collected from clinically healthy horses (0–88%).[37,44] Therefore, the usefulness of TW cytology for diagnosis of RAO and SPAOPD is limited. BAL fluid is preferred in diffuse pulmonary disease such as RAO and SPAOPD because BAL fluid cytology is more representative of lung histopathology.[43,44] BAL fluid cytology in healthy control horses reveals that lymphocytes and alveolar macrophages predominate and neutrophils represent < 10% of the total nucleated cell count (Table 29.5).[47,62,121] A marked absolute and relative neutrophilia (> 20%) is usually observed in BAL fluid from horses with RAO and SPAOPD (Table 29.5).[61,62,121] In affected horses the range of neutrophil percentages is wide (10–98%) but no significant differences exist between BAL fluid cytology collected from different regions of the lung.[47]

Necropsy examination

The classic histopathologic lesion in horses with RAO is bronchiolitis characterized by peribronchiolar lymphoplasmacytic, neutrophilic, and sometimes eosinophilic cell infiltration, bronchiolar goblet cell metaplasia, epithelial hyperplasia, and accumulation of mucopurulent exudate in the bronchioles' lumen.[120,122,123] Similar changes are also frequently detected in the large airways.[124] Other lesions reported in severely affected horses are peribronchiolar fibrosis and epithelial metaplasia. Horses with SPAOPD display histopathologic changes that are indistinguishable from RAO.[121] Emphysema is rarely present in RAO horses and both centrilobular and panlobular forms have been reported.[125–127] Lungs of affected horses tend to remain overinflated at post-mortem examination because of air trapping secondary to airway obstruction and not emphysema. In general, there is a good correlation between the degree and extent of histopathologic changes and clinical severity.[122–124]

Table 29.5 Bronchoalveolar lavage (BAL) fluid cytology in control horses and in horses with recurrent airway obstruction (RAO) and summer pasture-associated obstructive pulmonary disease (SPAOPD)

BAL technique	Environment/ number	Leukocytes (cells/mL)	Alveolar macroph. (%)	Lymphocytes (%)	Neutrophils (%)	Eosinophils (%)	Mast cells (%)
Controls							
2 × 250 mL saline-pump-endoscope	Pasture/10	309.2 ± 48.5	46.4 ± 4.0	44.5 ± 5.7	8.7 ± 2.8		
2 × 250 mL saline-pump-endoscope	Stable/10	200.2 ± 25.1	31.6 ± 7.4	40.8 ± 6.3	27.6 ± 7.8		
2 × 250 mL saline-pump-endoscope	Stable/5	290 ± 90	48.6 ± 7.4	42.9 ± 7.8	7.2 ± 5.9	0.3 ± 0.4	1.0 ± 1.0
2 × 250 mL saline-pump-endoscope	Pasture/5	200 ± 100	58.2 ± 9.8	35.9 ± 8.4	4.7 ± 3.5	0.2 ± 0.2	1.0 ± 1.0
300 mL saline-pump-endoscope	Stable/7	90 (50–140)	49.7 (36–74.3)	39.7 (20–51.3)	1.0 (0.7–4.0)	0.0 (0.0–0.7)	9.3 (0.7–12.3)
3 × 100 mL saline-syringe-endoscope	Pasture/6		22.5 (19–50)	61 (40–70)	6 (3–26)	0 (0–6)	4.5 (0–6)
RAO/SPAOPD							
2 × 250 mL saline-pump-endoscope	Pasture RAO/5	110 ± 43.5	29.9 ± 3.9	40.7 ± 6.0	29.4 ± 7.2		
2 × 250 mL saline-pump-endoscope	Stable RAO/5	132.5 ± 60.6	**15.3 ± 7.0**	**13.0 ± 5.6**	**71.6 ± 12.2**		
3 × 100 mL saline-pump-endoscope	Pasture RAO ponies/6	199 ± 61	28.6 ± 6.8	60.3 ± 24.1	5.8 ± 2.3	1.0 ± 0.4	4.0 ± 1.1
3 × 100 mL saline-pump-endoscope	Stable RAO ponies/6	316 ± 49	10.4 ± 3.5	21.8 ± 4.7	**58.2 ± 13.9**	2.8 ± 1.9	2.8 ± 0.8
300 mL saline-pump-endoscope	Stable RAO/6	105 (70–240)	11.9 (1.7–57.3)	22.2 (3.7–36.3)	**64.2 (5.7–94.3)**	0.0 (0.0–0.7)	2.2 (0.0–4.3)
2 × 250 mL saline-pump-endoscope	Stable RAO/5	2340 ± 3690	**14.6 ± 12.6**	**22.1 ± 17.9**	**61.3 ± 29.1**	0.0 ± 0.0	1.6 ± 1.9
2 × 250 mL saline-pump-endoscope	Pasture RAO/5	410 ± 390	28.2 ± 10.3	30.5 ± 15.0	37.5 ± 23.6	0.2 ± 0.4	3.7 ± 2.9
3 × 100 mL saline-syringe-endoscope	Pasture SPAOPD/8		**10.5 (2–38)**	**28.5 (3–80)**	**65 (5–92)**	0 (0–0)	2 (0–3)

Values are expressed as mean ± standard deviation or median (range); Bold values are significantly different from control values ($P < 0.05$).
Data from references 47, 61, 62, 121, and 134.

However, lesions are usually extensive but multifocal in nature, making interpretation based on small size samples (e.g. percutaneous lung biopsy) hazardous.[123]

Ultrastructural changes are characterized by loss of ciliated cells in the larger airways and replacement by a hyperplastic epithelium.[124] Examination of terminal airways and alveoli shows degenerative changes affecting non-ciliated bronchiolar epithelial cells (Clara cells) suggesting that Clara cells may be the target for antigens and inflammatory mediators during the disease process.[123]

Diagnostic confirmation

Horses presenting an abnormal increase in respiratory efforts should be examined to rule out upper and lower airway causes (Fig. 29.8). Upper airway obstruction may be associated with loud abnormal respiratory sounds (stridor). Lower airway diseases are often associated with abnormal breath sounds upon thoracic auscultation. Typically, upper airway obstruction results in increased inspiratory efforts whereas intrathoracic airway obstruction is associated with increased expiratory efforts. Fixed obstructions result in sounds, respiratory efforts, and respiratory times that are comparable during inspiration and expiration. Variable (dynamic) obstructions are characterized by a marked difference between inspiratory and expiratory sounds. Endoscopic examination should be performed rapidly in order to localize the disease process.

A decrease in lung sounds in the ventral thorax is usually indicative of pleural effusion or diaphragmatic hernia. Decreased lung sounds dorsally associated with increased resonance upon percussion of the thorax are consistent with pneumothorax. Diagnosis may be confirmed by ultrasonography of the thoracic cavity. The presence of abnormal lung sounds (crackles, wheezes) in horses with fever and respiratory distress suggests infectious pulmonary disease (e.g. bronchopneumonia, pulmonary abscess, interstitial pneumonia, necrotizing pneumonia).[128,129] A horse with labored breathing, normal rectal temperature, and abnormal lung sounds should be treated with a fast-acting bronchodilator (e.g. aerosolized albuterol, intravenous atropine) to assess the role of bronchoconstriction. Marked improvement in clinical signs strongly suggests reversible obstructive pulmonary disease such as RAO and SPAOPD. Marginal or no improvement may be associated with restrictive pulmonary diseases (e.g. pleural effusion, pulmonary edema, interstitial pneumonia, pulmonary fibrosis, silicosis, mediastinal mass), or non-respiratory diseases (e.g. cardiac failure). Thoracic radiography and cardiac ultrasonography are indicated to characterize the disease process and evaluate the severity of the lesion.

Horses in respiratory distress with no abnormal respiratory sounds should be further evaluated. Horses with

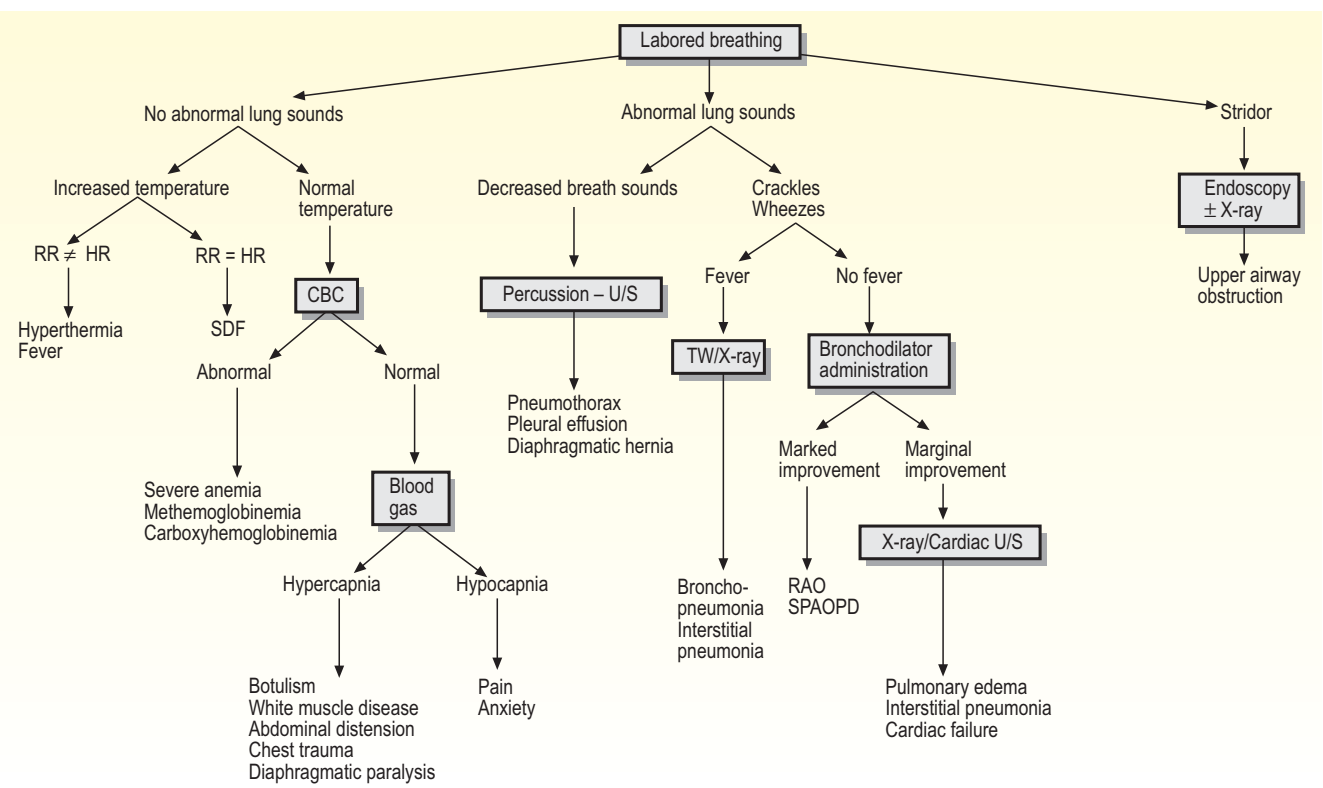


Fig. 29.8
Diagnostic approach in horses with labored breathing. CBC, complete blood count; HR, heart rate; RAO, recurrent airway obstruction; RR, respiratory rate; SDF, synchronous diaphragmatic flutter; SPAOPD, summer pasture-associated obstructive pulmonary disease; TW, tracheal wash; U/S: ultrasound; X-ray: radiographs.

synchronous diaphragmatic flutter present with pronounced abdominal contractions that might be mistaken for increased respiratory effort. However, in this case spasmodic contractions of the flank are synchronous with the first heart sound and are independent of the normal respiratory cycle.[130] A markedly elevated rectal temperature may be associated with conditions causing hyperthermia (e.g. exercise, hot environment) or fever and contribute to respiratory distress. Collection of blood for packed cell volume measurement and hematology is valuable to detect anemia and diseases resulting in decreased oxygen-carrying capacity of the blood (methemoglobinemia, carboxyhemoglobinemia). Only severe anemia resulting in packed cell volume < 8–10% may cause labored breathing at rest. Anemia does not lower arterial oxygen tension but does cause hypoxemia (a decrease in oxygen content in blood) and a decrease in the delivery of oxygen to tissues (i.e. tissue hypoxia). Therefore, anemic horses have a normal Pa_{O_2} and hyperventilation results from acidification of cerebrospinal fluid secondary to increased anaerobic metabolism. An arterial blood gas sample is indicated in horses with normal hematologic findings. Hypercapnia may be associated with conditions impairing respiratory muscle function (e.g. botulism, nutritional muscular dystrophy, diaphragmatic paralysis) or chest wall movement (e.g. abdominal distension, chest trauma). Hypocapnia indicates hyperventilation and may be in response to painful conditions (e.g. colic) or to anxiety.

Treatment and prognosis

Therapeutic aims

The goals of therapy are to control airway inflammation and relieve airflow obstruction. Treatment of RAO and SPAOPD should place emphasis on environmental changes.[53] Medical therapy is useful to control clinical signs in severely affected animals and when improvement in environmental management is limited. The main classes of drugs recommended for RAO and SPAOPD are corticosteroids to treat airway inflammation and bronchodilators to relax airway smooth muscle. Improvement of mucociliary clearance may also help reduce airway obstruction.

The type of activities the horse is performing as well as the initial complaint from the owner should be taken into consideration before therapy is recommended. For example, a RAO-affected horse used for showjumping that started exhibiting decreased performance and coughing while being maintained in a low-dust environment should benefit from medical therapy. However, a brood mare exhibiting an acute RAO crisis 2 weeks after being housed in the barn for the winter may only need simple environmental control measures (e.g. changing bedding and feed) to be implemented in order to resolve clinical signs even though lung function and BAL fluid cytology may take weeks to improve.

Therapy

Environmental changes Several measures help reduce exposure of the horse's airways to respirable particles and are discussed in detail below (RAO prevention). Placing RAO horses in crisis into a low-dust environment (e.g. wood shavings bedding and pelleted diet) results in significant improvement in lung function within 3 days, even if environmental changes only take place in the affected horse's stall.[131] Horses become free of clinical signs within 1 to 2 weeks in optimal indoor housing or outside on pasture.[59,132] Some horses may only improve partially after being placed on pasture, especially chronic long-standing cases. Medical therapy will help most of those cases to become free of clinical disease (remission), at which point medication can be discontinued. Subsequently, horses may remain free of clinical disease for extended periods if they are kept in a low-dust environment. Because of the nature of the disease, susceptible horses may suffer another bout of the disease when exposed to allergens.

Horses suffering from SPAOPD are affected during the summer while at pasture, presumably from inhaling plant allergens such as pollen and thermophilic molds.[66] In those cases, removal from pasture and confinement to a low-dust indoor environment is recommended. However, medical therapy is often needed to provide clinical resolution.[66,133] The management of affected horses may be complicated by the fact that some animals suffer from both RAO and SPAOPD.[133]

Systemic medical therapy Most horses are easy to treat by the oral or injectable route and the cost of systemic therapy is usually less than that of aerosol therapy because of the need to purchase a delivery device (i.e. face mask) for aerosol administration. However, systemic therapy with corticosteroids or bronchodilators may result in adverse effects because of the dosages required for clinical efficacy.

Corticosteroids Corticosteroids are potent inflammation inhibitors with known efficacy for the treatment of heaves. Triamcinolone acetonide is a potent long-acting corticosteroid that may improve lung function for 2 to 4 weeks after administration of a single dose (0.09 mg/kg, i.m.) to RAO horses maintained on straw bedding and fed hay.[134] Neutrophil percentage in BAL fluid may also be significantly decreased within 2 weeks of treatment. Depending on the dose of triamcinolone used, endogenous cortisol production may be suppressed for 2 to 4 weeks but adrenal gland response to ACTH administration is maintained.[134]

Dexamethasone (0.1 mg/kg, i.v., every 24 hours) induces a marked improvement in clinical signs and lung function of RAO horses by the third day of treatment.[54] These beneficial effects may persist for at least a week after treatment is discontinued. A reduction in BAL fluid neutrophilia is evident within 3 days of therapy and after 1 week, proliferation of pro-inflammatory lymphocytes is prevented.[135] Dexamethasone results in marked adrenal suppression of endogenous cortisol production starting 2 hours after administration and persisting approximately 3 days after treatment ends. However, adrenal gland response to exogenous ACTH is maintained.[136,137] Treatment of RAO horses with dexamethasone 21-isonicotinate (0.04 mg/kg, i.m., every 72 hours) reduces airway obstruction 3 days after treatment initiation with a maximum effect obtained after 7 days.[138] Oral forms of dexamethasone are commonly used in the field for the treatment of

RAO but pharmacokinetic or efficacy data are currently not available.

Oral prednisone has for a long time been advocated for the treatment of RAO. However, several reports have now documented its poor efficacy.[131,138,139] In a crossover study, RAO horses in crisis were placed in a low-dust environment for 14 days while half of them received prednisone tablets (2.2 mg/kg, by mouth, every 24 hours) and the other half were left untreated. Pulmonary function improved significantly between day 3 and day 14 in both groups. However, no significant effect of prednisone treatment was detected.[131] The only beneficial effect of prednisone treatment was a significant decrease in the number of the BAL fluid neutrophils. The reason for this lack of efficacy is related to the pharmacokinetic characteristics of the drug.[140] Prednisone is poorly absorbed after oral administration of tablets or liquid forms and the active metabolite prednisolone is detected in the serum in small quantities in very few horses (1/5 with tablet form, 0/5 with liquid form). Conversely, both liquid and tablet forms of prednisolone are well absorbed in the horse with a bioavailability > 50%.[140] Significant adrenal suppression may be detected after treatment with prednisone tablets, but it is short-lived and less pronounced than with prednisolone tablets.

Deleterious side effects associated with corticosteroid therapy may develop depending on drug potency, dose used, and treatment duration. Long-acting and potent corticosteroids (e.g. triamcinolone, dexamethasone) are more likely to cause adverse effects such as immune suppression, iatrogenic Cushing's disease, adrenal cortex suppression and possibly laminitis.[137,141,142] For these reasons, triamcinolone acetonide administration should not be repeated at less than 3-month interval.[143] Responsiveness of adrenal glands to ACTH persists during dexamethasone therapy using doses up to 30 mg per day for 31 days. Therefore, adrenal atrophy is unlikely to develop if therapy lasts less than a month.[144] Discontinuation of dexamethasone after an extended treatment period should be done carefully to avoid acute adrenocortical insufficiency. Dexamethasone doses as low as 0.01 mg/kg result in adrenal suppression for up to 24 hours as compared with < 24 hours for prednisolone.[144] Therefore, discontinuation of prolonged dexamethasone therapy should be performed by slowly and gradually decreasing the dose until the least suppressive amount (0.01 mg/kg) is given every third day for a minimum of 2 weeks. Alternatively, dexamethasone therapy may be replaced by an equipotent dose of prednisolone (1 mg dexamethasone ≈ 7.5 mg prednisolone) that will be tapered down to alternate day treatment. Before treatment is discontinued, an ACTH stimulation test should be performed to assess the adrenocortical reserve necessary for the horse to cope with stress.

Bronchodilators Bronchodilators are indicated to relax airway smooth muscle and relieve airflow obstruction, but they should not be used alone because they have no anti-inflammatory properties and do not reduce airway hyperresponsiveness.[76] In addition, prolonged use of a certain type of bronchodilator (e.g. β_2-agonists) as sole medication induces airway receptor downregulation and renders the drug less effective. This phenomenon is prevented by combined use of β_2-agonists with corticosteroids. Bronchodilator administration is also beneficial in horses that exhibit mild clinical signs, particularly those involved in athletic activities, because significant bronchospasm may be present.

The three classes of drugs available as systemic bronchodilators are anticholinergics, β_2-agonists, and methylxanthines. Atropine (0.01–0.02 mg/kg, i.v.) is an anticholinergic drug that has been used systemically in horses with heaves and shown to provide rapid and marked improvement in lung function (mean reduction in ΔP_{plmax} of 68–83%) and clinical signs.[96,145,146] Effects occur within 10 minutes of administration, peak around 30 minutes and last a maximum of 1–2 hours. Potentially serious side effects such as ileus and abdominal pain usually develop when higher dosages are used (22–88 mg)[147] but are rare with low dose atropine (≤ 0.02 mg/kg) unless administration is repeated. Atropine may be used as a single dose for the rapid relief of severe airway obstruction and for diagnostic and prognostic purposes. However, fast-acting aerosolized bronchodilators (e.g. albuterol) are safer and at least as effective alternatives.

Clenbuterol hydrochloride syrup (Ventipulmin) was approved by the Food and Drug Administration (FDA) in 1998 for the treatment of heaves in horses in the USA. Injectable and oral formulations have been available in other countries for many years. In an open field trial involving 239 horses with heaves 75% improved clinically after administration of oral clenbuterol (0.8–3.2 μg/kg, every 12 hours for 10–30 days) and 25% did not respond to treatment.[148] The percentage of horses responding to treatment increased as the dose of clenbuterol was augmented (24% at 0.8 μg/kg to 75% at 3.2 μg/kg). A controlled clinical trial failed to demonstrate any benefit of the drug (0.4 mg/horse, by mouth, every 12 hours, $n = 7$) after 10 days of treatment.[139] Clenbuterol may also help airway mucociliary clearance by increasing ciliary beat frequency.[149] Mild side effects such as sweating, muscle tremors, and excitement occur in less than 9% of horses treated with oral clenbuterol.[148] More concerning side effects are cardiovascular remodeling detected by echocardiography immediately post-exercise in healthy horses treated with medium doses of clenbuterol (2.4 μg/kg, by mouth every 12 hours) for 8 weeks.[150] At the end of the 8-week treatment period, horses receiving clenbuterol had elevated left ventricular mass, calculated stroke volume, aortic root diameter (+ 24–30%), and larger left ventricular diameter at end systole and diastole (+ 24–40%) compared with non-treated control horses, suggesting a deleterious effect of clenbuterol on cardiac function.

Administration of the β-adrenergic drug isoproterenol (0.1–0.2 mg/kg, i.v.) to heavey horses results in clinical and lung function improvement within 15 minutes. However, results are variable between animals and heart rate more than doubles because of stimulation of cardiac β_1-receptors.[145] Terbutaline, a β_2-receptor agonist, has been used orally, intravenously and by nebulization in horses.[146] Efficacy of the oral route for the treatment of heaves is unlikely because bioavailability is less than 1%.[151]

Both intravenous (0.01 mg/kg) and aerosol (0.02 mg/kg) routes of administration may improve lung function of heavey horses for up to 6 hours but marked adverse reactions such as central nervous system (CNS) stimulation, sweating, and trembling are likely to occur with the i.v. route.[146,151]

Methylxanthine and derivatives may be beneficial in horses with heaves. However, plasma levels necessary for bronchodilation vary widely between horses and the range between effective and toxic concentration is narrow.[152,153] Aminophylline (5–12 mg/kg i.v.) and theophylline (5–10 mg/kg, by mouth) administered every 12 hours improve lung function and clinical signs in up to 50% of affected horses.[145,154] Common side effects are hyperesthesia, hyperexcitability, and muscle tremors. Pentoxifylline (36 mg/kg, by mouth, every 12 hours for 14 days) administered to RAO-affected horses results in significant improvement in lung function and is not associated with adverse effects.[155]

Enhancement of mucociliary clearance Horses with RAO and SPAOPD accumulate large amounts of mucopurulent secretions with higher viscoelasticity in their airways, therefore contributing to airflow obstruction.[156] Mucociliary clearance may be enhanced by stimulation of the ciliary apparatus or by decreasing mucus viscoelasticity, but the latter appears to be the most important factor.[157] Different types of drugs may enhance clearance of respiratory secretions including mucolytics (e.g. acetylcysteine, dembrexine hydrochloride) and drugs capable of improving mucociliary transport (e.g. β_2-agonists). However, none have been shown to be beneficial for the treatment of heaves.

Other treatments Furosemide (frusemide, 1 mg/kg i.v. or aerosol) also results in significant improvement in the lung mechanics of RAO horses but not in arterial blood gases.[158] Antihistamine drugs are commonly used to treat RAO horses in the field, but they appear to have limited usefulness and no controlled study has proved their efficacy.

A technique of overhydration consisting in the intravenous administration of 30–40 L of isotonic saline solution over a 3- to 4-hour period may benefit heavey horses.[159,160] But the method is not without risks (e.g. pulmonary edema, electrolyte abnormalities, death) and thus far, no controlled study has demonstrated its efficacy for the treatment of heaves.

Aerosol therapy Administration of therapeutic substances via inhalation has the advantage of delivering high concentrations of the drug directly into the lungs while minimizing the amount absorbed systemically and therefore, reducing the risk of adverse effects. In addition, systemic side effects and drug residue are decreased. Clinical response to aerosol medications is a function of the dose deposited in the airways, which is dependent on the delivery device, the particle size characteristics of the inhaled aerosol, the pattern of breathing, and airway disease.[161]

Deposition of therapeutic aerosols within the respiratory tract occurs mainly by inertial impaction and gravitational sedimentation.[162] Inertial impaction is largely responsible for particle deposition in nasal passages, nasopharynx, and central airways. Impaction of aerosolized particles on airway walls can occur if their size is sufficiently large (≥ 1 μm) or the air stream rapidly changing direction (e.g. high flow rate, branching airways, turbulent flow). Smaller particles (≥ 0.5 μm) that are able to reach peripheral airways and alveoli may deposit on airway surfaces by gravitational sedimentation when the air stream is sufficiently slow. Aerosols with mass median aerodynamic diameter (MMAD) > 5 μm are mainly deposited in the upper airways while the majority of particles < 1 μm are exhaled.[162] The deposition of particles in small conducting airways and alveoli is maximal when aerosol MMAD is between 1 and 5 μm.

The most important factor for aerosol deposition is the speed of inhalation.[162] As inspiratory flow rate or breathing frequency increases more particles are deposited in the upper airways. Penetration of aerosol into peripheral airways is improved when inhaled volume increases. Obviously, manipulation of these factors in the horse is limited.

Airway narrowing increases aerosol deposition in central airways and results in poor deposition in peripheral airways.[161] In horses with severe airway obstruction (i.e. RAO), aerosol deposition after administration of inhaled albuterol (360 μg) results in rapid (5 minutes) improvement in peripheral airway deposition.[163] Improved lung deposition of therapeutic aerosols is also likely to occur after administration of a bronchodilator in horses with IAD exhibiting significant airflow obstruction or bronchial hyper-responsiveness.

Therapeutic aerosols may be produced by nebulizing a solution, administrating aerosols prepackaged in metered dose inhalers (MDIs), and inhaling the drug using dry powder inhalers (DPIs). Several types of devices are used to improve delivery of aerosol to the horse's lung such as facemask, nosepiece, and extension tubing (spacer or holding chamber). The fraction of drug deposited into the lungs varies between 0.3 and 7.4% for nebulizers and 6.1 and 23.3% for MDI delivery devices (6.1% AeroMask, 8.2% Equine Haler, 23.3% 3M Equine device).[164–167] Spacers and holding chambers are designed to alter the size distribution of particles originating from the MDI or nebulizer, resulting in a reduction in upper airway deposition and an increase in the mass of drug contained in respirable particles.[161] A valve is usually present between the spacer and the horse's nostril; therefore, precise synchronization between MDI actuation and onset of inhalation is not required.

Corticosteroids Five different inhaled corticosteroids are available in the USA: beclomethasone dipropionate, budesonide, flunisolide, fluticasone proprionate, and triamcinolone acetonide (Table 29.3). A common test of potency for inhaled corticosteroids (McKenzie skin blanching) allows relative ranking of the compounds from least to most potent: flunisolide = triamcinolone acetonide < beclomethasone dipropionate = budesonide < fluticasone propionate.[168] At the time of this writing, only clinical trials with beclomethasone and fluticasone have been reported in the horse.

Clinical trials in horses with heaves indicate that beclomethasone dipropionate at dosages ranging from 500–1500 μg twice a day (3M Equine device) to 3750 μg twice a day (AeroMask) results in significant clinical and lung function improvement as well as reduction in pulmonary inflammation.[169,170] Therapeutic effects are measurable within 24 hours of administration. Administration of a low

dose of beclomethasone dipropionate (500 μg twice a day) to horses with heaves results in similar efficacy as high dose (> 1500 μg twice a day) but with less adrenal suppression.[169]

Fluticasone propionate has been used successfully for the treatment of heaves in horses using 2000 μg twice daily (AeroMask).[171] Treatment of horses with inhaled fluticasone (AeroMask) using 3000 μg twice a day results in adrenal suppression. However, no adrenal suppression is detectable with 2000 μg twice a day.[171,172]

Bronchodilators Two main classes of inhaled bronchodilators have been used in the horse: β_2-agonists and anticholinergics (Table 29.3). Bronchodilators should not be used as only therapy for RAO because they do not suppress airway inflammation and do not reduce airway hyperresponsiveness.[76] In addition, prolonged use of β_2-agonists without corticosteroids induces receptor downregulation, which renders the drug less effective. In horses with significant airway obstruction, bronchodilators should be administered prior to corticosteroids in order to optimize lung deposition.

β_2-agonists induce airway smooth muscle relaxation regardless of bronchoconstriction mechanism and also inhibit mast cell degranulation.[76] Albuterol, pirbuterol, and fenoterol are short-acting bronchodilators (1 hour) with rapid onset of action (5 minutes).[173–175] Some horses may benefit from the effects of albuterol for up to 7 hours.[176] Salmeterol and formoterol are long-acting β_2-agonists (6–8 hours) suitable for twice daily dosing but with slow onset of action (15 minutes).[177]

Ipratropium bromide is an anticholinergic drug chemically derived from atropine but devoid of side effects when administered by inhalation. Nebulization of 2 μg/kg causes bronchodilation for approximately 6 hours with a maximum effect obtained 1 hour after administration.[178] The effects of anticholinergic drugs on airway smooth muscle are additive to β_2-agonists.[76]

Prognosis

A follow-up survey involving 51 RAO-affected horses revealed that the median survival time following diagnosis was 8 years and that 87% of horses would be expected to survive 3 years after being diagnosed with RAO.[179] Seventy-nine percent of respondents reported recurring episodes of heaves and 21% believed that the condition had resolved. And while 21% of diagnosed horses were retired, 74% were still used in various athletic activities. These findings are considered good considering that > 77% of horses were still fed hay and housed indoors for at least part of the day.[179] Some investigators found that horses diagnosed with more severe disease were less likely to survive 2–4 years, but other investigators did not.[120,179]

Etiology and pathophysiology

Etiology

RAO is associated with exposure to high levels of organic molds particularly abundant in moldy hay and poorly ventilated stables.[180] Susceptible horses are allergic to inhaled spores and exposure to an environment rich in molds triggers clinicals signs within a few hours to a few days.[53,59] Clinical signs usually resolve within a few days of horses being removed from the dusty environment. Numerous studies have documented that traditional horse management exposes them to high dust levels originating mainly from bedding and feed.[16,17,84,181–186] In addition, horses are exposed to higher levels of dust around the nose (breathing zone) in the stable because of their feeding behavior.[84] As water content of hay at baling increases mold growth rises to reach a maximum for hay baled at 35–50% moisture.[187] Approximately 70 species of fungi and actinomycetes have been identified and among them thermophilic molds such as *Aspergillus fumigatus*, *Faenia rectivirgula* and *Thermoactinomyces vulgaris* are commonly present.[187] These spores have a small diameter (MMAD < 5 μm), allowing them to be inhaled in peripheral airways (respirable particles) where they may trigger an inflammatory reaction.[188] Furthermore, BAL fluid neutrophilia increases in a dose-dependent fashion as the quantity of inhaled dust rises.[189]

Several studies suggest that RAO and SPAOPD are caused by a mold allergy. Analysis of BAL fluid and sera collected from RAO-affected horses reveals significantly higher levels of IgE and IgA against mold allergens than in control horses consistent with a type I hypersensitivity reaction.[190,191] Unexpectedly, tracheal wash fluid collected from SPAOPD-affected horses contains a lower concentration of IgE than that from controls.[192] Immunohistochemical studies of lung tissues have shown high levels of IgA and IgG(Fc) in the airways of RAO-affected horses and the number of immunoglobulin staining cells increases with disease severity.[193,194] Quantification of serum precipitating antibodies against common environmental allergens and evaluation of response to intradermal challenge with these allergens are of little value for diagnosis and treatment of heaves because there is considerable overlap between control and affected horses.[195–197] Comparison of cytokine profiles in BAL fluid of horses exposed to dust challenge revealed an increased mRNA expression for interleukin-4 (IL-4) and IL-5 and a decreased expression for IFNγ in horses with heaves consistent with a Th2-type response.[198] Th2-type lymphocyte responses regulate allergic reactions by stimulating IgE production and promoting recruitment and activation of mast cells and eosinophils as in human asthma. These findings provide further support for an allergic basis of RAO.

Endotoxins are present in large quantities in the horses' environment and may potentiate the inflammatory response to inhaled molds.[16] Inhalation challenge using hay dust fractions suggests that endotoxin and other substances (e.g. β-glucans) are more important than particles for neutrophil recruitment to the lungs of RAO-affected horses.[199] Research in humans and other species indicates that timing and dose of inhaled endotoxins also play a modulatory role in the induction of airway inflammation as early exposure during childhood may prevent later development of asthma in people and exposure later in life worsen it.[200]

A study involving German Warmblood and Lipizzaner horses found RAO prevalence among offspring to be low

when neither parent is affected by the disease, but when one or both of the parents are affected the offspring are 3.2 and 4.6 times more likely to suffer from RAO, respectively ($P < 0.05$).[91] These findings strongly suggest that, as in human asthma, genetic susceptibility may be an important and heritable factor contributing to the development of heaves.

Pathophysiology

RAO susceptible horses develop signs of airway obstruction when exposed to a dusty environment rich in molds (e.g. hay, straw) and these signs are reversible if horses are placed in a low-dust environment (e.g. pasture).[53,59] Clinical signs associated with airway obstruction such as cough, increased respiratory efforts, and mucopurulent secretions are the result of airway inflammation. In addition, pulmonary inflammation is associated with airway hyper-responsiveness to both specific (e.g. molds, other allergens) and non-specific stimuli (e.g. histamine, endotoxin). Hence, RAO in horses is similar to asthma in people except that the equine disease is characterized by neutrophilic inflammation and asthma is associated with eosinophilic inflammation, although airway neutrophilia is a common feature of acute severe asthma and with grain-dust induced asthma in people.[201,202]

The cascade of events leading to pulmonary dysfunction starts shortly after susceptible horses are exposed to allergens. Circulating neutrophils are recruited to the lungs within 4 hours of an allergen challenge and are detectable in BAL fluid in 5 hours.[83,203] In addition, BAL fluid from horses with heaves contains increased numbers of cells expressing mRNA for IL-4 and IL-5 and decreased numbers of cells expressing mRNA for IFNγ consistent with a predominant Th2-type lymphocyte response as in human asthma.[198] Numerous inflammatory mediators are increased in respiratory secretions or blood of RAO horses after allergen challenge. However, the complex relationships between effector cells, inflammatory mediators, and clinical signs are still unclear. Histamine concentration in BAL fluid is elevated in RAO horses 5 hours after allergen challenge, but administration of antihistamines is usually poorly effective.[204] Various metabolites of arachidonic acid degradation such as prostaglandin E_2, thromboxane B_2, and 15-hydroxyeicosatetraenoic acid are increased in BAL fluid or plasma of affected horses. However, cyclo-oxygenase blockade does not improve clinical signs of the disease.[205–207] Recruitment of neutrophils to the airways may be explained by increased levels of chemotactic substances such as IL-8, macrophage inflammatory protein-2, leukotriene B_4 and platelet-activating factor present in BAL fluid of RAO horses in crisis.[208–210] In turn, primed neutrophils that migrate to the lungs may release reactive oxygen species leading to oxidative stress and proteases (e.g. MMP-9, MMP-8, MMP-13) responsible for further tissue damage.[211–213]

In asthma, airway inflammation is associated with overexpression of numerous proteins involved in immunologic and inflammatory processes. Increased gene expression is a prerequisite for protein overexpression, which in turn is a consequence of increased activation of transcription factors such as NF-κB, AP-1, cAMP, and others.[214] NF-κB is overexpressed in bronchial cells of RAO horses in crisis and the level of NF-κB activity is strongly correlated with the degree of lung dysfunction.[215] RAO horses in crisis improve rapidly after being removed from the allergenic environment. However, resolution of airway inflammation, in particular neutrophilia, usually lags behind resolution of lung dysfunction by weeks to months.[61,62] Persistence of airway granulocytes is correlated with sustained NF-κB activity which is markedly decreased after granulocyte cell death.[215] Furthermore, activated granulocytes release high levels of IL-1β and TNFα leading to NF-κB activation which in turn results in IL-1β and TNFα expression.[216] The prolonged survival of granulocytes in RAO affected horses may result from expression of anti-apoptotic proteins that may protect these cells or delay apoptosis.

Epidemiology

RAO is an occupational disease of horses housed indoors and fed hay. It is more commonly diagnosed in parts of the world where summers are frequently humid (e.g. northern Europe, northeast USA) than in areas with a warm and dry climate (e.g. Australia).[217] Presumably, wet summers lead to higher quantities of moldy hay being harvested, although this assumption has not been proven yet. Conversely, SPAOPD is commonly diagnosed in horses living in hot and humid climates (e.g. southern USA) where they spend most of the time on pasture and the highest prevalence of the disease is observed during the summer months.[94] Nevertheless, the condition is also diagnosed in areas where RAO is traditionally believed to be more prevalent and some horses may suffer from both conditions.[133]

Prevalence of RAO has been reported as high as 55% of horses in Switzerland based on endoscopy and tracheal wash cytology.[218] Considering the case definition used by the authors, the prevalence was probably overestimated because horses with IAD would have been diagnosed as RAO. In a North American survey conducted on 166 horses selected at random at a slaughterhouse, RAO was diagnosed histopathologically in 19 horses (incidence of 12%).[43]

RAO and SPAOPD tend to be diagnosed in horses > 7 years of age and there is no apparent breed or sex predilection.[11,94] However, in a case-controlled study of horses diagnosed with RAO at 19 North American Veterinary Teaching Hospitals ($n = 2888$) we found that Thoroughbred horses were significantly more likely to be diagnosed with the disease than were other breeds (odds ratio, 2.4; $P < 0.001$; Couëtil, in press).

Prevention

Inhaled dust particles play a central role in the pathophysiology of RAO and management of the disease should always include recommendations to decrease environmental exposure. Particle deposition in the respiratory tract is related to their mean aerodynamic diameter (MMAD), which depends on particle size, shape, and density. Large particles

(MMAD > 5 μm) will be mainly deposited in the nasal passages. Smaller ones (MMAD < 5 μm) are called respirable particles because they tend to be deposited in the lower airways where they can exert their pro-inflammatory effects. Among respirable dust particles, mold spores from hay and straw including *Aspergillus fumigatus*, *Faenia rectivirgula* (previously called *Micropolyspora faeni*) and *Thermoactinomyces vulgaris* have been directly implicated.[84,188] Two main approaches help reduce exposure of the horse's airways to respirable particles. The first appraoch is to use feedstuff and bedding that generate low dust levels. For example, changing bedding material from straw to cardboard can cut respirable dust levels in half and reduce mold concentration to negligible levels.[181] The second approach is to increase removal of airborne particles by improving ventilation in the building.[182]

The ideal environment for horses with RAO is pasture because exposure to dust is significantly less than in stalls, regardless of feed and bedding quality.[16,183] If for practical reasons the horse cannot be kept on pasture at all times, ventilation in the barn and stall, the type of bedding, feedstuff, and general management should be scrutinized in order to minimize allergen exposure. However, owners need to realize that for RAO horses kept on pasture, exposure to organic dust for even a few hours, such as when bringing horses indoors to be fed or during periods of inclement weather, may be sufficient to recruit inflammatory cells to the lungs resulting in airway hyper-responsiveness and clinical signs.[83,110]

Horses with SPAOPD are generally affected between June and September when they spend more than half of each day on pasture.[94] Consequently, the recommended environment for these horses during the summer is low-dust indoor housing.[66,133]

Simple changes such as switching bedding from straw to wood shavings and feeding pellets or silage instead of hay can decrease respirable dust at least five-fold.[16,84] The relative amounts of respirable particles in different types of feed and bedding materials, from the least dusty to the dustiest, are concentrate with molasses > whole grain – silage (×2) > cardboard bedding (×2.7) > alfalfa pellets (×4.5) > rolled grain – good straw (×6) > wood shavings (×15) > good hay (×30).[181,184] Concentrate with molasses was given a reference value of 1 and numbers in parentheses represent the numbers of fold increase in respirable particles for the different types of feed and bedding. If hay has to be part of the horse's diet, the amount of dust generated can be reduced by feeding it after soaking it or preferably keeping it immersed in a tub of water. An obvious potential problem with this approach is the generation of more mold in the stall if previously wet hay gets mixed with the bedding. Tub water has to be changed every day. RAO horses maintained in clinical remission at pasture and then housed long-term in a very low-dust environment (i.e. cardboard bedding, grass silage, grain with molasses) do not show detectable changes in BAL fluid cytology or pulmonary function.[181] But housing susceptible horses in an environment usually considered low-dust, such as wood shavings bedding and fed grass silage, may result in bronchial hyper-responsiveness despite horses maintaining normal tidal breathing lung mechanics.[185,186] Environmental control targeting only the affected horse's stall and not the rest of the stable may be sufficient to improve clinical signs of RAO horses but not to normalize lung function and pulmonary inflammation.[131]

The activity in the barn also affects dust exposure with peak levels during the day especially at the time of feeding and cleaning of the stalls, when dust levels can increase more than 10-fold.[183] Therefore, dust-generating tasks such as cleaning stalls and sweeping floors should be performed when RAO-susceptible horses are outside the barn. Grooming also generates airborne dust particles and should be done outside or using a vacuum cleaner system.

Exercise-induced pulmonary hemorrhage (EIPH)

- Exercise-induced pulmonary hemorrhage is a common disorder of race horses, among which it occurs worldwide.
- EIPH may, rarely, manifest as epistaxis after exercise and may be a cause of poor performance. It rarely causes death.
- Diagnosis is based on demonstration of blood in the airways either by tracheobronchoscopy after exercise or by examination of tracheal aspirate or bronchoalveolar lavage fluid.
- Furosemide (frusemide) is commonly used to treat EIPH, although its efficacy under field conditions has not been demonstrated.
- EIPH is caused by rupture of pulmonary capillaries with subsequent development of pulmonary inflammation, fibrosis and angiogenesis contributing to continued hemorrhage during exercise.

Recognition of disease

History and presenting complaint

Poor athletic performance and epistaxis are the most common presenting complaints for horses with exercise-induced pulmonary hemorrhage (EIPH). While poor performance may be attributable to any of a large number of causes, epistaxis associated with exercise is almost always secondary to EIPH.

Epistaxis due to EIPH occurs during or shortly after exercise and is usually first noticed at the end of a race, particularly when the horse is returned to the paddock or winner's circle and is allowed to lower its head. It is usually bilateral and resolves within hours of the end of the race. Epistaxis may occur on more than one occasion, especially when horses are raced or exercised at high speed soon after an initial episode.

Failure of race horses to perform to the expected standard (poor performance) is often, accurately or not, attributed to EIPH. Many horses with poor performance have cytologic

evidence of EIPH on microscopic examination of tracheobronchial aspirates or BAL fluid or have blood evident on endoscopic examination of the tracheobronchial tree performed 30 to 90 minutes after strenuous exercise or racing.[219,220] However, it is important to recognize that EIPH is very common in race horses and it should be considered the cause of poor performance only after other causes have been eliminated. Severe EIPH undoubtedly results in poor performance and, on rare occasions, death of Thoroughbred race horses.[221] However, the effect of less severe EIPH on race performance of Thoroughbred or Standardbred horses has not been conclusively determined. A relationship between finishing position and incidence of EIPH, diagnosed by bronchoscopic examination, was not detected for 191 Thoroughbred race horses that finished in first, second, or third place.[222] Furthermore, there was no relationship between the proportion of horses with EIPH and placing (first, second, or third versus other) in another 98 horses.[222] Similarly, there was no relationship between finishing position and proportion of horses with EIPH in 191 Thoroughbreds examined after racing.[223] There was no relationship between severity of EIPH, assessed on tracheobronchoscopic examination, and race performance in 258 Thoroughbreds or 296 Standardbred race horses.[224] Together, these studies do not demonstrate a clear relationship between the presence of EIPH, or its severity, and race performance.

In contrast to the studies discussed above, among 452 Thoroughbred horses examined after racing in Hong Kong, those finishing in the first three positions had less severe EIPH than did horses finishing in lower positions.[225] Of horses finishing in the first three places, 43.9% had evidence of EIPH on tracheobronchoscopic examination after racing whereas 55.9% of horses finishing in fourth to fourteenth place had evidence of EIPH.

Results of studies in Standardbred race horses indicate either a lack of effect of EIPH on performance or an association between EIPH and superior performance. There was not a relationship between presence of EIPH and finishing position in 29 Standardbred race horses with intermittent EIPH examined on at least two occasions,[226] nor in 92 Standardbred race horses examined on one occasion.[227] However, of 965 Standardbred race horses examined after racing, those finishing first or second were 1.4 times more likely (95% CI 0.9–2.2) to have evidence of EIPH on tracheobronchoscopic examination than were horses that finished in seventh or eighth position.[228]

Physical examination

Apart from epistaxis in a small proportion of affected horses, there are few abnormalities detectable on routine physical examination of horses with EIPH. Rectal temperature and heart and breathing rates may be elevated as a consequence of exercise in horses examined soon after exercise, but values of these variables in horses with EIPH at rest are not noticeably different to horses with no evidence of EIPH.[229] Affected horses may swallow more frequently during recovery from exercise than do unaffected horses, probably as a result of blood in the larynx and pharynx.[230] Coughing is common in horses recovering from strenuous exercise and horses with EIPH are reported to have a hacking cough, although this observation may not be very specific.[222] After recovery from exercise, horses with EIPH are no more likely to cough than are unaffected horses.[231] Other clinical signs related to respiratory abnormalities are uncommon in horses with EIPH. Respiratory distress is rare in horses with EIPH and when present indicates severe hemorrhage or other serious lung disease such as pneumonia, pneumothorax or rupture of a pulmonary abscess. Lung sounds are abnormal in a small number of EIPH-affected horses and when present are characterized by increased intensity of normal breath sounds during rebreathing examination.[229] Tracheal rales may be present in horses with EIPH but are also heard in unaffected horses.[230]

Epistaxis associated with exercise is almost always attributable to pulmonary hemorrhage. The severity of epistaxis ranges from flecks or a small amount of blood at one nostril present after the horse lowers its head at the end of exercise to profuse hemorrhage from both nostrils occurring during exercise (Fig. 29.9). Epistaxis occurs in a small proportion of race horses.[222,223,230,232–236] The prevalence of epistaxis in race horses varies between 0.1 and 9.0%, with the frequency depending on the breed, age and sex of horses selected for study, the type of racing, and the timing and frequency of observation of horses after racing. Epistaxis occurs in 0.13% of Thoroughbred race horses in Japan,[232] 5.9% of Thoroughbreds in Hong Kong,[225] 0.8% of Thoroughbreds in California,[222] 9.0% of Thoroughbreds in Pennsylvania,[223] and 3.5% of Quarter Horses.[234] Epistaxis is more common in older horses, with horses 5 years of age or older being 6.4 times as likely as 2-year-olds to have epistaxis.[223,225,230,232,235] Female Thoroughbreds are 1.4 times as likely as stallions to have epistaxis.[232] Epistaxis is more common after races < 1600 m than in longer races.[232] However, horses in steeplechase races, which are typically

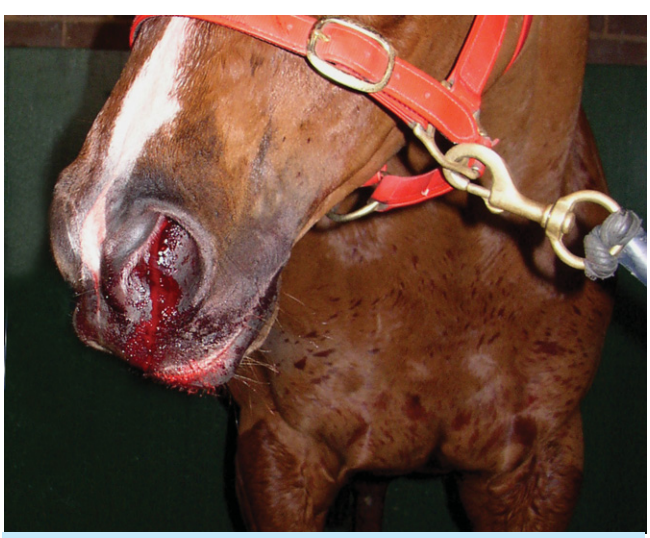


Fig. 29.9
Horse with epistaxis secondary to EIPH. Note blood splattered on the horse's chest.

longer than 2000 m, are at greater risk of epistaxis than are horses in flat races.[230,232,235,237]

Horses that have experienced one episode of epistaxis are more likely to have a second episode. For this reason most racing jurisdictions do not permit horses with epistaxis to race for a period of weeks to months after the initial instance, with more prolonged enforced rest after a subsequent episode of epistaxis and retirement from racing after a third bout. The recurrence rate after one episode of epistaxis in Thoroughbred horses is approximately 13.5% despite affected horses not being permitted to race for one month after the initial episode of epistaxis.[232] This high rate of recurrence suggests that the inciting pulmonary lesions have not healed.

Diagnostic tests

There are a variety of techniques available for determining the presence and severity of EIPH including direct visualization of the airways through a flexible endoscope or examination of bronchial lavage fluid or tracheal aspirates for evidence of hemorrhage. The utility of these diagnostic tests varies and choice of examination technique depends on the time between the horse racing and the examination and the desired sensitivity of the test. For instance, tracheobronchoscopic examination is most appropriate if a horse is examined within 1–2 hours of exercise whereas examination of airway washings is most appropriate if the examination is days to a week after strenuous exercise. Radiography, pulmonary scintigraphic examination and lung function tests are useful in eliminating other respiratory diseases as a cause of poor performance, but are minimally useful in confirming a diagnosis of EIPH or in determining the severity of hemorrhage.

Tracheobronchoscopy Observation of blood in the trachea or large bronchi of horses 30–120 minutes after racing or strenuous exercise provides a definitive diagnosis of EIPH. The amount of blood in the large airways varies from a few small specks on the airway walls to a stream of blood occupying the ventral one-third of the trachea (Fig. 29.10). Blood may also be present in the larynx and nasopharynx. If there is a strong suspicion of EIPH and blood is not present on a single examination conducted soon after exercise, the examination should be repeated in 60–90 minutes. Some horses with EIPH do not have blood present in the rostral airways immediately after exercise, but do so when examined 1–2 hours later. Blood is detectable by tracheobronchoscopic examination for 1–3 days in most horses, with some horses having blood detectable for up to 7 days.

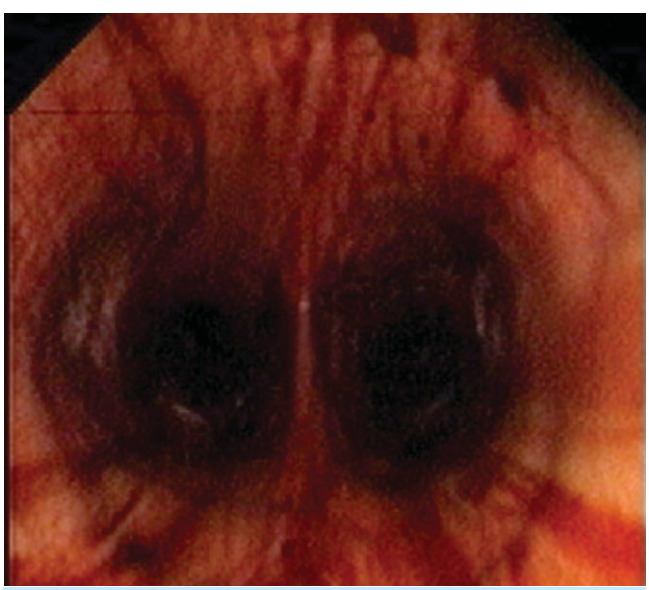


Fig. 29.10
Tracheobronchoscopic image of the carina of a horse with severe EIPH.

Tracheobronchoscopic examination is performed using a 1–1.5 m flexible endoscope. Endoscopes of 1 m length allow visualization of the rostral trachea to the level of the thoracic inlet, but do not permit direct examination of the caudal trachea and large bronchi. Use of an endoscope of at least 1.5 m length is recommended to allow direct examination of all the large airways. The examination is performed with the horse restrained while the endoscope is passed through the ventral meatus into the nasopharynx. Most horses will tolerate passage of an endoscope into the caudal trachea with minimal restraint such as application of a nose twitch. Some horses may require administration of sedatives or tranquilizers. Administration of tranquilizers will alter pharyngeal and laryngeal function and may impair assessment of abnormalities of the upper airway. The nasopharynx and larynx are then examined for the presence of blood or other abnormalities and the endoscope is passed through the larynx into the cranial trachea. The trachea is examined as the endoscope is passed caudally so that the carina and cranial aspects of the left and right bronchi are visualized.

Bronchoscopic examination can be used to estimate the severity of EIPH through use of a grading system.[222,225,226,238] A commonly used grading system has a scale of four levels from 0 (no hemorrhage visible) to 3 (streak of blood > 5 mm wide) and its repeatability on consecutive examinations in Thoroughbred horses has been demonstrated. Of 56 horses examined at least twice, 21 (38%) had identical scores on each examination, 26 (41%) had scores that differed by one grade and nine had scores that differed by two grades.[238] It is assumed that a higher score represents more severe hemorrhage, but while the repeatability of this scoring system has been established, the relationship between the amount of blood in the large airways and the actual amount of hemorrhage has not been established.

Examination of airway secretions or lavage fluid The presence of red cells or macrophages containing either effete red cells or the breakdown products of hemoglobin (hemosiderophages) in tracheal or BAL fluid provides evidence of EIPH (Fig. 29.11). Detection of red cells or hemosiderophages in tracheal aspirates or bronchoalveolar lavage fluid is believed to be both sensitive and specific in the diagnosis of EIPH.[220,239] Examination of airway fluids indicates the presence of EIPH in a greater proportion of horses than does tracheobronchoscopic examination after strenuous exercise or racing. The greater sensitivity of examination of airway fluid

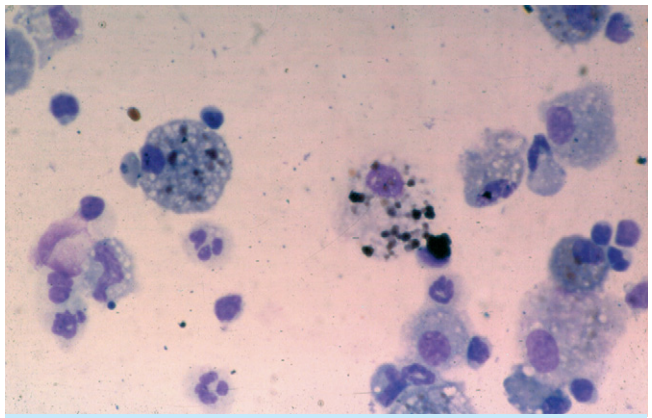


Fig. 29.11
Hemosiderophages in bronchoalveolar lavage fluid of a Standardbred race horse.

is probably attributable to the ability of this examination to detect the presence of small amounts of blood or its residual products and the longevity of these products in the airways. While endoscopic examination may detect blood in occasional horses up to 7 days after an episode of EIPH, cellular evidence of pulmonary hemorrhage persists for weeks after a single episode.[220,239–242] Red blood cells and macrophages containing red cells are present in bronchoalveolar lavage fluid or tracheal aspirates for at least one week after strenuous exercise or instillation of autologous blood into airways and hemosiderophages are present for at least 21 days and possibly longer.[220,239–242]

Recent studies have reported on the use of red cell numbers in BAL fluid as a quantitative indicator of EIPH.[241,243–246] However, this indicator of EIPH severity has not been validated nor demonstrated to be more reliable or repeatable than tracheobronchoscopic examination and visual scoring. Furthermore, considerable concern exists over the suitability of red cell counts in BAL fluid for assessment of severity of EIPH given that an unknown area, although presumably small, of the lung is examined by lavage and there is a risk that this area of lung may not be representative of the lung as a whole, similar to the situation of examination of bronchoalveolar lavage fluid of horses with pneumonia.[247]

Tracheal aspirates may be obtained any time after exercise by either aspiration during tracheobronchoscopic examination or aspiration through a percutaneous intratracheal needle and catheter. Aspirates obtained through an endoscope may not be sterile, depending on the collection technique. BAL fluid can be obtained either through an endoscope wedged in the distal airway or through a cuffed tube inserted blindly into a distal airway. Collection of fluid through an endoscope has the advantage of permitting examination of the distal airways and selection of the area of lung to be lavaged. However, it does require the use of an endoscope that is longer (2 m) than those readily available in most equine practices. A commercial BAL catheter does not require use of an endoscope and can be readily used in field situations.

For both endoscopic and lavage tube collection of BAL fluid the horse is restrained and sedated (xylazine 0.5–1.0 mg/kg i.v., detomidine 20–40 μg/kg i.v.). Some clinicians administer butorphanol (0.02–0.5 mg/kg i.v.) or local anesthetic (lidocaine (lignocaine), 20 ml of a 2% solution diluted with saline to a total volume of 100 ml and administered into the trachea) to suppress coughing. Application of a nose twitch may be necessary in some horses. The endoscope or lavage tube is passed into the trachea and then advanced caudally until it wedges in the distal airway. The cuff of the lavage tube is then inflated and a quantity of fluid (150–300 ml) of isotonic fluid (phosphate buffered 0.9% sodium chloride or similar) rapidly injected. After allowing the horse several breaths, the fluid is aspirated with the first 20 ml being discarded. Blind passage of the lavage tube usually results in its lodging in the dorsocaudal lung region.[248]

Radiography Thoracic radiography is of limited use in detecting horses with EIPH. Radiographs may demonstrate the presence of densities in the caudodorsal lung fields of some horses (Fig. 29.12),[249] but many affected horses have minimal to undetectable radiographic abnormalities. Examination of thoracic radiographs of horses with EIPH may be useful in ruling out the presence of another disease process, such as a pulmonary abscess, contributing to the horse's pulmonary hemorrhage or poor athletic performance.

Pulmonary scintigraphy Scintigraphic examination of lungs has the potential to detect horses with EIPH but to date technical limitations have precluded its routine use for this purpose.[250,251]

Exercise testing During incremental exercise on a treadmill, horses with EIPH have more severe exercise-induced arterial hypoxemia, hypercapnia and higher blood lactate concentrations than do control horses.[252] These changes indicate abnormalities in gas exchange in horses with EIPH but are not sufficiently large to be useful clinically. Blood gas tensions in horses with EIPH are within the normal ranges.

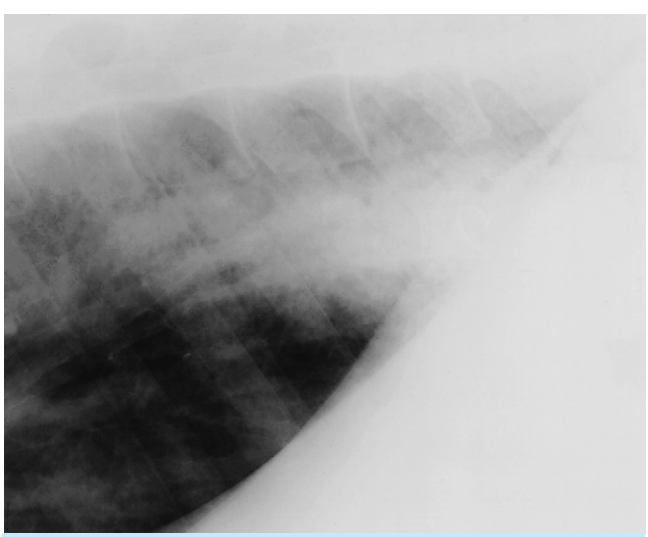
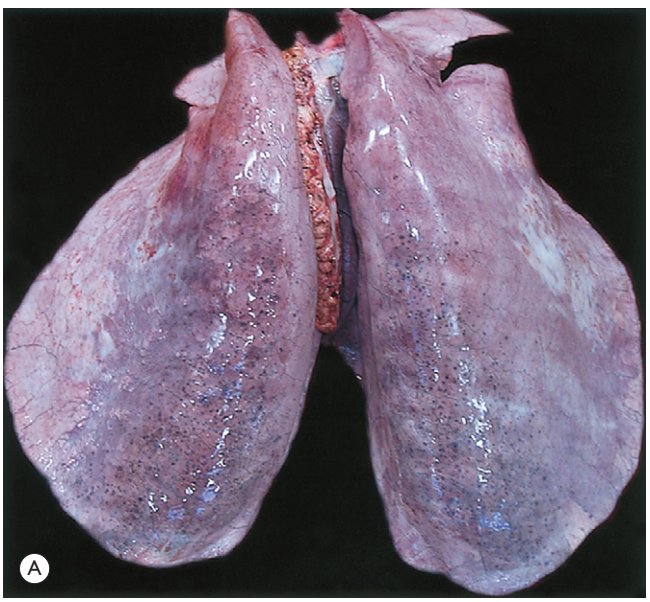


Fig. 29.12
Thoracic radiograph of a 5-year-old Thoroughbred race horse. Radiographic signs of EIPH are evident as the wedge-shaped density in the dorsocaudal lung fields.

Necropsy examination

Exercise-induced pulmonary hemorrhage is a rare cause of death of race horses. Necropsy examination of affected horses is usually incidental to examination for another cause of death. Pertinent abnormalities in horses with EIPH are restricted to the respiratory tract. Grossly, horses examined within hours of strenuous exercise, such as horses necropsied because of catastrophic musculoskeletal injuries incurred during racing, may have severe petechiation in the caudodorsal lung fields (Fig. 29.13). Horses with chronic disease have blue/gray or blue/brown discoloration of the visceral pleural surfaces of the caudodorsal lung fields that is often sharply demarcated, especially on the diaphragmatic surface (Fig. 29.14).[253] The discoloration affects both lungs equally with 30 to 50% of the lung fields being discolored in severe cases.[253] Affected areas do not collapse to the same extent as unaffected areas and, in the deflated lung, have a spleen-like consistency.[253] On the cut surface, the discolored areas of lung are predominantly contiguous with the dorsal pleural surface and extend ventrally into the lung parenchyma. Areas of affected lung may be separated by normal lung. There is proliferation of bronchial vessels, predominantly arteries and arterioles, in affected areas.[254] Histologically, affected areas exhibit bronchiolitis, hemosiderophages in the alveolar lumen and interstitial spaces, and fibrosis of interlobular septa, pleura and around vessels and bronchioles.[255]



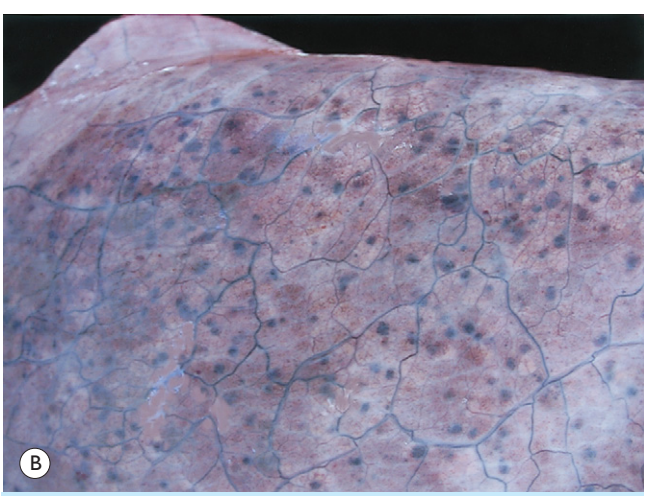


Fig. 29.13
(A) Lungs of a Thoroughbred race horse euthanased immediately after racing because of a catastrophic musculoskeletal injury. Lesions of acute EIPH are evident in dorsocaudal lung fields. Photograph courtesy of Prof. R. Slocombe. (B) Closer view of lungs in Figure 29.14A demonstrating focal nature of hemorrhage. Photograph courtesy of Prof. R. Slocombe.

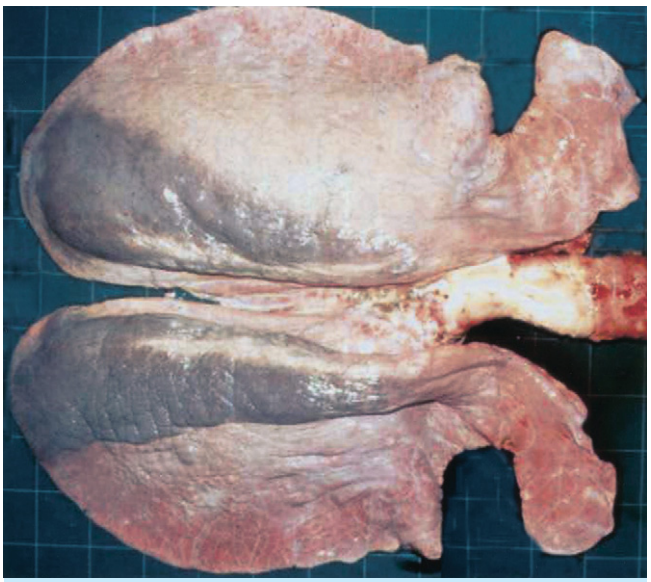


Fig. 29.14
Lungs of a Thoroughbred race horse with exercise-induced pulmonary hemorrhage. The lesions are restricted to the caudodorsal lung fields and produce a blue-gray discoloration of the visceral pleural surface.

Table 29.6 Causes of epistaxis or hemorrhage into airways of horses

Hemorrhage into trachea or bronchi:
Exercise-induced pulmonary hemorrhage
Pulmonary abscess
Trauma
Pneumonia
Pulmonary foreign body
Hemangiosarcoma
Pulmonary neoplasia
Epistaxis:
All of the above
Guttural pouch mycosis
Ethmoidal hematoma
Thrombocytopenia
Trauma
Neoplasia

Table 29.7 Pharmacotherapeutic and management interventions used to prevent exercise-induced pulmonary hemorrhage in horses

Putative mechanism and contributing factor	Intervention	Evidence of efficacy
High pulmonary capillary pressure		
High cardiac output	Furosemide (frusemide)	Increasing evidence of efficacy of furosemide in control of EIPH
	Dehydration	
	Other diuretics	
Insufficient pulmonary vasodilation	Antihypertensive agents:	No studies to investigate efficacy or effect on PAP
	Guanabenz	
	Clonidine	
	Enalapril	No effect on PAP during intense exercise
	Nitric oxide donors/analogs:	NG reduces PAP of standing horses. No evidence of effect on
	Nitroglycerin (NG)	PAP during exercise. NO blockade by L-NAME does not affect
	Nitroprusside	PAP during intense exercise
	L-arginine	
	Phosphodiesterase inhibitors:	No known effects on PAP or EIPH
	Sildenafil (Viagra)	
	Aminophylline	
Increased blood viscosity (reduced red cell deformability, echinocytosis)	Pentoxifylline	No effect on PAP during intense exercise. Effect on EIPH not reported
Low alveolar pressure – increased upper airway resistance		
Upper airway abnormalities (increased inspiratory resistance)	Surgical correction of obstruction	No demonstrated efficacy on EIPH
Resistance at nares	Nasal dilator strips (Flair)	Decreases red cell count in bronchoalveolar lavage fluid collected after intense exercise
Low alveolar pressure – intrathoracic obstruction		
Bronchoconstriction	Bronchodilatory drugs:	No demonstrated efficacy on EIPH. Clenbuterol does not affect PAP during exercise
	Clenbuterol	
	Albuterol	
	Ipratropium	
	Pyrroglycolate	
Lower airway inflammation	Anti-inflammatory drugs:	
	Corticosteroids	No demonstrated efficacy of corticosteroids in preventing EIPH
	Cromolyn sodium	Cromolyn sodium has demonstrated lack of efficacy
	Low allergenic stall bedding (paper)	No efficacy in reducing EIPH
Interstitial inflammation and bronchial angiogenesis		
Progressive lung injury	Rest	No demonstrated efficacy in reducing EIPH
	Corticosteroids	No demonstrated efficacy in reducing EIPH
Coagulopathy or platelet dysfunction		
Excessive fibrinolysis	Aminocaproic acid	Inhibits fibrinolysis. No demonstrated efficacy in preventing EIPH
	Estrogens	Rationale unclear. No demonstrated efficacy in preventing EIPH
Increased platelet aggregation	Aspirin	Inhibits platelet aggregation. No demonstrated effect in preventing EIPH
Capillary fragility	Hesperidin-citrus bioflavinoids	No effect on EIPH in 45 horses

PAP, pulmonary artery pressure; EIPH, exercise-induced pulmonary hemorrhage, NO, nitric oxide.

Diagnostic confirmation

Presence of EIPH is most immediately confirmed by tracheobronchoscopic examination of the horse after strenuous exercise. Detection of red blood cells or hemosiderophages in tracheal aspirates or BAL fluid is also indicative of EIPH. The finding of hemorrhage in the airways of a horse soon after exercise allows a strong presumptive diagnosis of EIPH. Other causes of hemorrhage into airways are listed in Table 29.6.

Treatment and prognosis

Therapeutic aims

The aims of treatment are to reduce the severity of hemorrhage and minimize the adverse sequelae to hemorrhage. Sequelae to hemorrhage include airway and interstitial inflammation and fibrosis.

Treatment

Therapy for EIPH is controversial in that a wide variety of treatments is used but there is no conclusive evidence of efficacy for any of them in horses under field, i.e. racing, conditions (Table 29.7). Therapy of EIPH is usually a combination of attempts to reduce the severity of subsequent hemorrhage and efforts to minimize the effect of recent hemorrhage.

Treatment of EIPH is problematic for a number of reasons. First, the pathogenesis of EIPH has not been determined although the available evidence supports a role for stress failure of pulmonary capillaries (see below). Second, there is a lack of information using large numbers of horses under field conditions that demonstrates an effect of any medication or management practice (with the exception of bedding) on EIPH. There are numerous studies of small numbers of horses (< ~40) under experimental conditions but these studies often lacked the statistical power to detect treatment effects and, furthermore, the relevance of studies conducted on a treadmill to horses racing competitively is questionable. Treatments for EIPH are usually intended to address a specific aspect of the pathogenesis of the disease and will be discussed in that context.

Prevention of stress failure of the pulmonary capillaries Stress failure of pulmonary capillaries, and subsequent subsequent hemorrhage, is believed to occur as a result of the high transmural pressures in pulmonary capillaries that develop in the lungs of horses during strenuous exercise. There is therefore interest in reducing the pressure difference across the pulmonary capillary membrane in an effort to reduce EIPH. Theoretically, this can be achieved by reducing the pressure within the capillary or increasing (making less negative) the pressure within the intrathoracic airways and alveolus.

Reducing pulmonary capillary pressure Furosemide (frusemide) administration as prophylaxis of EIPH is permitted in a number of racing jurisdictions worldwide (Fig. 29.15).[256] Within the USA and Canada, almost all Thoroughbred, Standardbred and Quarter Horse racing jurisdictions permit administration of furosemide before racing. Approximately 85% of all Thoroughbred race horses in the USA and Canada receive furosemide at some stage of their career and, on average, 75% of horses in a race receive furosemide.[257] Although accurate numbers are not available, it appears that a smaller proportion of Standardbred and Quarter Horse race horses receive furosemide before racing. Furosemide is administered to 22–32% of Standardbred race horses and 19% of racing Quarter Horses in two racing jurisdictions.[258–260]

The efficacy of furosemide in treatment of EIPH is uncertain. While field studies of large numbers of horses do not demonstrate an effect of furosemide on the prevalence of EIPH,[224,261] studies of Thoroughbred horses running on a treadmill provide evidence that furosemide reduces the severity of EIPH.[245,246] Under field conditions, based on tracheobronchoscopic evaluation of the severity of bleeding, furosemide has been reported to reduce or have no influence on the severity of bleeding.[224,238] This apparent inconsistency may be attributable to measurement of red blood cell counts in BAL fluid of horses that have run on a treadmill not being

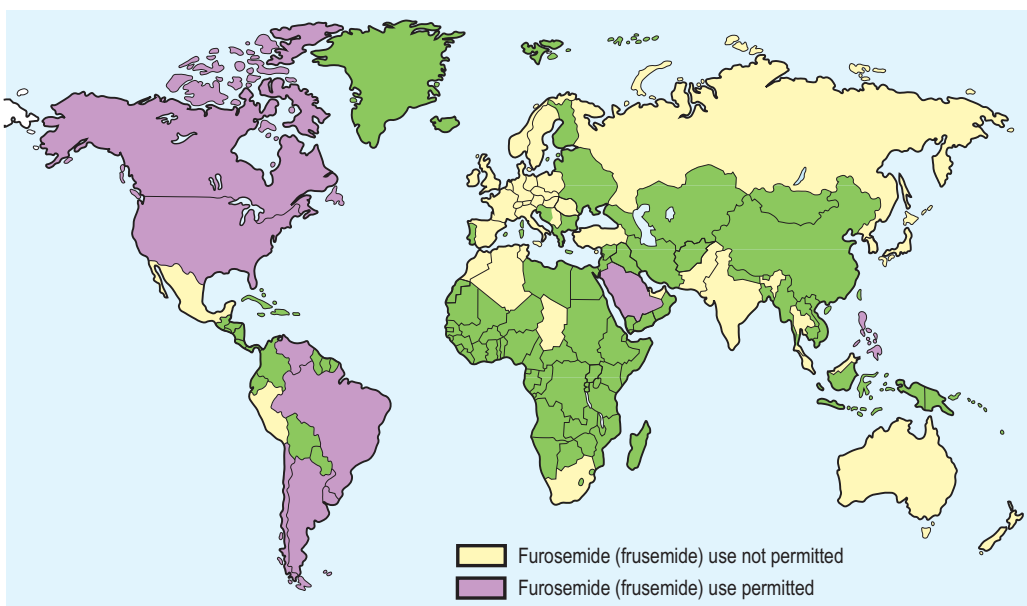


Fig. 29.15
Map depicting racing jurisdictions (purple) that permit administration of furosemide (frusemide) on the day of racing. Source: www.horseracingintfed.com.

representative of effects of furosemide under field conditions. The weight of evidence from field studies does not support a role for furosemide in preventing or reducing the severity of EIPH.

The mechanism by which furosemide may reduce the severity of EIPH is unknown although it is speculated that furosemide, by attenuating the exercise-induced increase in pulmonary artery and pulmonary capillary pressure of horses, reduces the frequency or severity of pulmonary capillary rupture.[262–264]

Furosemide is associated with superior performance in both Thoroughbred and Standardbred race horses.[257,258] Thoroughbred horses treated with furosemide were 1.4 times as likely to win the race, earned more money and had a standardized 6 furlong race time 0.56 to 1.09 seconds less than untreated horses.[257] Similarly, furosemide reduced one mile race times of Standardbred pacers by 0.31 to 0.74 seconds.[258]

Antihypertensive agents used in control of systemic (not pulmonary artery) hypertension in humans have been used in an effort to prevent EIPH in horses. Drugs including guanabenz and clonidine have been administered to horses to prevent EIPH, but the efficacy of these drugs in preventing EIPH or reducing pulmonary capillary pressure of exercising horses has not been demonstrated. Enalapril is effective in inhibiting angiotensin-converting enzyme (ACE) activity in horses, but does not affect pulmonary artery pressure of exercising horses.[265] Similarly, the efficacy of enalapril in preventing EIPH has not been demonstrated.

Nitric oxide is a potent vasodilator in many vascular beds. Administration of nitroglycerin (a nitric oxide donor) reduces pulmonary artery pressure of standing horses, but does not affect pulmonary artery pressure of horses during intense exercise.[266] L-Arginine is a nitric oxide donor with no demonstrated efficacy in reducing pulmonary capillary pressure or EIPH in horses. The effect of L-NAME, an inhibitor of nitric oxide synthetase, on pulmonary artery pressure during maximal exercise is controversial with either no effect or a decrease in pulmonary artery pressure reported.[267,268] Interestingly, L-NAME administration caused an increase in severity of EIPH.[267] Sildenafil, a phosphodiesterase inhibitor that accentuates the effect of nitric oxide and is used in the treatment of erectile dysfunction in men, has been administered to horses in an apparent attempt to reduce EIPH. However, its efficacy in preventing EIPH or reducing pulmonary capillary pressure has not been demonstrated.

An increase in pulmonary capillary pressure secondary to altered rheostatic properties of blood during exercise has been suggested as a possible contributing factor for EIPH.[269] Furosemide increases blood viscosity whereas pentoxifylline increases red blood cell deformability and may attenuate the increase in blood viscosity that occurs during exercise.[270–272] However, pentoxifylline does not affect pulmonary capillary pressure of exercising horses and did not affect the prevalence of EIPH in a small experimental study.[273]

Increasing alveolar inspiratory pressure Airway obstruction, either intrathoracic or extrathoracic, increases airway resistance and results in a more negative intrathoracic (pleural) pressure during inspiration to maintain tidal volume and alveolar ventilation. Causes of extrathoracic airway obstruction include laryngeal hemiplegia and other abnormalities of the upper airway (see Chapter 27), whereas intrathoracic obstruction is usually a result of bronchoconstriction and inflammatory airway disease. Horses with partial extrathoracic inspiratory obstruction or bronchoconstriction and airway inflammation associated with recurrent airway obstructive disease (heaves) have pleural (and hence alveolar) pressures that are lower (more negative) than those in unaffected horses or in horses after effective treatment.

Partial inspiratory obstruction, such as produced by laryngeal hemiplegia, exacerbates the exercise-induced decrease in intrapleural pressures with a consequent increase

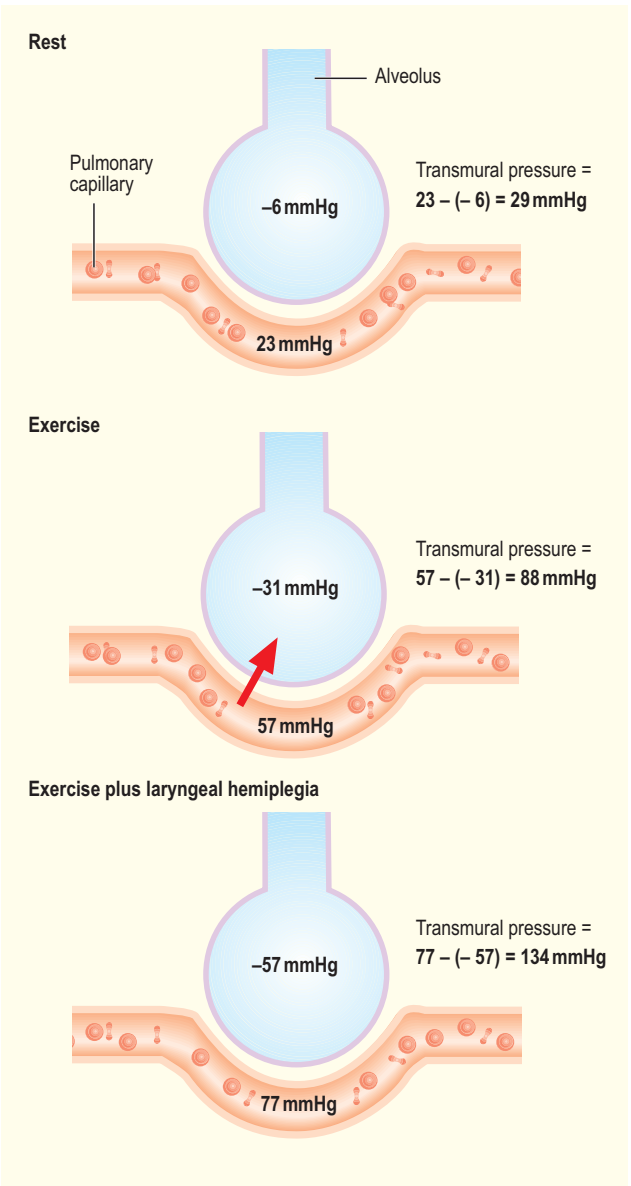


Fig. 29.16
Schematic representation of determinants of transmural pressure in a horse at rest, during intense exercise, and during intense exercise with left laryngeal hemiplegia. Data from Ducharme et al.[276]

in transmural capillary pressures (Fig. 29.16).[274–276] These changes may exacerbate the severity of EIPH although an association between upper airway obstructive disease and EIPH has not been demonstrated. Surgical correction of airway obstruction is expected to resolve the more negative intrapleural pressure but its effect on EIPH is unknown.

Recently, the role of the nares in contributing to upper airway resistance, and hence lowering inspiratory intrapleural pressure during intense exercise has attracted the attention of some investigators (Fig. 29.17). Application of nasal dilator bands (Flair strips) reduces nasal resistance by dilating the nasal valve,[277] and reduces red cell count of BAL fluid collected from horses after intense exercise on a treadmill.[244,245] However, the effect of this intervention in horses racing competitively has not been demonstrated.

The role of small airway inflammation and bronchoconstriction in the pathogenesis of EIPH is unclear. However, horses with EIPH are often treated with drugs intended to decrease lower airway inflammation and relieve bronchoconstriction. Beta-adrenergic bronchodilatory drugs such as clenbuterol and albuterol are effective in inducing bronchodilation in horses with bronchoconstriction, but their efficacy in preventing EIPH is either unknown or, in very small studies, is not evident. Clenbuterol does not alter the hemodynamic responses of horses to exertion nor attenuate exercise-induced arterial hypoxemia in normal horses.[278,279] Ipratropium, a parasympatholytic drug administered by inhalation, showed promise in a very small study (two horses) of preventing EIPH.[280] Corticosteroids, including dexamethasone, fluticasone and beclomethasone, administered by inhalation, parenterally or enterally reduce airway inflammation and obstruction, but have no demonstrated efficacy in preventing EIPH. Cromolyn sodium (sodium cromoglicate) has no efficacy in preventing EIPH.[281]

Water vapor treatment (inhalation of water saturated air) has been proposed as a treatment for EIPH because of its putative effect on small airway disease. However, water vapor treatment has no effect on EIPH.[282]

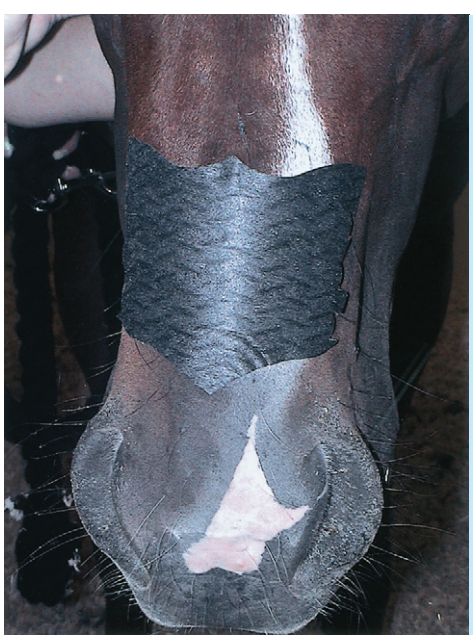


Fig. 29.17 Horse wearing a nasal dilator (Flair) strip. Photograph courtesy of Dr S. Holcombe.

The use of bedding of low allergenic potential (shredded paper) to prevent EIPH has no apparent effect on the prevalence of EIPH.[283] While it is suggested that the severity of EIPH may be reduced by preventing or minimizing small airway disease, studies to demonstrate such an effect have not been reported. However, optimizing the air quality in barns and stables and preventing infectious respiratory disease appear sensible precautions.

Interstitial inflammation and bronchial angiogenesis

Hemorrhage into interstitial tissues induces inflammation with subsequent development of fibrosis and bronchial artery angiogenesis.[240,254,284] The role of these changes in perpetuating EIPH in horses is unclear, but is likely to be of some importance. Treatments to reduce inflammation and promote healing with minimal fibrosis have been proposed. Rest is an obvious recommendation and many racing jurisdictions have rules regarding enforced rest for horses with epistaxis. While the recommendation for rest is intuitive, there is no information that rest reduces the severity or incidence of EIPH in horses with prior evidence of this disorder.

Similarly, corticosteroids are often administered, either by inhalation, enterally or parenterally, in an attempt to reduce pulmonary inflammation and minimize fibrosis. Again, the efficacy of this intervention in preventing or minimizing severity of EIPH has not been documented.

Excessive bleeding

Coagulopathy and fibrinolysis Exercise induces substantial changes in blood coagulation and fibrinolysis.[285] However there is no evidence that horses with EIPH have defective coagulation or increased fibrinolysis.[286,287] Regardless, aminocaproic acid, a potent inhibitor of fibrin degradation, has been administered to horses to prevent EIPH. The efficacy of aminocaproic acid in preventing EIPH has not been demonstrated. Similarly, estrogens are given to horses with the expectation of improving hemostasis although the effect of estrogens on coagulation in any species is unclear. There is no evidence that estrogens prevent EIPH in horses.

Vitamin K is administered to horses with EIPH presumably with the expectation that it will decrease coagulation times. However, as EIPH is not associated with prolonged bleeding times, it is unlikely that this intervention will affect the prevalence or severity of EIPH.

Platelet function Aspirin inhibits platelet aggregation in horses and increases bleeding time.[288] Seemingly paradoxically, aspirin is sometimes administered to horses with EIPH because of concerns that increased platelet aggregation contributes to EIPH.[289] There is no evidence that aspirin either exacerbates or prevents EIPH.

Capillary integrity Capillary fragility increases the risk of hemorrhage in many species. Various bioflavinoids have been suggested to increase capillary integrity and prevent bleeding. However, hesperidin and citrus bioflavinoids have no efficacy in prevention of EIPH in horses.[290] Similarly, vitamin C is administered to horses with EIPH without scientific evidence of any beneficial effect.

Overview of treatment Selection of therapy for horses with EIPH is problematic. Given that most horses have some degree of pulmonary hemorrhage during most bouts of intense exercise, the decision must be made not only as to the type of treatment and its timing but also which horses to treat. Moreover, the apparent progressive nature of the disease with continued work highlights the importance of early and effective prophylaxis and emphasizes the need for studies of factors, such as air quality and respiratory infections, in inciting the disorder.

The currently favored treatment for EIPH is administration of furosemide (frusemide) before intense exercise. Its use is permitted in race horses in a number of countries. Increasingly persuasive laboratory evidence of an effect of furosemide to reduce red cell count in BAL fluid collected from horses soon after intense exercise supports the contention that furosemide is effective in reducing the severity of EIPH in race horses. However, it should be borne in mind that neither the relationship between severity of EIPH and red cell count in BAL fluid nor the efficacy of furosemide in reducing severity of EIPH in race horses in the field has been demonstrated. In fact, there is strong evidence that furosemide does not reduce the prevalence of EIPH and other evidence that it does not reduce the severity of EIPH under field conditions. The association between furosemide administration and superior performance in Standardbred and Thoroughbred race horses should be borne in mind when recommending use of this drug.

Rest is an obvious recommendation for horses with EIPH, but the hemorrhage is likely to recur when the horse is next strenuously exercised. The duration of rest and the optimal exercise program to return horses to racing after EIPH is unknown, although some jurisdictions require exercise no more intense than trotting for 2 months. Firm recommendations cannot be made on duration of rest because of a lack of objective information.

Although a role for lower airway disease (either infectious or allergic) in the genesis of EIPH has not been demonstrated, control of infectious diseases and minimization of non-infectious lower airway inflammation appears prudent.

Prognosis

The prognosis for racing for horses with clinically significant EIPH is guarded because of the progressive nature of the disease. Horses that have experienced severe EIPH on one occasion are likely to do so again regardless of treatment. However, the risk of horses experiencing a repeated bout of severe hemorrhage and the effect of EIPH on career longevity are unknown.

Pathophysiology and etiology

The likely proximate cause of EIPH is rupture of alveolar capillary membranes with subsequent extravasation of blood into interstitial and alveolar spaces (Fig. 29.18).[291] The source of blood in such instances is the pulmonary circulation. Bleeding from bronchial circulation during exercise has been suggested based on histologic evidence of bronchial angiogenesis in horses that have experienced previous episodes of EIPH.[292] Whether there is a contribution of the bronchial circulation to EIPH has not been determined. Regardless of the contribution of bronchial circulation to blood in the airways, the likely initial lesion is in capillaries associated with the pulmonary circulation. Hemorrhage into the interstitial space and alveoli, with subsequent rostral movement of blood in the airways, results in blood in the trachea and bronchi and, infrequently, epistaxis.

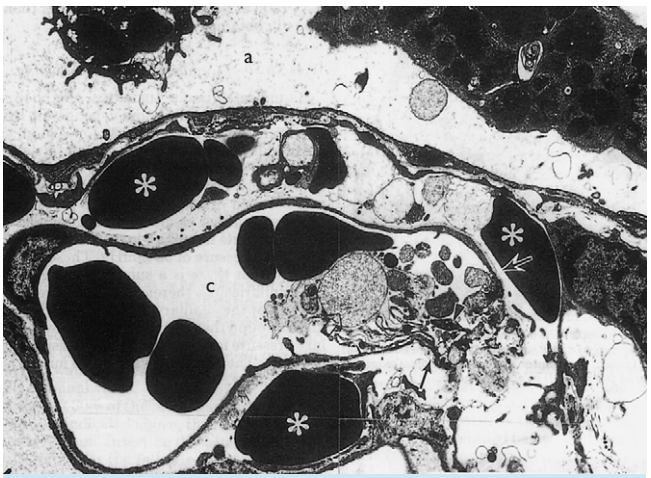


Fig. 29.18
Electron micrograph demonstrating rupture of an alveolar capillary (c, thin arrows) with extravasation of red blood cells (*) into pulmonary interstitium. The 'a' is the alveolar airspace and the arrow mark the site of disruption of the pulmonary capillary epithelium. Reproduced with permission from West et al.[291]

Rupture of alveolar capillaries occurs secondary to an exercise-induced increase in transmural pressure (pressure difference between the inside of the capillary and the alveolar lumen) (Fig. 29.16). If the transmural stress exceeds the tensile strength of the capillary wall, the capillary ruptures.[293] The proximate cause of alveolar capillary rupture is the high transmural pressure generated by positive intracapillary pressures (largely attributable to capillary blood pressure) and the lower intra-alveolar pressure (generated by the negative pleural pressures associated with inspiration). During exercise, the absolute magnitudes of both pulmonary capillary pressure and alveolar pressure increase, with a consequent increase in transmural pressure.[276,293] (Fig. 29.16) Strenuous exercise is associated with marked increases in pulmonary artery pressure in horses.[243,263,294] Values for mean pulmonary arterial pressure at rest of 20–25 mmHg increase to greater than 90 mmHg during intense exercise because of the large cardiac output achieved by exercising horses. Although pulmonary capillary pressure cannot be measured directly, it can be estimated from pulmonary artery wedge pressures. Different techniques for estimating pulmonary capillary pressure produce varying values, but invariably exercise induces a marked increase in pulmonary

capillary pressure.[276,295,296] Combined with the increase in pulmonary capillary pressure is a marked decrease (more negative) in pleural, and therefore alveolar, pressures during exercise. Pleural pressures of normal horses during inspiration decrease from approximately –0.7 kPa (–5.3 mmHg) at rest to as low as –8.5 kPa (–64 mmHg) during strenuous exercise.[297] Together, the increases in pulmonary capillary pressure and decreases (more negative) in intrapleural (alveolar) pressure contribute to a marked increase in stress in the alveolar wall. Although the alveolar wall and pulmonary capillary of horses are stronger than those of other species, rupture may occur because the wall stress in the alveolus exceeds the mechanical strength of the capillary.[298]

Other theories of the pathogenesis of EIPH include (Table 29.8): small airway disease, upper airway obstruction, hemostatic abnormalities, changes in blood viscosity and erythrocyte shape, intrathoracic shear forces associated with gait, and bronchial artery angiogenesis.[292,299] It is likely that the pathogenesis of EIPH involves several processes, including pulmonary hypertension, lower alveolar pressure and changes in lung structure, that summate to induce stress failure of pulmonary capillaries.

Obstruction of either the upper or lower airways has been proposed as a cause of EIPH.[300] Inspiratory airway obstruction results in more negative intrapleural, and therefore alveolar, pressures. This effect is exacerbated by exercise with the result that alveolar transmural pressure is greater in horses with airway obstruction (Fig. 29.16).[274,276] The higher transmural pressure in such horses may increase the severity of EIPH, although this has not been demonstrated. Moreover, while inspiratory airway obstruction may predispose to EIPH, the prevalence of this condition is much less than that of EIPH, indicating that it is not the sole factor inducing EIPH in most horses.

Horses with moderate to severe EIPH have histologic evidence of inflammation of the small airways,[255,301] and there is a clear association between presence of EIPH and inflammatory changes in bronchoalveolar or tracheal aspirate fluid.[239,302] However, because instillation of autologous blood into the airways induces a marked inflammatory response in normal horses,[240] it is unclear if inflammation alone induces or predisposes to EIPH or if the inflammation is a result of EIPH. Theoretically, small airway inflammation and bronchoconstriction have the potential to produce intrathoracic airway obstruction and, therefore, a more negative alveolar pressure. Given that small airway disease is common in horses, there is the potential for an important effect of factors such as viral infections, air pollution and allergic airway disease to contribute to the initiation or propagation of EIPH.

Exercise is accompanied by marked changes in blood flow characteristics attributable to an increase in hematocrit and decrease in red cell deformability.[269,303] These changes cause an increase in microvascular shear stress and thus could, conceivably, contribute to capillary rupture.[303] However, there is at present no direct evidence that indicates that this is an important feature of EIPH.

The characteristic location of lesions of EIPH in the caudodorsal lung fields has led to the proposal that hemorrhage is a result of tissue damage occurring when waves of stress, generated by forelimb foot strike, are focused and amplified into by the narrowing cross-sectional area of the caudal lung lobes.[299] According to the theory, the locomotory impact of the forelimbs results in transmission of forces through the scapula to the body wall, from where they pass into the lungs and caudally and dorsally. As the wave of pressure passes into the narrower caudodorsal regions of the lungs it generates progressively greater shearing forces which disrupt tissue and cause EIPH.[299] However, studies of intrapleural pressures have not demonstrated the presence of a systemic pressure wave passing through the lung and do not provide support for this hypothesis.[304]

Horses with EIPH have been suspected of having defects in either hemostasis or fibrinolysis. However, while exercise induces substantial changes in blood coagulation and fibrinolysis,[285] these is no evidence that horses with EIPH have defective coagulation or increased fibrinolysis.[286,287]

Overview Regardless of the cause, rupture of pulmonary capillaries and subsequent hemorrhage into airways and interstitium causes inflammation of both airways and interstitium with subsequent development of fibrosis and alteration of tissue compliance (Fig. 29.19). Heterogeneity of compliance within the lungs, and particularly at the junction of normal and diseased tissue, results in development of abnormal shear stress with subsequent tissue damage. These changes are exacerbated by inflammation and obstruction of small airways with resulting uneven inflation of the lungs.[305] The structural abnormalities, combined with pulmonary hypertension and the large intrathoracic forces associated with respiration during strenuous exercise, cause repetitive damage at the boundary of normal and diseased tissue with further hemorrhage and inflammation. The process, once started, is lifelong and continues for as long as the horse continues to perform strenuous exercise.[292]

Table 29.8 Potential factors inducing or contributing to the severity of exercise-induced pulmonary hemorrhage

Pulmonary capillary hypertension
Rheologic properties of blood
Negative intrapleural (alveolar) pressures
Extrathoracic airway obstruction (e.g. laryngeal hemiplegia)
Intrathoracic airway obstruction (e.g. bronchoconstriction)
Small airway inflammatory disease
viral or bacterial infections
allergy
air pollution (dust, ozone)
Coagulopathy
abnormal platelet function
capillary fragility
Bronchial neovascularization
Pulmonary fibrosis and altered compliance
Locomotory forces
foot strike
abdominal piston

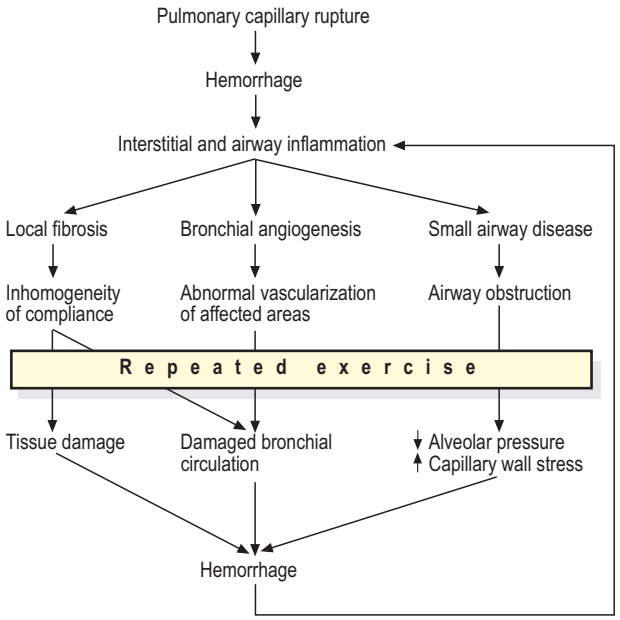


Fig. 29.19
Proposed pathogenesis of EIPH.

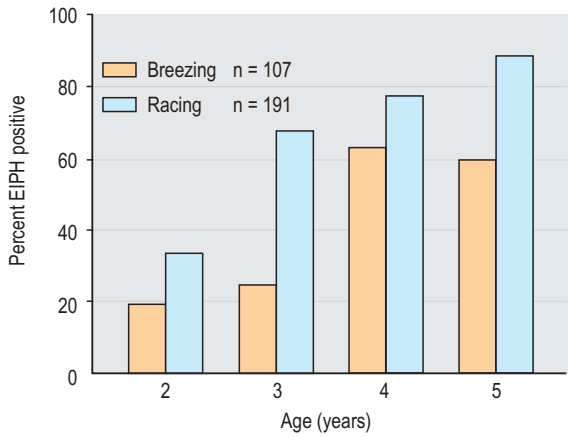


Fig. 29.20
Relationship between prevalence of EIPH and age and speed (racing or breezing) in Thoroughbred horses. Reproduced with permission from Raphel and Soma.[223]

Epidemiology

Exercise-induced pulmonary hemorrhage is a disorder of horses that run at high speed, such as Thoroughbred or Standardbred race horses. The disease is almost unknown in endurance horses or draft breeds. As a general rule, the more intense the exercise or higher the speed attained, the greater the proportion of horses with EIPH.

The prevalence of EIPH varies with the method used to detect it and the frequency with which horses are examined. Almost all Thoroughbred race horses in active training have hemosiderophages in BAL fluid, indicating that all have some degree of EIPH.[220] The prevalence of EIPH decreases when diagnosis is based on endoscopic examination of horses after exercise or racing.

Exercise-induced pulmonary hemorrhage is very common in Thoroughbred race horses with estimates of prevalence, based on a single endoscopic examination of the trachea and bronchi, of 43–75%.[223,225,306] The prevalence increases with the frequency of examination with over 80% of horses having evidence of EIPH on at least one occasion after examination after each of three consecutive races.[261] The prevalence of EIPH in Standardbred race horses is assumed to be lower, with 26–34% of horses reported to have blood in the trachea after racing.[227,307] However, these studies were based on a single examination and one[307] only reported as positive those horses with blood covering more than one-half of the tracheobronchial tree. When examined after each of three races, 87% of Standardbred race horses have evidence of EIPH on at least one occasion,[226] suggesting that EIPH is as common in Standardbred race horses as it is in Thoroughbred race horses.

Exercise-induced pulmonary hemorrhage occurs in approximately 62% of racing Quarter Horses, and has been observed in Quarter Horses used for barrel racing.[234] The disorder occurs in racing Appaloosa horses.[233] Approximately 11% of polo ponies are affected with EIPH.[308]

Age is an important risk factor for EIPH with the prevalence of the disorder being higher in older horses (Fig. 29.20).[223,225,306] There is no consistent effect of sex on prevalence of EIPH.[223,225,227,306]

Among Thoroughbred race horses the prevalence of EIPH increases with increasing speed.[223,301] The prevalence of EIPH is greater in Thoroughbreds after racing than after breezing (galloping) (Fig. 29.20) and lesions of EIPH are not detected in young Thoroughbred race horses that have not trained at speeds above 7 meters per second.[223,301]

Prevention

Aspects of prevention of EIPH are discussed under 'Treatment and prognosis'. At present, there are no recognized and accepted approaches for prevention of EIPH in young horses. Development of strategies for prevention will depend on an understanding of the inciting causes of EIPH.

Interstitial pneumonia

- Interstitial pneumonia is a rare disease of horses that can be caused by infections, toxins, or immune-mediated mechanisms, but most cases remain undiagnosed.
- Acute cases often present for acute respiratory distress whereas chronic cases have a history of progressive weight loss and increasing respiratory difficulty.
- History, clinical examination, lung function testing, and thoracic radiographs help reach a presumptive diagnosis

of interstitial pneumonia, but histology of a lung biopsy is required to confirm diagnosis.
- Treatment is usually unrewarding and prognosis is poor.

Recognition of the disease

History and presenting complaint

Interstitial pneumonia is an uncommon cause of pulmonary disease in horses, with both acute and chronic presentations having been described. Affected animals may vary in age from foals as young as 1 month to horses over 20 years and present with acute or chronic onset of tachypnea, weight loss, exercise intolerance, increased respiratory efforts, fever and cough.[309–312] Clinical presentation may vary from horses developing acute respiratory distress in less than 24 hours to horses exhibiting progressive weight loss and exercise intolerance over a period of months. Animals usually fail to improve in response to antimicrobial and anti-inflammatory therapy.

Physical examination

Horses presenting acute forms of the disease usually exhibit respiratory distress characterized by nostril flaring, tachypnea, increased respiratory efforts, and cyanotic mucous membranes.[310,313] Fever, tachycardia, and abnormal breath sounds (e.g. wheezes, crackles) upon thoracic auscultation are frequently found during physical examination. Other horses display decreased breath sound intensity over the entire lung field despite obvious breathing difficulty.[311] Chronic cases often exhibit progressive weight loss and increasing breathing difficulties. Horses may be asymptomatic in the early stages of chronic interstitial pneumonia (e.g. silicosis).[314]

Special examination

Thoracic radiographs often reveal a severe, diffuse interstitial pattern occasionally forming a miliary to nodular pattern (Fig. 29.21).[310,314] Areas of alveolar opacities with air bronchogram may be seen in addition to bronchointerstitial patterns. Repeating radiographs may be useful to follow disease progression. However, it is a poor predictor of lung function and radiographic findings may be normal in a horse with significant exercise intolerance. Ultrasonography of the chest may reveal an irregular lung surface with small hyperechoic areas.[311]

Transcutaneous lung biopsy often provides a definitive diagnosis. However, complications such as pulmonary hemorrhage, pneumothorax, and rarely death can occur.[315,316] Histologic findings in acute severe cases reveal diffuse, necrotizing bronchiolitis and alveolitis, hyaline membrane formation, interstitial edema and fibrosis, and type II pneumocyte hyperplasia.[310,311,317] Lesions secondary to silicosis are characterized by areas of fibrosis with multiple granulomatous lesions containing macrophages with intracytoplasmic, eosinophilic, birefringent crystalline material.[314]

Lung function testing is useful to characterize the type and severity of pulmonary disease. Interstitial pneumonia results in decreased lung elasticity and as a result greater distending pressure is required from inspiratory muscles in order to achieve any volume change (restrictive lung disease). These changes may be detected by measurement of lung mechanics during tidal breathing. Typical changes are decreased dynamic lung compliance (C_{dyn}), increased changes in transpulmonary pressure (ΔP_{plmax}), and normal pulmonary resistance (R_L; Fig. 29.22). In contrast, horses with obstructive lung disease such as RAO exhibit increased ΔP_{plmax} mainly because of increased R_L. Decreased lung elasticity also limits the maximum volume of air that the horse can inhale (vital capacity) but does not affect the ability to exhale rapidly. As a result forced vital capacity (FVC) is reduced but the ratio forced expiratory volume in 1.5 second ($FEV_{1.5}$):FVC is normal or high (Fig. 29.23). Horses with RAO in crisis have a mildly reduced FVC and a markedly decreased $FEV_{1.5}$:FVC ratio.

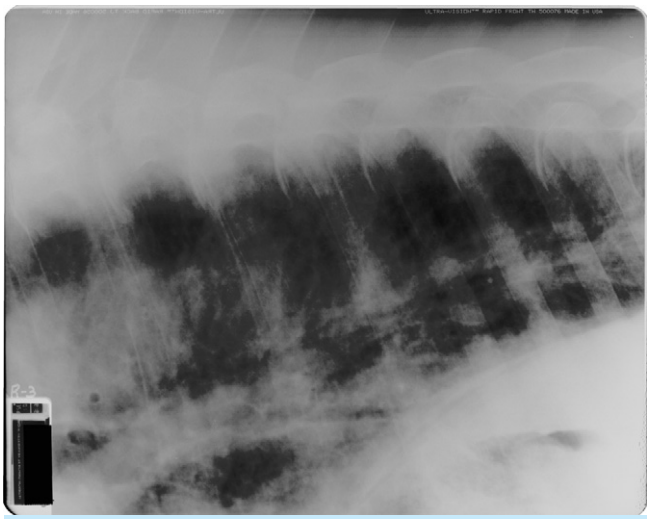


Fig. 29.21
Thoracic radiograph of 14-year-old Thoroughbred horse diagnosed with interstitial pneumonia. Radiographic findings indicate a marked, diffuse broncho-interstitial pattern in the dorsocaudal lung fields.

Laboratory examination

Hematologic findings include leukocytosis, neutrophilia, and hyperfibrinogenemia.[310,312] Occasionally, thrombocytopenia and abnormal clotting times may be detected in severely affected animals with bleeding diathesis (e.g. epistaxis, petechia, ecchymosis).[310] Common abnormalities detected on arterial blood gas analyses include hypoxemia and hyper- or hypocapnia.[312,318]

Various bacteria (e.g. *Streptococcus zooepidemicus*, *Rhodococcus equi*, *Escherichia coli*) may be isolated from respiratory secretions collected by TW or BAL in foals. However, bacteria, viruses, or fungi are usually not cultured from adult horses.[310,312] Cytological analyses often show inflammatory changes characterized by increased number of non-degenerative neutrophils and no visible pathogens. Accumulation of intracellular crystalline materials in pulmonary alveolar macrophages is commonly detected in horses with silicosis.[314]

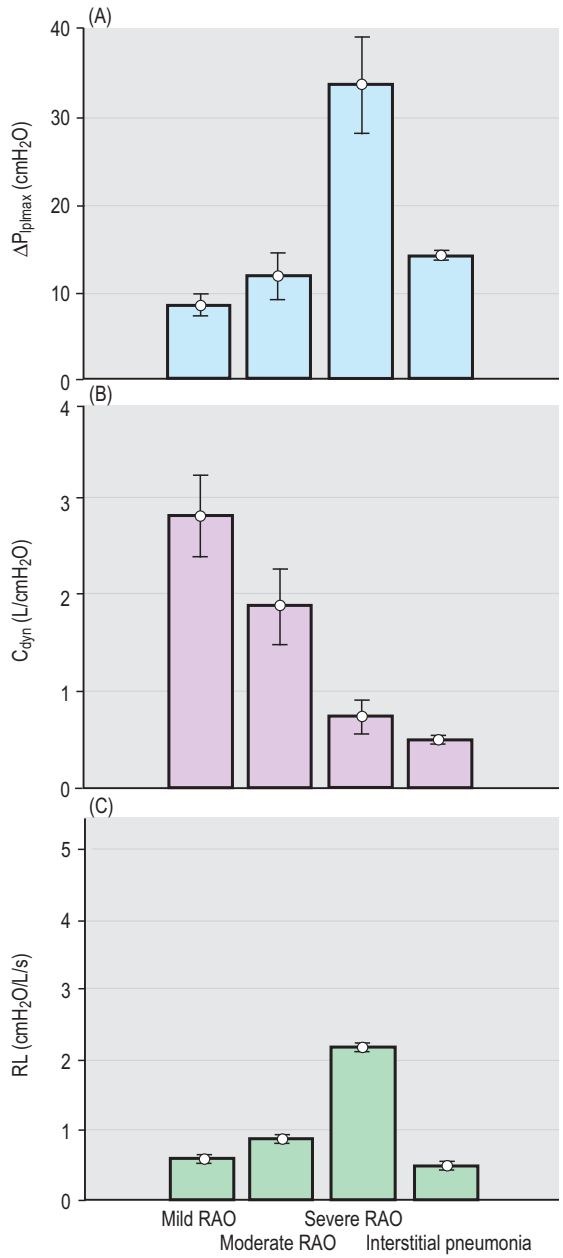


Fig. 29.22
Lung mechanics during tidal breathing in horses with RAO and one horse with interstitial pneumonia. (A) Maximum transpulmonary, pressure changes. (B) Dynamic compliance. (C) Pulmonary resistance.

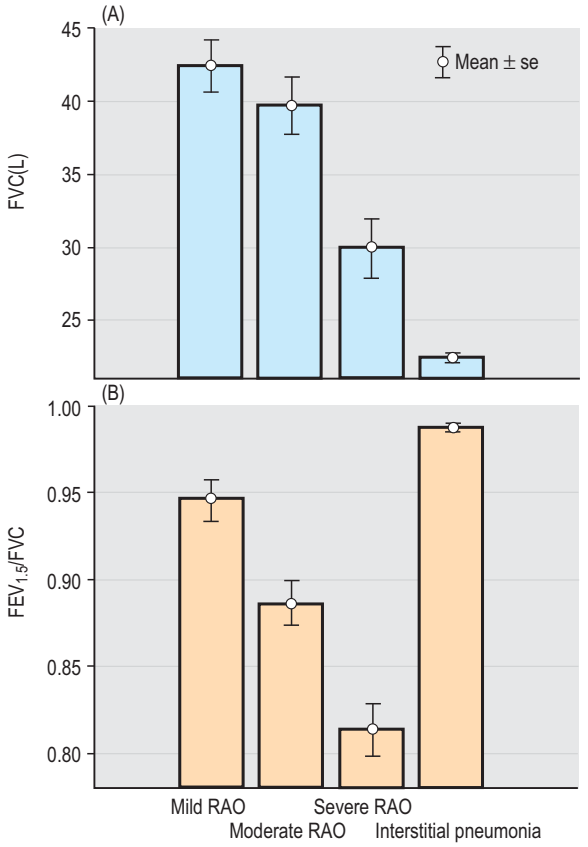


Fig. 29.23
Forced expiration parameters in horses with RAO and in one horse with interstitial pneumonia. (A) Forced vital capacity. (B) Forced expiratory volume in 1.5 s ($FEV_{1.5}$)/forced vital capacity (FVC).

Necropsy examination

Gross pathologic findings include diffusely enlarged and abnormally heavy lungs that fail to collapse upon opening of the thorax, variable amounts of pink foamy liquid in airways, a mottled, lobulated appearance of the lungs, and in some cases, interstitial emphysema.[317,318] Main histologic findings in chronic cases are interstitial fibrosis. Acute lesions include severe, diffuse bronchiolitis, alveolar septal necrosis with neutrophilic infiltration, interstitial edema, hyaline membrane formation, and type II pneumocyte hyperplasia. Cases of silicosis are characterized by diffuse granulomatous pneumonia with areas of pulmonary fibrosis and granulomatous tracheobronchial lymphadenitis.[314,319] Granulomas are composed mainly of macrophages containing refractile particles (≤ 1 μm).

Diagnostic confirmation

The diagnostic approach concerning horses with respiratory distress has been discussed in detail in the RAO section (see 'Diagnostic confirmation'; Fig. 29.8). The main test consists in the administration of a fast-acting bronchodilator (e.g. aerosolized albuterol) to rule out reversible obstructive pulmonary diseases such as RAO and SPAOPD. Thoracic radiography and transcutaneous biopsy are often necessary to confirm a diagnosis of interstitial pneumonia.

Treatment and prognosis

Therapeutic aims

The main goals are to improve tissue oxygenation, decrease pulmonary inflammation, treat underlying infections and

potential complications, and avoid additional stressors.[313] The latter includes strict stall rest in a well-ventilated, cool and dust-free environment.

Therapy

Treatment of tissue hypoxia includes oxygen supplementation through nasal or transtracheal insufflation and bronchodilator administration. In order to improve arterial blood oxygen tension minimum oxygen flow rates of 5 L/min in foals and 12 L/min in adults may be required and should be adjusted based on clinical response or preferably repeated arterial blood gas analysis. Long-acting inhaled bronchodilators are indicated to help decrease the work of breathing (see discussion in the RAO 'Therapy' section). Non-steroidal anti-inflammatory drugs (e.g. flunixin meglumine) may be beneficial. However, corticosteroids appear to be more effective at decreasing pulmonary inflammation and preventing fibrosis, and their use is associated with positive outcome.[311,318] Both inhaled (Table 29.3) and systemic corticosteroids may be administered using similar dosages as for RAO horses in crisis. Antimicrobial therapy is recommended to treat primary or opportunistic infections. Broad-spectrum treatment should be initiated while waiting for tracheal wash cytology and culture results, and should last at least 3 to 6 weeks.[313] Intravenous fluid therapy should be used with caution because cases of severe interstitial pneumonia often exhibit pulmonary hypertension and additional fluids may lead to or aggravate pulmonary edema. Furosemide (frusemide) therapy may be useful in such cases.[320]

Prognosis

Horses with interstitial pneumonia have a poor prognosis. However, some cases have been successfully treated and able to return to athletic activities. One study describes survival of 9 out of 23 cases of interstitial pneumonia in foals.[310] Based on review of the literature, survival rate in adult horses appears to be less favorable.

Prevention

Avoidance of exposure to environmental or toxic causes of interstitial pneumonia (e.g. silicosis, hypersensitivity pneumonitis, smoke inhalation, pneumotoxins) is recommended. However, because the majority of cases of interstitial pneumonia are of unknown etiology, preventive measures are limited to general respiratory hygiene (e.g. low-dust environment, good ventilation) and prophylaxis against respiratory pathogens.

Etiology and pathophysiology

Etiology

A potential cause is found in only a minority of interstitial pneumonia cases. Infectious agents associated with interstitial pneumonia include viruses (e.g. *Morbillivirus*), bacteria (*Streptococcus zooepidemicus*, *Rhodococcus equi*, *Escherichia coli*), parasites (*Parascaris equorum*, *Dictyocaulus arnfieldi*), protozoa (*Pneumocystis carinii*), and fungi (*Aspergillus* spp., *Cryptococcus* spp., *Histoplasma* spp.).[69,317,318,321] Pneumotoxins may be released after ingestion of certain plants such as *Perilla frutescens* and *Eupatorium adenophorum*.[322,323] Alternatively, inhalation of chemicals (e.g. smoke, silicon dioxide crystals) or organic antigens (fungi, endotoxins) may directly injure the lungs and result in intersitial pneumonia.[314,324,325]

Pathophysiology

Interstitial pneumonia may result from direct injury of the alveolar epithelium (pneumocytes I and II), from inhaled toxins or from hematogenous injury to pulmonary capillaries or alveolar basement membrane.[326] Acute lung injury begins with an exudative phase resulting from disruption of the alveolar–capillary barrier. Exudate may form hyaline membranes that become partially attached to alveolar and airway walls. Inflammatory cells, in particular neutrophils, accumulate in the alveolar walls and may cause further tissue damage by the release of proteases and reactive oxygen species.[213,327] A proliferative phase characterized by type II pneumocyte hyperplasia follows the exudative phase within a few days, resulting in thickened alveolar walls. If the horse survives the initial pulmonary insult, the lesions may progress towards alveolar fibrosis characteristic of the chronic phase of interstitial pneumonia.

Epidemiology

Most of the reported cases are sporadic in occurrence. However, multiple cases may occur when horses are exposed to common environmental toxins such as pasture rich in pneumotoxic plants or regions with a high level of crystalline silicates. Cases of interstitial pneumonia have been described in young foals to old horses of various breeds and sex.

References

1. Rush Moore B, Krakowka S, Robertson JT, Cummins JM. Cytologic evaluation of bronchoalveolar lavage fluid obtained from Standardbred racehorses with inflammatory airway disease. Am J Vet Res 1995; 56:562–567.
2. Hare JE, Viel L, O'Byrne PM, Conlon PD. Effect of sodium cromoglycate on light racehorses with elevated metachromatic cell numbers on bronchoalveolar lavage and reduced exercise tolerance. J Vet Pharmacol Therap 1994; 17:237–244.
3. Robinson N. International workshop on equine chronic airway disease. Equine Vet J 2001; 33:5–19.
4. Viel L. Small airway disease as a vanguard for chronic obstructive pulmonary disease. Vet Clin North Am: Equine Pract 1997; 13:549–560.

5. Burrell MH. Endoscopic and virologic observations on respiratory disease in a group of young Thoroughbred horses in training. Equine Vet J 1985; 17:99–103.
6. Chapman P, Green C, Main J, et al. Retrospective study of the relationships between age, inflammation and the isolation of bacteria from the lower respiratory tract of thoroughbred horses. Vet Rec 2000; 146:91–95.
7. MacNamara B, Bauer S, Iafe J. Endoscopic evaluation of exercise-induced pulmonary hemorrhage and chronic obstructive pulmonary disease in association with poor performance in racing Standardbreds. J Am Vet Med Assoc 1990; 196:443–445.
8. Burrell M, Wood J, Whitwell K, et al. Respiratory disease in thoroughbred horses in training: the relationships between disease and viruses, bacteria and environment. Vet Rec 1996; 139:308–313.
9. Sellon DC. Investigating outbreaks of respiratory disease in older foals. Proc Am Assoc Equine Pract 2001; 47:447–455.
10. Couetil L, Rosenthal F, DeNicola D, Chilcoat C. Clinical signs, evaluation of bronchoalveolar lavage fluid, and assessment of pulmonary function in horses with inflammatory respiratory disease. Am J Vet Res 2001; 62:538–546.
11. Dixon P, Railton D, McGorum B. Equine pulmonary disease: a case control study of 300 referred cases. Part 2: Details of animals and of historical and clinical findings. Equine Vet J 1995; 27:422–427.
12. Christley RM, Hodgson DR, Rose RJ, et al. Coughing in thoroughbred racehorses: risk factors and tracheal endoscopic and cytological findings. Vet Rec 2001; 148:99–104.
13. Vrins A, Doucet M, Nunez-Ochoa L. A retrospective study of bronchoalveolar lavage cytology in horses with clinical findings of small airway disease. J Vet Med Assoc 1991; 38:472–479.
14. Bracher V, von Fellenberg R, Winder CN, et al. An investigation of the incidence of chronic obstructive pulmonary disease (COPD) in random populations of Swiss horses. Equine Vet J 1991; 23:136–141.
15. Art T, Anderson L, Woakes A, et al. Mechanics of breathing during strenuous exercise in thoroughbred horses. Respir Physiol 1990; 82:279–294.
16. McGorum B, Ellison J, Cullen R. Total and respirable airborne dust endotoxin concentrations in three equine management systems. Equine Vet J 1998; 30:430–434.
17. Clarke A. A review of environmental and host factors in relation to equine respiratory disease. Equine Vet J 1987; 19:435–441.
18. Fogarty U, Buckley T. Bronchoalveolar lavage findings in horses with exercise intolerance. Equine Vet J 1991; 23:434–437.
19. Gerber V. Mucus in equine lower airway disease. World Equine Airway Symposium, Edinburgh, UK, 2001.
20. Gerber V, Robinson NE, Luethi E, et al. Comparison of airway inflammation and mucus between younger versus older stabled clinically healthy horses. WEAS 2001 conference proceedings. 2001.
21. Christley RM, Hodgson DR, Rose RJ, et al. A case-control study of respiratory disease in Thoroughbred racehorses in Sydney, Australia. Equine Vet J 2001; 33:256–264.
22. Wagner P, Gillespie J, Landgren G, et al. Mechanism of exercise-induced hypoxemia in horses. J Appl Physiol 1989; 66:1227–1233.
23. Art T, Lekeux P. Ventilatory and arterial blood gas tension adjustments to strenuous exercise in standardbreds. Am J Vet Res 1995; 56:1332–1337.
24. Nyman G, Bjork M, Funkquist P. Gas exchange during exercise in Standardbred trotters with mild bronchiolitis. Equine Vet J 1999; Suppl 30:96–101.
25. Persson S. On blood volume and working capacity in horses. Studies of methodology and physiological and pathological variations. Acta Vet Scand 1967; Suppl 189.
26. Persson S. Evaluation of exercise tolerance and fitness in the performance horse. In: Snow D, Persson S, Rose R, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 441–457.
27. Funkquist P, Nyman G, Persson SGB. Hemodynamic responses to exercise in trotters with red cell hypervolemia and exercise induced pulmonary hemorrhage. Proceedings of the 10th International Conference of Racing Analysts and Veterinarians. Newmarket: R and W Publications; 1994; 165–167.
28. Davis J, Manohar M. Effect of splenectomy on exercise-induced pulmonary and systemic hypertension in ponies. Am J Vet Res 1988; 49:1169–1172.
29. Nyman G, Lindberg R, Weckner D, et al. Pulmonary gas exchange correlated to clinical signs and lung pathology in horses with chronic bronchiolitis. Equine Vet J 1991; 23:253–260.
30. Eberly V, Tyler W, Gillespie J. Cardiovascular parameters in emphysematous and control horses. J Appl Physiol 1966; 21:883–889.
31. Persson SGB, Lindberg R. Lung biopsy pathology and exercise tolerance in horses with chronic bronchiolitis. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 457–464.
32. Hoffman A, Mazan M. Programme of lung function testing horses suspected with small airway disease. Equine Vet Educ 1999; 11:322–328.
33. Hoffman A, Mazan M, Ellenberg S. Association between bronchoalveolar lavage cytologic features and airway reactivity in horses with a history of exercise intolerance. Am J Vet Res 1998; 59:176–181.
34. Couëtil L, DeNicola D. Blood gas, plasma lactate, and bronchoalveolar lavage cytology analyses in racehorses with respiratory disease. Equine Vet J 1999; 30:77–82.
35. Christley RM, Hodgson DR, Evans DL, Rose RJ. Effects of training on the development of exercise-induced arterial hypoxemia in horses. Am J Vet Res 1997; 58:653–657.
36. Morris EA, Seeherman HJ. Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. Equine Vet J 1991; 23:169–174.
37. Dixon PM, Railton DI, McGorum BC. Equine pulmonary disease: a case control study of 300 referred cases. Part 3: Ancillary diagnostic findings. Equine Vet J 1995; 27:428–435.
38. Beech J. Tracheobronchial aspirates. In: Beech J, ed. Equine respiratory disorders. Philadelphia: Lea and Febiger; 1991; 41–53.
39. Mair T, Stokes C, Bourne F. Cellular content of secretions obtained by lavage from different levels of the equine respiratory tract. Equine Vet J 1987; 19:458–462.
40. Mansmann R, Knight H. Transtracheal aspiration in the horse. J Am Vet Med Assoc 1972; 160:1527–1529.
41. Christley RM, Hodgson DR, Rose RJ, et al. Comparison of bacteriology and cytology of tracheal fluid samples collected by percutaneous transtracheal aspiration or via an endoscope using a plugged, guarded catheter. Equine Vet J 1999; 31:197–202.
42. Chapman P, Green C, Main J, et al. Retrospective study of the relationships between age, inflammation and the isolation of

bacteria from the lower respiratory tract of thoroughbred horses. Vet Rec 2000; 146:91–95.
43. Larson V, Busch R. Equine tracheobronchial lavage: comparison of lavage cytology and pulmonary histopathologic findings. Am J Vet Res 1985; 46:144–146.
44. Derksen F, Brown C, Sonea B. Comparison of transtracheal aspirate and bronchoalveolar lavage cytology in 50 horses. Equine Vet J 1989; 21:23–26.
45. Winder N, Gruenig G, Hermann M, et al. Comparison of respiratory secretions cytology and pulmonary histology in horses. J Vet Med Assoc 1989; 36:32–38.
46. Sweeney C, Rossier Y, Ziemer E, Lindborg S. Effects of lung site and fluid volume on results of bronchoalveolar lavage fluid analysis in horses. Am J Vet Res 1992; 53:1376–1379.
47. McGorum B, Dixon P, Halliwell R, Irving P. Comparison of cellular and molecular components of bronchoalveolar lavage fluid harvested from different segments of the equine lung. Res Vet Science 1993; 55:57–59.
48. Viel L. Structural-functional correlations of the lung in horses with small airway disease. University of Guelph, Canada. 1983.
49. Sweeney C, Beech J. Bronchoalveolar lavage. In: Beech J, ed. Equine respiratory disorders. Philadelphia: Lea and Febiger; 1991:55–61.
50. Rush Moore B. Lower respiratory tract disease. Vet Clin North Am Equine Pract 1996; 12:457–472.
51. Gillespie J, Tyler W, Eberly V. Pulmonary ventilation and resistance in emphysematous and control horses. J Appl Physiol 1966; 21:416–422.
52. Derksen F, Robinson N, Slocombe R, et al. Pulmonary function tests in standing ponies: reproducibility and effect of vagal blockade. Am J Vet Res 1982; 43:598–602.
53. Tesarowski DB, Viel L, McDonell WN. Pulmonary function measurements during repeated environmental challenge of horses with recurrent airway obstruction (heaves). Am J Vet Res 1996; 57:1214–1219.
54. Rush B, Raub E, Rhoads W, et al. Pulmonary function in horses with recurrent airway obstruction after aerosol and parenteral administration of beclomethasone dipropionate and dexamethasone, respectively. Am J Vet Res 1998; 59:1039–1043.
55. Petsche V, Derksen F, Robinson N. Tidal breathing flow-volume loops in horses with recurrent airway obstruction (heaves). Am J Vet Res 1994; 55:885–891.
56. Gillespie J. The role of the respiratory system during exertion. J South Afr Vet Assoc 1974; 45:305–309.
57. Couetil L, Rosenthal F, Simpson C. Forced expiration: a test for airflow obstruction in horses. J Appl Physiol 2000; 88: 1870–1879.
58. Hoffman A, Kuehn H, Riedelberger K, et al. Flowmetric comparison of respiratory inductance plethysmography and pneumotachography in horses. J Appl Physiol 2001; 91:2767–2775.
59. Derksen FJ, Robinson NE, Armstrong PJ, et al. Airway reactivity in ponies with recurrent airway obstruction (heaves). J Appl Physiol 1985; 58:598–604.
60. Hare J, Viel L. Pulmonary eosinophilia associated with increased airway responsiveness in young racing horses. J Vet Intern Med 1998; 12:163–170.
61. Derksen F, Scott J, Miller D, et al. Bronchoalveolar lavage in ponies with recurrent airway obstruction (heaves). Am Rev Respir Dis 1985; 132:1066–1070.
62. Tremblay G, Ferland C, Lapointe J-M, et al. Effect of stabling on bronchoalveolar cells obtained from normal and COPD horses. Equine Vet J 1993; 25:194–197.
63. Dixon P, Railton D, McGorum B. Equine pulmonary disease: a case control study of 300 referred cases. Part 1: Examination, techniques, diagnostic criteria and diagnoses. Equine Vet J 1995; 27:416–421.
64. Wilson W. Equine influenza. Vet Clin North Am Equine Pract 1993; 9:257–282.
65. Kastner S, Haines D, Archer J, Townsend H. Investigations on the ability of clenbuterol hydrochloride to reduce clinical signs and inflammation associated with equine influenza A infection. Equine Vet J 1999; 31:160–168.
66. Seahorn T, Beadle R. Summer pasture-associated obstructive pulmonary disease in horses: 21 cases. J Am Vet Med Assoc 1993; 202:779–782.
67. Burks B. Parasitic pneumonitis. Compend Contin Educ Pract Vet 1998; 20:378–382.
68. Hermann M, Gruning G, Bracher V, et al. Eosinophile granulozyten im tracheobronchialsekret von pferden: anhaltspunkt fur eine parasitare lungenerkrankung? Schweiz Arch Tierheilk 1988; 130:19–28.
69. Darien B. Eosinophilic pneumonitis in foals and horses. Compend Contin Educ Pract Vet 1994; 16: 1210–1212.
70. Beech J, Sweeney C. Infections caused by bacteria, mycoplasmas, parasites, and fungi. In: Beech J, ed. Equine respiratory disorders. Malvern: Lea and Febiger; 1991; 181–207.
71. Lyons E, Tolliver S, Drudge J, et al. Parasites in lungs of dead equids in Kentucky: emphasis on *Dictyocaulus arnfieldi*. Am J Vet Res 1985; 46:924–927.
72. Rush Moore B, Krakowka S, Cummins J. Changes in airway inflammatory cell populations in Standardbred racehorses after interferon administration. Vet Immunol Immunopathol 1996; 49:347.
73. Rush Moore B, Krakowka S, McVey D, et al. Inflammatory markers in bronchoalveolar lavage fluid of Standardbred racehorses with inflammatory airway disease: response to interferon-alpha. Equine Vet J 1997; 29:142–147.
74. Evans D, Rollins J, Huff G, et al. Inactivated *Propionobacterium acnes* (Immunoregulin) as adjunct to conventional therapy in the treatment of equine respiratory diseases. Equine Pract 1988; 10:17–21.
75. Klimczak C. Immunostimulant quickly aids weanling equine respiratory disease complex (ERDC) cases. Equine Vet Sci 1992; 12:68–69.
76. Barnes P. Current therapy for asthma. In: Hansel T, Barnes P, eds. New drugs for asthma, allergy and COPD. New York: Karger; 2001; 6–10.
77. Wood J, Burrell M, Roberts C, et al. Streptococci and Pasteurella spp. associated with disease of the equine lower respiratory tract. Equine Vet J 1993; 25:314–318.
78. Sweeney C, Beech J, Roby K. Bacterial isolates from tracheobronchial aspirates of healthy horses. Am J Vet Res 1985; 46:2562.
79. Nuytten J, Muylle E, Oyaert W, et al. Cytology, bacteriology and phagocytic capacity of tracheo-bronchial aspirates in healthy horses and horses with chronic obstructive pulmonary disease (COPD). Zentralbl Veterinarmed A 1983; 30:114–120.
80. Holcombe S, Jackson C, Gerber V, et al. Stabling is associated with airway inflammation in young Arabian horses. Equine Vet J 2001; 33:244–249.
81. Couetil LL, Hunt MA, Rosenthal FS. Effects of dust and endotoxin exposures on lung function and airway cytology of horses. In: Lunn DP, Wade JF, eds. Equine immunology (No. 4), Havemeyer Foundation Monograph Series. Newmarket, UK: R and W Publications. 2001; 86.
82. Pirie R, Dixon P, Collie D. Pulmonary and systemic effects of inhaled endotoxin in control and heaves horses. Equine Vet J 2001; 33:311–318.

83. McGorum B, Dixon P, Halliwell R. Responses of horses affected with chronic obstructive pulmonary disease to inhalation challenges with mould antigens. Equine Vet J 1993; 25:261–267.
84. Woods P, Robinson N, Swanson M, et al. Airborne dust and aeroallergen concentration in a horse stable under two different management systems. Equine Vet J 1993; 25:208–213.
85. Mills P, Roberts C, Smith N. Effects of ozone and airway inflammation on glutathione status and iron homeostasis in the lungs of horses. Am J Vet Res 1996; 57:1359–1363.
86. Davis M, Foster W. Inhalation toxicology in the equine respiratory tract. In: Lekeux P, ed. Equine respiratory diseases. Ithaca, NY: International Veterinary Information Services (www.ivis.org); 2002.
87. Tyler WS, Jones JH, Birks EK. Effects of ozone on exercising horses: a preliminary report. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology. Davis, CA: ICEEP Publications; 1991; 490–502.
88. Hobo S, Oikawa M-A, Kuwano A, et al. Effect of transportation on the composition of bronchoalveolar lavage fluid obtained from horses. Am J Vet Res 1997; 58:531–534.
89. Raidal S, Bailey G, Love D. Effect of transportation on lower respiratory tract contamination and peripheral blood neutrophil function. Aust Vet J 1997; 75:433–438.
90. Raidal S, Love D, Bailey G. Effect of a single bout of high intensity exercise on lower respiratory tract contamination in the horse. Aust Vet J 1997; 75:293–295.
91. Marti E, Gerber H, Essich G, et al. The genetic basis of equine allergic disease. 1: Chronic hypersensitivity bronchitis. Equine Vet J 1991; 23:457–460.
92. Morrison J. Asthma and COPD genetics and genomics: an overview. In: Hansel T, Barnes P, eds. New drugs for asthma, allergy and COPD. New York: Karger; 2001; 358–360.
93. Robinson NE. Pathogenesis and management of airway disease. Proc Am Assoc Equine Pract 1997; 43:106–115.
94. Seahorn T, Groves M, Harrington K, Beadle R. Chronic obstructive pulmonary disease in horses in Louisiana. J Am Vet Med Assoc 1996; 208:248–251.
95. McPherson E, Lawson G, Murphy J, et al. Chronic obstructive pulmonary disease (COPD): Identification of affected horses. Equine Vet J 1978; 10:47–53.
96. Broadstone R, Scott J, Derksen F, Robinson N. Effects of atropine in ponies with recurrent airway obstruction. J Appl Physiol 1988; 65:2720–2725.
97. Littlejohn A, Bowles F. Studies on the pathophysiology of chronic obstructive pulmonary disease in the horse: VI. The alveolar dead space. Onderstepoort J Vet Res 1982; 49:71–72.
98. Votion D, Ghafir Y, Vandenput S, et al. Analysis of scintigraphical lung images before and after treatment of horses suffering from chronic pulmonary disease. Vet Rec 1999; 144:232–236.
99. Art T, Duvivier D, Votion D, et al. Does an acute COPD crisis modify the cardiorespiratory and ventilatory adjustments to exercise in horses? J Appl Physiol 1998; 84:845–852.
100. Aliverti A, Macklem P. How and why exercise is impaired in COPD. Respiration 2001; 68:229–239.
101. Harms C, Wetter T, McClaran S, et al. Effect of respiratory muscle work on cardiac output and its distribution during maximal exercise. J Appl Physiol 1998; 85:609–618.
102. Broadstone R, Gray P, Robinson N, Derksen F. Effects of xylazine on airway function in ponies with recurrent airway obstruction. Am J Vet Res 1992; 53:1813–1817.
103. Lavoie J, Phan S, Blais D. Effects of a combination of detomidine and butorphanol on respiratory function in horses with or without chronic obstructive pulmonary disease. Am J Vet Res 1996; 57:705–709.
104. Reitemeyer H, Klein H-J, Deegen E. The effect of sedatives on lung function in horses. Acta Vet Scand 1986; 82:111–120.
105. Pickles K, Pirie R, Rhind S, et al. Cytological analysis of equine bronchoalveolar lavage fluid. Part 1: comparison of sequential and pooled aliquots. Equine Vet J 2002; 34:288–291.
106. Wisner E, O'Brien T, Lakritz J, et al. Radiographic and microscopic correlation of diffuse interstitial and bronchointerstitial pulmonary patterns in the caudodorsal lung of adult Thoroughbred horses in race training. Equine Vet J 1993; 25:293–298.
107. Robinson N, Olszewski M, Boehler D, et al. Relationship between clinical signs and lung function in horses with recurrent airway obstruction (heaves) during a bronchodilator trial. Equine Vet J 2000; 32:393–400.
108. Couetil L, Rosenthal F, DeNicola D, Chilcoat C. Clinical signs, evaluation of bronchoalveolar lavage fluid, and assessment of pulmonary function in horses with inflammatory respiratory disease. Am J Vet Res 2001; 62:538–546.
109. Young S, Tesarowski D, Viel L. Frequency dependence of forced oscillatory respiratory mechanics in horses with heaves. J Appl Physiol 1997; 82:983–987.
110. Fairbairn S, Lees P, Page C, Cunningham F. Duration of antigen-induced hyperresponsiveness in horses with allergic respiratory disease and possible links with early airway obstruction. J Vet Pharmacol Therap 1993; 16:469–476.
111. Armstrong P, Derksen F, Slocombe R, Robinson N. Airway responses to aerosolized methacholine and citric acid in ponies with recurrent airway obstruction (heaves). Am Rev Respir Dis 1986; 133:357–361.
112. Doucet M, Vrins A, Ford-Hutchinson A. Histamine inhalation challenge in normal horses and in horses with small airway disease. Can J Vet Res 1991; 55:285–293.
113. Klein H-J, Deegen E. Histamine inhalation provocation test: method to identify nonspecific airway reactivity in equids. Am J Vet Res 1986; 47:1796–1800.
114. Mazan M, Hoffman A, Manjerovic N. Comparison of forced oscillation with the conventional method for histamine bronchoprovocation testing in horses. Am J Vet Res 1999; 60:174–180.
115. Gallivan G, Viel L, McDonell W. An evaluation of the multiple-breath nitrogen washout as a pulmonary function test in horses. Can J Vet Res 1990; 54:99–105.
116. Denac-Sikiric VM. Die funktionelle residualkapazitat und helium-einmishchzeit gesunder und lungenkranker pferde. Zbl Vet Med A 1976; 23:193–205.
117. Willoughby R, McDonnell W. Pulmonary function testing in horses. Vet Clin North Am Large Anim Pract 1979; 1:171–197.
118. Leith DE, Gillespie JR. Respiratory mechanics of normal horses and one with chronic obstructive lung disease. Fed Proc 1971; 30:556.
119. Gillespie J, Tyler W. Chronic alveolar emphysema in the horse. Adv Vet Sci Comp Med 1969; 13:99.
120. Naylor J, Clark E, Clayton H. Chronic obstructive pulmonary disease: usefulness of clinical signs, bronchoalveolar lavage, and lung biopsy as diagnostic and prognostic aids. Can Vet J 1992; 33:591–598.
121. Rodrigues Costa L, Seahorn T, Moore R, et al. Correlation of clinical score, intrapleural pressure, cytologic findings of bronchoalveolar fluid, and histopathologic lesions of pulmonary tissue in horses with summer pasture-associated obstructive pulmonary disease. Am J Vet Res 2000; 61:167–173.
122. Thurlbeck W, Lowell F. Heaves in horses. Am Rev Respir Dis 1964; 89:82–88.

123. Kaup F, Drommer W, Damsch S, Deegen E. Ultrastructural findings in horses with chronic obstructive pulmonary disease (COPD) II: pathomorphological changes of the terminal airways and the alveolar region. Equine Vet J 1990; 22:349–355.
124. Kaup F, Drommer W, Deegen E. Ultrastructural findings in horses with chronic obstructive pulmonary disease (COPD) I: alterations of the larger conducting airways. Equine Vet J 1990; 22:343–348.
125. Breeze R. Heaves. Vet Clin North Am Large Anim Pract 1979; 1:219–230.
126. Foley F, Lowell F. Equine centrilobular emphysema. Am Rev Respir Dis 1966; 93:17–21.
127. Port C, Ketels K, Coffin D, Kane P. A comparison study of experimental and spontaneous emphysema. J Toxicol Environ Health 1977; 2:589–604.
128. Carr E, Carlson G, Wilson W, Read D. Acute hemorrhagic pulmonary infarction and necrotizing pneumonia in horses: 21 cases (1967–1993). J Am Vet Med Assoc 1997; 210:1774–1778.
129. Hoffman A, Viel L, Prescott J, et al. Association of microbiologic flora with clinical signs, endoscopic, and pulmonary cytologic findings in foals with distal respiratory tract infections. Am J Vet Res 1993; 54:1615–1622.
130. Mansmann R, Carlson G, White N. Synchronous diaphragmatic flutter in horses. J Am Vet Med Assoc 1974; 165:265–270.
131. Jackson C, Berney C, Jefcoat A, Robinson N. Environment and prednisone interactions in the treatment of recurrent airway obstruction (heaves). Equine Vet J 2000; 32:432–438.
132. Thomson J, McPherson E. Effect of environmental control on pulmonary function of horses affected with chronic obstructive pulmonary disease. Equine Vet J 1984; 16:35–38.
133. Mair T. Obstructive pulmonary disease in 18 horses at summer pasture. Vet Rec 1996; 138:89–91.
134. Lapointe J-M, Lavoie J-P, Vrins AA. Effects of triamcinolone acetonide on pulmonary function and bronchoalveolar lavage cytologic features in horses with chronic obstructive pulmonary disease. Am J Vet Res 1993; 54:1310–1316.
135. Rush B, Flaminio J, Matson C, et al. Cytologic evaluation of bronchoalveolar lavage fluid from horses with recurrent airway obstruction after aerosol and parenteral administration of beclomethasone dipropionate and dexamethasone, respectively. Am J Vet Res 1998; 59:1033–1038.
136. Rush B, Worster A, Flaminio M, et al. Alteration in adrenocortical function in horses with recurrent airway obstruction after aerosol and parenteral administration of beclomethasone dipropionate and dexamethasone, respectively. Am J Vet Res 1998; 59:1044–1047.
137. Toutain PL, Brandon RA, de Pomyers H. Dexamethasone and prednisolone in the horse: pharmacokinetics and action on the adrenal gland. Am J Vet Res 1984; 45:1750–1756.
138. Robinson N, Jackson C, Jefcoat A, et al. Efficacy of three corticosteroids for the treatment of recurrent airway obstruction (heaves). Equine Vet J 2002; 34:17–22.
139. Traub-Dargatz J, McKinnon A, Thrall M, et al. Evaluation of clinical signs of disease, bronchoalveolar and tracheal wash analysis, and arterial blood gas tensions in 13 horses with chronic obstructive pulmonary disease treated with prednisone, methyl sulfonmethane, and clenbuterol hydrochloride. Am J Vet Res 1992; 53:1908–1916.
140. Peroni D, Stanley S, Kollias-Baker C, Robinson N. Prednisone per os is likely to have limited efficacy in horses. Equine Vet J 2002; 34:283–287.
141. Derksen FJ. Chronic obstructive pulmonary disease. In: Beech J, ed. Equine respiratory disorders. Philadelphia: Lea and Febiger; 1991; 223–235.
142. Eyre P, Elmes PJ, Strickland S. Corticosteroid-potentiated vascular response of the equine digit: a possible pharmacological basis for laminitis. Am J Vet Res 1979; 40:138.
143. Lavoie J. Chronic obstructive pulmonary disease. In: Robinson N, ed. Current therapy in equine medicine. Philadelphia: WB Saunders; 1997; 431–435.
144. Madigan J, Dybdal N. Endocrine and metabolic diseases. In: Smith B, ed. Large animal internal medicine. St Louis: Mosby; 1990; 1296–1306.
145. Pearson E, Riebold T. Comparison of bronchodilators in alleviating clinical signs in horses with chronic obstructive pulmonary disease. J Am Vet Med Assoc 1989; 194:1287–1291.
146. Murphy J, McPherson E, Dixon P. Chronic obstructive pulmonary disease (COPD): Effects of bronchodilator drugs on normal and affected horses. Equine Vet J 1980; 12:10–14.
147. Ducharme N, Fubini S. Gastrointestinal complications associated with the use of atropine in horses. J Am Vet Med Assoc 1983; 182:229–231.
148. Erichsen D, Aviad A, Schultz R, Dillon G. Clinical efficacy and safety of clenbuterol HCl when administered to effect in horses with chronic obstructive pulmonary disease (COPD). Equine Vet J 1994; 26:331–336.
149. Turgut K, Sasse H. Influence of clenbuterol on mucociliary transport in horses with chronic obstructive pulmonary disease. Vet Rec 1989; 12:526–530.
150. Sleeper M, Kearns C, McKeever K. Chronic clenbuterol administration negatively alters cardiac function. Med Sci Sports Exerc 2001; 34:643–650.
151. Torneke M, Ingvast-Larsson J, Johansson J, Appelgren L. Pharmacokinetics and pharmacodynamics of terbutaline in healthy horses. Am J Vet Res 2000; 61:761–765.
152. McKiernan B, Koritz G, Scott J, et al. Plasma theophylline concentration and lung function in ponies with recurrent obstructive lung disease. Equine Vet J 1990; 22:194–197.
153. Ayres J, Pearson E, Riebold T, Chang S-F. Theophylline and dyphylline pharmacokinetics in the horse. Am J Vet Res 1985; 46:2500–2506.
154. Nuytten J, Deprez P, Picavet T, et al. Euphillin treatment of horses suffering from COPD. Vlaams Diergeneeskundig Tijdschift 1988; 57:271–277.
155. Leguillette R, Deseveaux C, Lavoie J. Effects of pentoxifylline on pulmonary function and results of cytological examination of bronchoalveolar lavage fluid in horses with recurrent airway obstruction. Am J Vet Res 2002; 63:459–463.
156. Gerber V, King M, Schneider D, Robinson N. Tracheobronchial mucus viscoelasticity during environmental challenge in horses with recurrent airway obstruction. Equine Vet J 2000; 32:411–417.
157. Gerber V, Gehr P, Straub R, et al. Microscopic investigation of mucus qualities, mucus transport velocity and ciliary beat frequency on horse tracheal epithelium. Respir Physiol 1997; 107:67–74.
158. Broadstone R, Robinson N, Gray P, et al. Effect of furosemide on ponies with recurrent airway obstruction. Pulm Pharmacol 1991; 4:203–208.

159. Deegen E. Neure methoden der behandlung chronisch hustender pferde. Prakt Tierarzt 1982; 63:55–57.
160. Bosler K. Langzeiterfolg der NaCl-hyperinfusions-therapie beim pferd mit chronisch obstruktiver bronchitis. Pferdeheilkunde 1986; 2:197–200.
161. Dolovich M. Lung dose, distribution, and clinical response to therapeutic aerosols. Aerosol Sci Technol 1993; 18:230–240.
162. Newman S. Aerosol deposition considerations in inhalation therapy. Chest 1985; 88:152S–160S.
163. Rush B, Hoskinson J, Davis E, et al. Pulmonary distribution of aerosolized technetium Tc 99m pentetate after administration of a single dose of aerosolized albuterol sulfate in horses with recurrent airway obstruction. Am J Vet Res 1999; 60:764–769.
164. Viel L, Tesarowski DB. Radioaerosol deposition in equids. In: Bakhaus R, ed. Proceedings of the 40th annual convention. Lexington; American Association of Equine Practitioners; 1994; 93–94.
165. Votion D, Ghafir Y, Munsters K, et al. Aerosol deposition in equine lungs following ultrasonic nebulisation versus jet aerosol delivery system. Equine Vet J 1997; 29:388–393.
166. Funch-Nielsen H, Roberts C, Weekes JS, et al. Evaluation of a new spacer device for delivery of drugs into the equine respiratory tract. World Equine Airway CRS Symposium; 2001; 56.
167. Geor R, Johnston G. Deposition of radiolabelled aerosols within the equine respiratory tract. Urbana, IL: Comparative Respiratory Society; 1993.
168. Kelly H. Comparison of inhaled corticosteroids. Ann Pharmacother 1998; 32:220–232.
169. Rush B, Raub E, Thomsen M, et al. Pulmonary function and adrenal gland suppression with incremental doses of aerosolized beclomethasone dipropionate in horses with recurrent airway obstruction. J Am Vet Med Assoc 2000; 217:359–364.
170. Ammann VJ, Vrins AA, Lavoie J-P. Effects of inhaled beclomethasone dipropionate on respiratory function in horses with chronic obstructive pulmonary disease (COPD). Equine Vet J 1998; 30:152–157.
171. Viel L, Celly CS, Staempfli H, Tesarowski DB. Therapeutic efficacy of inhaled fluticasone propionate in horses with chronic obstructive pulmonary disease. Proc Am Assoc Equine Pract 1999; 45:306–307.
172. Laan TTJM. Serum cortisol concentrations in response to fluticasone propionate inhalation therapy in horses. Proceedings of the World Equine Airway and VCRS Symposium, Edinburgh, UK; 2001; 25.
173. Derksen F, Olszewski M, Robinson N, et al. Aerosolized albuterol sulfate used as a bronchodilator in horses with recurrent airway obstruction. Am J Vet Res 1999; 60:689–693.
174. Derksen F, Olszewski M, Robinson N, et al. Use of a hand-held, metered-dose aerosol delivery device to administer pirbuterol acetate to horses with heaves. Equine Vet J 1996; 28:306–310.
175. Tesarowski D, Viel L, McDonnell W, Newhouse M. The rapid and effective administration of a beta2-agonist to horses with heaves using a compact inhalation device and metered-dose inhalers. Can Vet J 1994; 35:170–173.
176. Derksen FJ, Robinson NE, Olszewski MA, et al. Clinical studies with Torpex (aerosol albuterol sulfate): Duration of effect. Technical research review. Boehringer Ingelheim Vetmedica; 2002; 3–4.
177. Hendrikson S, Rush B. Efficacy of salmeterol xinafoate in horses with recurrent airway obstruction. J Am Vet Med Assoc 2001; 218:1961–1965.
178. Robinson N, Derksen F, Berney C, Goossens L. The airway response of horses with recurrent airway obstruction (heaves) to aerosol administration of ipratropium bromide. Equine Vet J 1993; 25:299–303.
179. Aviza G, Ainsworth D, Eicker S, et al. Outcome of horses diagnosed with and treated for heaves. Equine Vet Educ 2001; 3:318–320.
180. McPherson E, Lawson G, Murphy J, et al. Chronic obstructive pulmonary disease (COPD): factors influencing the occurrence. Equine Vet J 1979; 11:167–171.
181. Kirschvink N, Di Silvestro F, Sbai I, et al. The use of cardboard bedding material as part of an environmental control regime for heaves-affected horses: in vitro assessment of airborne dust and aeroallergen concentration and in vivo effects on lung function. Vet J 2002; 163:319–325.
182. Webster A, Clarke A, Madelin T, Wathes C. Air hygiene in stables 1: Effects of stable design, ventilation and management on the concentration of respirable dust. Equine Vet J 1987; 19:448–453.
183. Crichlow E, Yoshida K, Wallace K. Dust levels in a riding stable. Equine Vet J 1980; 12:185–188.
184. Vandenput S, Istasse L, Nicks B, Lekeux P. Airborne dust and aeroallergen concentrations in different sources of feed and bedding for horses. Vet Quart 1997; 19:154–158.
185. Vandenput S, Duvivier D, Votion D, et al. Environmental control to maintain stabled COPD horses in clinical remission: effects on pulmonary function. Equine Vet J 1998; 30:93–96.
186. Vandenput S, Votion D, Duvivier D, et al. Effect of a set environment control on pulmonary function and airway reactivity of COPD affected horses. Vet J 1998; 155:189–195.
187. Clarke A, Madelin T. Technique for assessing respiratory health hazards from hay and other source materials. Equine Vet J 1987; 19:442–447.
188. Derksen F, Robinson N, Scott J, Stick J. Aerosolized *Micropolyspora faeni* antigen as a cause of pulmonary dysfunction in ponies with recurrent airway obstruction (heaves). Am J Vet Res 1988; 49:933–938.
189. Pirie R, Collie D, Dixon P, McGorum B. Evaluation of nebulised hay dust suspensions (HDS) for the diagnosis and investigation of heaves. 2: Effects of inhaled HDS on control and heaves horses. Equine Vet J 2002; 34:337–342.
190. Halliwell R, McGorum B, Irving P, Dixon P. Local and systemic antibody production in horses affected with chronic obstructive pulmonary disease. Vet Immunol Immunopathol 1993; 38:201–215.
191. Eder C, Crameri R, Mayer C, et al. Allergen-specific IgE levels against crude mould and storage mite extracts and recombinant mould allergens in sera from horses affected with chronic bronchitis. Vet Immunol Immunopathol 2000; 73:241–253.
192. Seahorn T, Beadle R, McGorum B, Marley C. Quantification of antigen-specific antibody concentrations in tracheal lavage fluid of horses with summer pasture-associated obstructive pulmonary disease. Am J Vet Res 1997; 58:1408–1411.
193. Winder N, von Fellenberg R. Immunofluorescent evaluation of the lower respiratory tract of healthy horses and of horses with chronic bronchiolitis. Am J Vet Res 1986; 47:1271–1274.
194. Winder N, von Fellenberg R. Chronic small airway disease in the horse: Immunohistochemical evaluation of lungs with mild, moderate and severe lesions. Vet Rec 1988; 122:181–183.
195. McGorum B, Dixon P, Halliwell R. Evaluation of intradermal mould antigen testing in the diagnosis of equine chronic

obstructive pulmonary disease. Equine Vet J 1993; 25:273–275.
196. Madelin T, Clarke A, Mair T. Prevalence of serum precipitating antibodies in horses to fungal and thermophilic actinomycete antigens: effects of environmental challenge. Equine Vet J 1991; 23:247–252.
197. Jose-Cullineras E, Kohn C, Hillier A, et al. Intradermal testing in healthy horses and horses with chronic obstructive pulmonary disease, recurrent urticaria, or allergic dermatitis. J Am Vet Med Assoc 2001; 219:1115–1121.
198. Lavoie J, Maghni K, Desnoyers M, et al. Neutrophilic airway inflammation in horses with heaves is characterized by a Th2-type cytokine profile. Am J Respir Crit Care Med 2001; 164:1410–1413.
199. Pirie R, Dixon P, McGorum B. Evaluation of nebulised hay dust suspension (HDS) for the diagnosis and investigation of heaves. 3: Effect of fractionation of HDS. Equine Vet J 2002; 34:343–347.
200. Liu A. Endotoxin exposure in allergy and asthma: Reconciling a paradox. J Allergy Clin Immunol 2002; 109:379–392.
201. Park H, Jung K, Hwang S, et al. Neutrophil infiltration and release of IL-8 in airway mucosa from subjects with grain dust-induced occupational asthma. Clin Exp Allergy 1998; 28:724–730.
202. Louis R, Lau L, Bron A, et al. The relationship between airways inflammation and asthma severity. Am J Respir Crit Care Med 2000; 161:9–16.
203. Fairbairn S, Page C, Lees P, Cunningham F. Early neutrophil but not eosinophil or platelet recruitment to the lungs of allergic horses following antigen exposure. Clin Exp Allergy 1993; 23:821–828.
204. McGorum BC, Dixon PM, Halliwell RE. Quantification of histamine in plasma and pulmonary fluids from horses with chronic obstructive pulmonary disease, before and after 'natural (hay and straw) challenges'. Vet Immunol Immunopathol 1993; 36:223–237.
205. Gray PR, Derksen FJ, Broadstone RV, et al. Increased pulmonary production of immunoreactive 15-hydroxyeicosatetraenoic acid in an animal model of asthma. Am Rev Respir Dis 1992; 145:1092–1097.
206. Gray PR, Derksen FJ, Robinson NE, et al. The role of cyclooxygenase products in the acute airway obstruction and airway hyperreactivity of ponies with heaves. Am Rev Respir Dis 1989; 140:154–160.
207. Watson ED, Sweeney CR, Steensma KA. Arachidonate metabolites in bronchoalveolar lavage fluid from horses with and without COPD. Equine Vet J 1992; 24:379–381.
208. Franchini M, Gill U, von Fellenberg R, Bracher VD. Interleukin-8 concentration and neutrophil chemotactic activity in bronchoalveolar lavage fluid of horses with chronic obstructive pulmonary disease following exposure to hay. Am J Vet Res 2000; 61:1369–1374.
209. Fairbairn SM, Marr KA, Lees P, et al. Effects of platelet activating factor on the distribution of radiolabelled leucocytes and platelets in normal horses and asymptomatic horses with chronic obstructive pulmonary disease. Res Vet Sci 1996;61:107–113.
210. Franchini M, Gilli U, Akens MK, et al. The role of neutrophil chemotactic cytokines in the pathogenesis of equine chronic obstructive pulmonary disease (COPD). Vet Immunol Immunopathol 1998;66:53–65.
211. Raulo SM, Sorsa T, Tervahartiala T, et al. MMP-9 as a marker of inflammation in tracheal epithelial lining fluid (TELF) and in bronchoalveolar fluid (BALF) of COPD horses. Equine Vet J 2001; 33:128–136.
212. Raulo SM, Sorsa TA, Kiili MT, Maisi PS. Evaluation of collagenase activity, matrix metalloproteinase-8, and matrix metalloproteinase-13 in horses with chronic obstructive pulmonary disease. Am J Vet Res 2001; 62:1142–1148.
213. Art T, Kirschvink N, Smith N, et al. Cardiorespiratory measurements and indices of oxidative stress in exercising COPD horses. Equine Vet J Suppl 1999; 30:83–87.
214. Barnes P, Adcock I. Transcription factors and asthma. Eur Respir J 1998;12:221–234.
215. Bureau F, Bonizzi G, Kirschvink N, et al. Correlation between nuclear factor-kB activity in bronchial brushing samples and lung dysfunction in an animal model of asthma. Am J Respir Crit Care Med 2000; 161:1314–1321.
216. Bureau F, Delhalle S, Bonizzi G, et al. Mechanisms of persistent NF-kappa B activity in the bronchi of an animal model of asthma. J Immunol 2000; 165:5822–5830.
217. Robinson N, Derksen F, Olszewski M, Buechner-Maxwell V. The pathogenesis of chronic obstructive pulmonary disease of horses. Br Vet J 1996; 152:283–306.
218. Bracher V, von Fellenberg R, Winder C, et al. An investigation of the incidence of chronic obstructive pulmonary disease (COPD) in random populations of Swiss horses. Equine Vet J 1991; 23:136–141.
219. Martin BB, Jr, Beech J, Parente EJ. Cytologic examination of specimens obtained by means of tracheal washes performed before and after high-speed treadmill exercise in horses with a history of poor performance. J Am Vet Med Assoc 1999; 214:673–677.
220. McKane SA, Canfield PJ, Rose RJ. Equine bronchoalveolar lavage cytology: survey of thoroughbred racehorses in training. Aust Vet J 1993; 70:401–404.
221. Gunson DE, Sweeney CR, Soma LR. Sudden death attributable to exercise-induced pulmonary hemorrhage in racehorses: nine cases (1981–1983). J Am Vet Med Assoc 1988; 193:102–106.
222. Pascoe JR, Ferraro GL, Cannon JH, et al. Exercise-induced pulmonary hemorrhage in racing thoroughbreds: a preliminary study. Am J Vet Res 1981; 42:703–707.
223. Raphel CF, Soma LR. Exercise-induced pulmonary hemorrhage in Thoroughbreds after racing and breezing. Am J Vet Res 1982; 43:1123–1127.
224. Birks EK, Shuler KM, Soma LR, et al. EIPH: postrace endoscopic evaluation of Standardbreds and Thoroughbreds. Equine Vet J 2002; Suppl 34:375–378.
225. Mason DK, Collins EA, Watkins KL. Exercise-induced pulmonary haemorrhage in horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Publications; 1983; 57–63.
226. Lapointe JM, Vrins A, McCarvill E. A survey of exercise-induced pulmonary haemorrhage in Quebec standardbred racehorses. Equine Vet J 1994; 26:482–485.
227. Speirs VC. Pulmonary hemorrhage in Standardbred race horses. Aust Vet J 1982; 59:38–40.
228. Rohrbach BW. Exercise-induced pulmonary hemorrhage, chronic obstructive pulmonary disease, and racing performance. J Am Vet Med Assoc 1990; 196:1563–1564.
229. O'Callaghan MW, Pascoe JR, Tyler WS, Mason DK. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. I. Clinical profile of horses. Equine Vet J 1987; 19:384–388.
230. Cook WR. Epistaxis in the racehorse. Equine Vet J 1974; 6:45–58.
231. Christley RM, Hodgson DR, Rose RJ, et al. Coughing in thoroughbred racehorses: risk factors and tracheal endoscopic and cytological findings. Vet Rec 2001; 148:99–104.

232. Takahashi T, Hiraga A, Ohmura H, et al. Frequency of and risk factors for epistaxis associated with exercise-induced pulmonary hemorrhage in horses: 251,609 race starts (1992–1997). J Am Vet Med Assoc 2001; 218:1462–1464.
233. Hillidge CJ, Lane TJ, Whitlock TW. Exercise-induced pulmonary hemorrhage in the racing Appaloosa horse. J Equine Vet Sci 1986; 5:351–353.
234. Hillidge CJ, Lane TJ, Johnson E. Preliminary investigations of exercise-induced pulmonary hemorrhage in racing Quarter Horses. J Equine Vet Sci 1984; 4:21–23.
235. Pfaff G. The incidence of epistaxis in racehorses in South Africa. J South Afr Vet Assoc 1976; 47:215–218.
236. Pascoe JR, Wheat JD. Historical background, prevalence, clinical findings and diagnosis of exercise-induced pulmonary hemorrhage (EIPH) in racing horses. Proc Am Assoc Equine Pract 1980; 26:417–420.
237. Sweeney CR, Soma LR. Exercise-induced pulmonary haemorrhage in horses after different competitive exercises. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta; 1983; 51–56.
238. Pascoe JR, McCabe AE, Franti CE, Arthur RM. Efficacy of furosemide in the treatment of exercise-induced pulmonary hemorrhage in Thoroughbred racehorses. Am J Vet Res 1985; 46:2000–2003.
239. Fogarty U, Buckley T. Bronchoalveolar lavage findings in horses with exercise intolerance. Equine Vet J 1991; 23:434–437.
240. McKane S, Slocombe R. Sequential changes in bronchoalveolar cytology after autologous blood inoculation. Equine Vet J Suppl 1999; 30:126–130.
241. Meyer TS, Fedde MR, Gaughan EM, et al. Quantification of exercise-induced pulmonary haemorrhage with bronchoalveolar lavage. Equine Vet J 1998; 30:284–288.
242. Step DL, Freeman KP, Gleed RD, Hackett RP. Cytologic and endoscopic findings after intrapulmonary blood inoculations in horses. J Equine Vet Sci 1991; 11:340–345.
243. Langsetmo I, Meyer MR, Erickson HH. Relationship of pulmonary arterial pressure to pulmonary haemorrhage in exercising horses. Equine Vet J 2000; 32:379–384.
244. Kindig CA, McDonough P, Fenton G, et al. Efficacy of nasal strip and furosemide in mitigating EIPH in Thoroughbred horses. J Appl Physiol 2001; 91:1396–1400.
245. Geor RJ, Ommundson L, Fenton G, Pagan JD. Effects of an external nasal strip and frusemide on pulmonary haemorrhage in Thoroughbreds following high-intensity exercise. Equine Vet J 2001; 33:577–584.
246. Kindig CA, McDonough P, Fenton G, et al. Efficacy of nasal strip and furosemide in mitigating EIPH in Thoroughbred horses. J Appl Physiol 2001; 91:1396–1400.
247. Rossier Y, Sweeney CR, Ziemer EL. Bronchoalveolar lavage fluid cytologic findings in horses with pneumonia or pleuropneumonia. J Am Vet Med Assoc 1991; 198:1001–1004.
248. McKane SA, Rose RJ. Radiographic determination of the location of a blindly passed bronchoalveolar lavage catheter. Equine Vet Educ 1993; 5:329–332.
249. O'Callaghan MW, Pascoe JR, O'Brien TR, et al. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. VI. Radiological/pathological correlations. Equine Vet J 1987; 19:419–422.
250. O'Callaghan MW, Hornof WJ, Fisher PE, Pascoe JR. Exercise-induced pulmonary haemorrhage in the horses: results of a detailed clinical, post mortem and imaging study. VII. Ventilation/perfusion scintigraphy in horses with EIPH. Equine Vet J 1987; 19:423–427.
251. Votion DM, Roberts CA, Marlin DJ, Lekeux PM. Feasibility of scintigraphy in exercise-induced pulmonary haemorrhage detection and quantification: preliminary studies. Equine Vet J Suppl 1999; 30:137–142.
252. Couetil LL, Denicola DB. Blood gas, plasma lactate and bronchoalveolar lavage cytology analyses in racehorses with respiratory disease. Equine Vet J Suppl 1999; 30:77–82.
253. O'Callaghan MW, Pascoe JR, Tyler WS, Mason DK. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. II. Gross lung pathology. Equine Vet J 1987; 19:389–393.
254. O'Callaghan MW, Pascoe JR, Tyler WS, Mason DK. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. III. Subgross findings in lungs subjected to latex perfusions of the bronchial and pulmonary arteries. Equine Vet J 1987; 19:394–404.
255. O'Callaghan MW, Pascoe JR, Tyler WS, Mason DK. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. V. Microscopic observations. Equine Vet J 1987; 19:411–418.
256. Anonymous. International agreement on breeding and racing and appendices. 2002. International Federation of Horse Racing Authorities, France. 2002. Online: www.horseracingintfed.com, accessed 15 May 2003.
257. Gross DK, Morley PS, Hinchcliff KW, Wittum TE. Effect of furosemide on performance of Thoroughbreds racing in the United States and Canada. J Am Vet Med Assoc 1999; 215:670–675.
258. Soma LR, Birks EK, Uboh CE, et al. The effects of frusemide on racing times of Standardbred pacers. Equine Vet J 2000; 32:334–340.
259. Soma LR, Uboh CE, Nann L. Prerace venous blood acid–base values in Standardbred horses. Equine Vet J 1996; 28:390–396.
260. Sime D, Engen R, Miller-Graber P. Frequency and use of medications in horses racing in Prairie Meadows. Iowa State Univ Vet 1994; 54.
261. Sweeney CR, Soma LR, Maxson AD, et al. Effects of furosemide on the racing times of Thoroughbreds. Am J Vet Res 1990; 51:772–778.
262. Manohar M. Furosemide attenuates the exercise-induced increase in pulmonary artery wedge pressure in horses. Am J Vet Res 1993; 54:952–958.
263. Manohar M, Hutchens E, Coney E. Pulmonary haemodynamics in the exercising horse and their relationship to exercise-induced pulmonary haemorrhage. Br Vet J 1993; 149:419–428.
264. Gleed RD, Ducharme NG, Hackett RP, et al. Effects of frusemide on pulmonary capillary pressure in horses exercising on a treadmill. Equine Vet J 1999; Suppl 30: 102–106.
265. Muir WW, Sams RA, Hubbell JAE, et al. Effects of enalaprilat on cardiorespiratory, hemodynamic, and hematologic variables in exercising horses. Am J Vet Res 2001; 62:1008–1013.
266. Manohar M, Goetz TE. Pulmonary vascular pressures of strenuously exercising Thoroughbreds during intravenous infusion of nitroglycerin. Am J Vet Res 1999; 60:1436–1440.
267. Kindig CA, Erickson BK, Poole DC. Dissociation of exercise-induced pulmonary hemorrhage and pulmonary artery pressure via nitric oxide synthase inhibition. J Equine Vet Sci 2000; 20:715–721.

268. Manohar M, Goetz TE. L-NAME does not affect exercise-induced pulmonary-hypertension in thoroughbred horses. J Appl Physiol 1998; 84:1902–1908.
269. Fedde MR, Erickson HH. Increase in blood-viscosity in the sprinting horse – can it account for the high pulmonary arterial-pressure. Equine Vet J 1998; 30:329–334.
270. Weiss DJ, Geor RJ, Burger K. Effects of pentoxifylline on hemorheologic alterations induced by incremental treadmill exercise in thoroughbreds. Am J Vet Res 1996; 57:1364–1368.
271. Weiss DJ, Geor RJ, Burger K. Effects of furosemide on hemorheologic alterations induced by incremental treadmill exercise in thoroughbreds. Am J Vet Res 1996; 57:891–895.
272. Weiss DJ, Evanson OA, Geor RJ. The effects of furosemide and pentoxifylline on the flow properties of equine erythrocytes: in vitro studies. Vet Res Commun 1994; 18:373–381.
273. Manohar M, Goetz T, Rothenbaum P, Humphrey S. Intravenous pentoxifylline does not affect the exercise-induced pulmonary arterial, capillary or venous hypertension in Thoroughbred horses. J Vet Pharmacol Ther 2000; 23:317–322.
274. Hackett RP, Ducharme NG, Ainsworth DM, et al. Effects of extrathoracic airway obstruction on intrathoracic pressure and pulmonary artery pressure in exercising horses. Am J Vet Res 1999; 60:485–494.
275. Jackson JA, Ducharme NG, Hackett RP, et al. Effects of airway obstruction on transmural pulmonary artery pressure in exercising horses. Am J Vet Res 1997; 58:897–903.
276. Ducharme NG, Hackett RP, Gleed RD, et al. Pulmonary capillary pressure in horses undergoing alteration of pleural pressure by imposition of various airway resistive loads. Equine Vet J 1999; Suppl 30:27–33.
277. Holcombe SJ, Berney C, Cornelisse CJ, et al. Effect of commercially available nasal strips on airway resistance in exercising horses. Am J Vet Res 2002; 63:1101–1105.
278. Slocombe R, Covelli G, Bayly W. Respiratory mechanics of horses during stepwise treadmill exercise tests, and the effect of clenbuterol pretreatment on them. Aust Vet J 1992; 69:221–225.
279. Manohar M, Goetz TE, Rothenbaum P, Humphrey S. Clenbuterol administration does not attenuate the exercise-induced pulmonary arterial, capillary or venous hypertension in strenuously exercising Thoroughbred horses. Equine Vet J 2000; 32:546–550.
280. Sweeney CR, Soma LR, Bucan CA, Ray SG. Exercise-induced pulmonary hemorrhage in exercising Thoroughbreds: preliminary results with pre-exercise medication. Cornell Vet 1984; 74:263–268.
281. Hillidge C, Whitlock T, Lane T. Failure of inhaled disodium cromoglycate aerosol to prevent exercise-induced pulmonary hemorrhage in racing Quarter Horses. J Vet Pharmacol Ther 1987; 10:257–260.
282. Sweeney CR, Hall J, Fisher JR, et al. Efficacy of water vapor-saturated air in the treatment of exercise-induced pulmonary hemorrhage in Thoroughbred racehorses. Am J Vet Res 1988; 49:1705–1707.
283. Mason DK, Collins EA, Watkins KL. Effect of bedding on the incidence of exercise induced pulmonary haemorrhage in racehorses in Hong Kong. Vet Rec 1984; 115:268–269.
284. McKane SA, Slocombe RF. Alveolar fibrosis and changes in lung morphometry in response to intrapulmonary blood. Equine Vet J 2002; 34 (Suppl): 451–458.
285. McKeever KH, Hinchcliff KW, Kociba GJ, et al. Exercise-induced changes in clotting time and fibrinolytic activity in horses. Am J Vet Res 1990; 51:1335–1339.
286. Bayly WM, Meyers KM, Keck MT. Effects of furosemide on exercise-induced alterations in haemostasis in Thoroughbred horses exhibiting post-exercise epistaxis. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:64–70.
287. Johnstone IB, Viel L, Crane S, Whiting T. Hemostatic studies in racing standardbred horses with exercise-induced pulmonary hemorrhage. Hemostatic parameters at rest and after moderate exercise. Can J Vet Res 1991; 55:101–106.
288. Kopp K, Moore J, Byars T, Brooks P. Template bleeding time and thromboxane generation in the horse: effects of three non-steroidal anti-inflammatory drugs. Equine Vet J 1985; 17:322–324.
289. Mahony C, Rantanen NW, DeMichael JA, Kincaid B. Spontaneous echocardiographic contrast in the thoroughbred: high prevalence in racehorses and a characteristic abnormality in bleeders. Equine Vet J 1992; 24:129–133.
290. Sweeney CR, Soma LR. Exercise-induced pulmonary hemorrhage in thoroughbred horses: response to furosemide or hesperidin-citrus bioflavinoids. J Am Vet Med Assoc 1984; 185:195–197.
291. West JB, Mathieu-Costello O, Jones JH, et al. Stress failure of pulmonary capillaries in racehorses with exercise-induced pulmonary hemorrhage. J Appl Physiol 1993; 75:1097–1109.
292. Pascoe JR. Exercise-induced pulmonary hemorrhage: a unifying concept. Proc Am Assoc Equine Pract 1996; 42:220–226.
293. West JB, Mathieu-Costello O. Stress failure of pulmonary capillaries as a mechanism for exercise induced pulmonary haemorrhage in the horse. Equine Vet J 1994; 26:441–447.
294. Birks EK, Mathieu-Costello O, Fu Z, et al. Very high pressures are required to cause stress failure of pulmonary capillaries in thoroughbred racehorses. J Appl Physiol 1997; 82:1584–1592.
295. Manohar M. Pulmonary artery wedge pressure increases with high intensity exercise in the horse. Am J Vet Res 1993; 54:142–146.
296. Sinha AK, Hakim TS, Gleed RD, Dobson A. Pleural pressure changes during exercise do not affect measurement of mean pulmonary vascular pressures. Equine Vet J 1995; 18 (Suppl): 95–98.
297. Art T, Anderson L, Woakes AJ, et al. Mechanics of breathing during strenuous exercise in Thoroughbred horses. Respir Physiol 1990; 82:279–294.
298. Birks EK, Mathieu-Costello O, Fu Z, et al. Comparative aspects of the strength of pulmonary capillaries in rabbit, dog, and horse. Respir Physiol 1994; 97:235–246.
299. Schroter RC, Marlin DJ, Denny E. Exercise-induced pulmonary haemorrhage (EIPH) in horses results from locomotory impact induced trauma – a novel, unifying concept. Equine Vet J 1998;30:186–192.
300. Cook WR. Hypotheses on exercise-induced pulmonary hemorrhage in horses. J Am Vet Med Assoc 1988; 193:8–10.
301. Oikawa M. Exercise-induced haemorrhagic lesions in the dorsocaudal extremities of the caudal lobes of the lungs of young thoroughbred horses. J Comp Pathol 1999; 121:339–347.
302. Newton JR, Wood JLN. Evidence of an association between inflammatory airway disease and EIPH in young Thoroughbreds in training. Equine Vet J 2002; 34 (Suppl):417–424.
303. Weiss DJ, Smith CM. Haemorrheological alterations associated with competitive racing activity in horses:

implications for exercise-induced pulmonary haemorrhage (EIPH). Equine Vet J 1998; 30:7–12.
304. Jones JH, Cox TS, Takahashi T, et al. Heterogeneity of intrapleural pressures during exercise. Equine Vet J 2002; 34 (Suppl):391–396.
305. Robinson NE, Derksen FJ. Small airway obstruction as a cause of exercise-associated pulmonary hemorrhage. Proc Am Assoc Equine Pract 1980; 26:421–430.
306. Pascoe J, Ferraro G, Cannon J, et al. Exercise-induced pulmonary hemorrhage in racing thoroughbreds: a preliminary study. Am J Vet Res 1981; 42:703–707.
307. MacNamara B, Bauer S, Iafe J. Endoscopic evaluation of exercise-induced pulmonary hemorrhage and chronic obstructive pulmonary disease in association with poor performance in racing Standardbreds. J Am Vet Med Assoc 1990; 196:443–445.
308. Voynick BT, Sweeney CR. Exercise-induced pulmonary hemorrhage in polo and racing horses. J Am Vet Med Assoc 1986; 188:301–302.
309. Berry C, O'Brien T, Madigan J, Hager D. Thoracic radiographic features of silicosis in 19 horses. J Vet Intern Med 1991; 5:248–256.
310. Lakritz J, Wilson D, Berry C, et al. Bronchointerstitial pneumonia and respiratory distress in young horses: clinical, clinicopathologic, radiographic, and pathologic findings in 23 cases (1984–1989). J Vet Intern Med 1993; 7:277–288.
311. Donaldson MT, Beech J, Ennulat D, Hamir AN. Interstitial pneumonia and pulmonary fibrosis in a horse. Equine Vet J 1998; 30:173–175.
312. Cargile JL. Interstitial pneumonia in horses. Proceedings of the 11th American College of Veterinary Internal Medicine Forum, Lakewood, CO; 1993; 598–600.
313. Bruce E. Interstitial pneumonia in horses. Compend Cont Educ Pract Vet 1995; 17:1145–1153.
314. Berry CR, O'Brien TR, Madigan JE, Hager DA. Thoracic radiographic features of silicosis in 19 horses. J Vet Intern Med 1991; 5:248–256.
315. Schatzmann U, Straub R, Gerber H, Pauli B. Percutaneous lung biopsy in the horse. Vet Rec 1974; 94:588–590.
316. Savage CJ, Traub-Dargatz JL, Mumford EL. Survey of the large animal diplomates of the American College of Veterinary Internal Medicine regarding percutaneous lung biopsy in the horse. J Vet Intern Med 1998; 12:456–464.
317. Kelly D, Newsholme S, Baker J, Ricketts S. Diffuse alveolar damage in the horse. Equine Vet J 1995; 27:76–78.
318. Lakritz J, Wilson WD, Berry CR, et al. Bronchointerstitial pneumonia and respiratory distress in young horses: clinical, clinicopathologic, radiographic and pathological findings in 23 cases (1984–1989). J Vet Intern Med 1993; 7:277–288.
319. Schwartz LW, Knight HD, Whittig LD, et al. Silicate pneumoconiosis and pulmonary fibrosis in horses from the Monterey-Carmel peninsula. Chest 1981; 80:82–85.
320. Hinchcliff KW, Muir WW. Pharmacology of furosemide in the horse: a review. J Vet Intern Med 1991; 5:211–218.
321. Buergelt CD, Hines SA, Cantor G, et al. A retrospective study of proliferative interstitial lung disease of horses in Florida. Vet Pathol 1986; 23:750–756.
322. Breeze R, Brown C, Turk M. 3-Methylindole as a model of equine obstructive lung disease. Equine Vet J 1984; 16:108–112.
323. O'Sullivan BM. Crofton weed (*Eupatorium adenophorum*) toxicity in horses. Aust Vet J 1979; 55:19–21.
324. Kemper T, Spier S, Barratt-Boyes S, Hoffman R. Treatment of smoke inhalation in five horses. J Am Vet Med Assoc 1993; 202:91–94.
325. Winder C, Ehrensperger F, Hermann M, et al. Interstitial pneumonia in the horse: two unusual cases. Equine Vet J 1988; 20:298–301.
326. Lopez A. Respiratory system, thoracic cavity, and pleura. In: McGavin M, Carlton W, Zachary J, eds. Thompson's special veterinary pathology. St Louis: Mosby; 2001; 125–195.
327. von Fellenberg R. [Proteases and protease inhibitors of possible clinical relevance in COPD of horses]. Tierarztl Prax 1987; 15:399–407.
328. Clark CK, Lester GD, Vetro T, Rice B. Bronchoalveolar lavage in horses: effect of exercise and repeated sampling on cytology. Aust Vet J 1995; 72:249–252.
329. Sweeney C, Rossier Y, Ziemer E, Lindborg S. Effects of lung site and fluid volume on results of bronchoalveolar lavage fluid analysis in horses. Am J Vet Res 1992; 53:1376–1379.
330. Robinson NE, Derksen FJ, Berney C, Goossens L. The airway response of horses with recurrent airway obstruction (heaves) to aerosol administration of ipratropium bromide. Equine Vet J 1993; 25:299–303.

CHAPTER 30

Viral respiratory disease in athletic horses

Paul Morley

Importance of viral respiratory infections in athletic horses

Viral respiratory infections are one of the most common health problems in horses throughout the world. These infections are self-limiting and associated disease is not life-threatening, except in extreme cases. However, athletic horses generally have an increased risk of becoming infected and disease associated with these infections has greater consequences for athletes because of their intended use.

How big is the problem?

Infectious respiratory disease (IRD) is one of the most common reasons that athletic horses are removed from scheduled training and performances.[1–3] Interestingly, it has been suggested that IRD is a more frequent cause of performance disability among human athletes than all other diseases combined.[4–7] Even mild respiratory disease can affect equine athletes such that they are not able to attain peak performance. Most clinical occurrences of acute IRD in horses are primarily if not solely attributable to viral respiratory infections.[8] While bacteria and mycoplasma can be primary pathogens, bacteria may be more important in exacerbating clinical disease after a primary viral insult. Major exceptions would be disease caused by *Streptococcus equi* subsp. *equi* and *Rhodococcus equi*, although the latter is only a significant problem in foals.

The importance of respiratory disease among athletic horses is generally well recognized in the equine industries. In 1997 the United States Department of Agriculture (USDA) performed a survey to identify concerns that were of highest priority to the horse industry in the USA.[9] This needs assessment survey showed that problems in horses related to the respiratory system were the third most important health problem reported by all survey respondents (n = 2599), respiratory disease was the top health concern for respondents who used horses primarily for racing, and a majority of respondents considered respiratory disease agents, collectively (e.g. influenza virus, herpesvirus, etc.), to be their highest concern among infectious diseases.[9] A survey of 1200 equine practitioners in the USA found that veterinarians considered viral respiratory disease second only to colic in importance among medical problems of horses.[10] In addition to affecting the success of individual athletic performances, outbreaks of acute infectious respiratory disease can significantly disrupt entire athletic competitions. For example, dramatic outbreaks have been seen when novel strains of influenza virus are introduced into naïve populations (Fig. 30.1). The worldwide importance of viral IRD is further substantiated by the classification of equine influenza, equine rhinopneumonitis (herpesvirus), and equine arteritis as List B diseases for equids by the Office Internationale des Epizooties (OIE) because they are considered to significantly affect international trade of animals and animal products.

Why do equine athletes have an increased risk of viral infections?

First, equine athletes are typically young and often do not have the fully developed immunity to infectious agents that is acquired through repeated exposure to agents that commonly affect horses. Second, athletic horses are often congregated in large groups at training and performance facilities which increases the probability of introduction and exposure

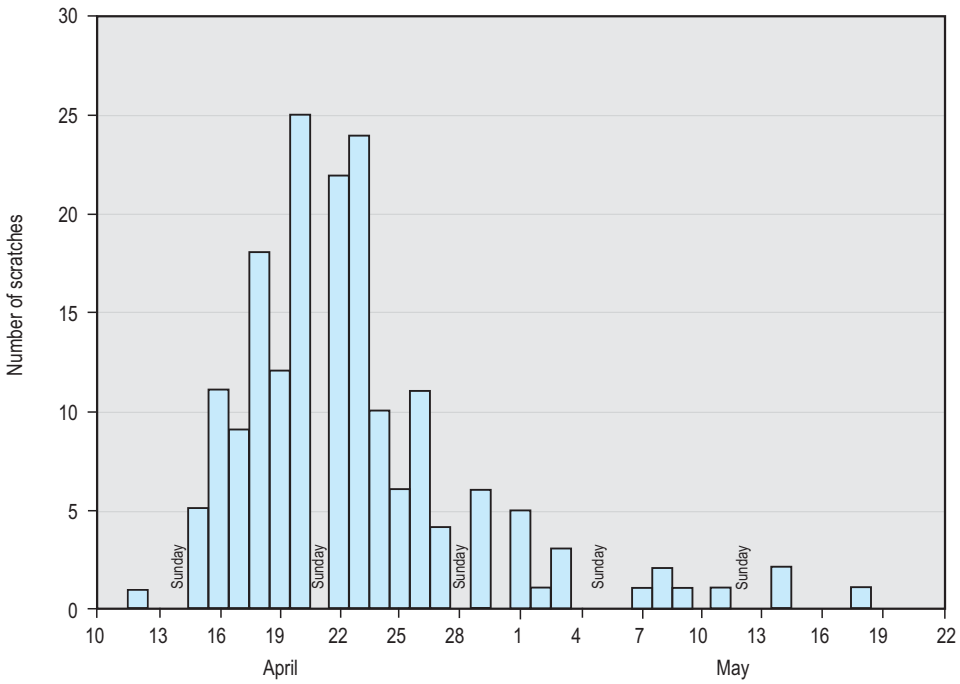


Fig. 30.1
Withdrawals from races (scratches) among 600 horses stabled at a racetrack during an influenza epidemic in April 1963. Similar epidemics were observed throughout North America following introduction of Influenza A/equine/Miami/63 (H3N8). Note the lower rate of scratches observed after the epidemic during May. Adapted from Scholtens et al[70] by permission of Oxford University Press.

to novel contagious pathogens. Third, intensive management of equine athletes at training facilities increases the probability of exposure through management practices such as the shared use of tack and other equipment, as well as through increased exposure via respiratory aerosols and contaminated surfaces. Fourth, environmental conditions encountered by equine athletes may impair non-specific clearance mechanisms through respiratory exposure to noxious chemicals (e.g. ammonia), dust, fungi, and molds. Drying and irritation of mucous membranes caused by airflow across their surfaces have been proposed as factors affecting non-specific immunity in human athletes,[11] and may also impact on the health of equine athletes. In addition, race horses are known to inhale significant quantities of small dirt particles when racing on dirt surfaces. These respiratory irritants may exacerbate non-infectious respiratory problems such as recurrent airway obstruction (heaves), which in turn are strongly believed to be a predisposing factor in viral respiratory infections in humans.[12,13] This is supported by the observation that the amount of airborne particulate matter in stabling environments significantly affected airway inflammation during an outbreak of equine herpesvirus type 1 (EHV1) infection.[14,15] Infected horses stabled in barns with adequate ventilation and lower air particulate counts had less lower airway inflammation when compared with infected horses stabled in less suitable environments.

The frequency of IRD among equine and human athletes may also be related to important effects that exercise has been shown to have on immune function. Physical stresses related to athletic activity have been repeatedly shown to be associated with transient changes of in vitro and in vivo measures of systemic and local immune function, including changes in catecholamine and cortisol release, neuropeptide hormone release, cytokine release and activity, secretion of mucosal antibody, and the functional activity of blood and pulmonary leukocytes.[16–23] These documented changes provide a basis for the 'open window' model proposed to describe cumulative effects of exercise on the immune system in humans.[16,24,25] According to this theoretical model, moderate exercise stimulates immune function during the event and for a short time after. In contrast, heavy exertion is related to an initial stimulation followed by a longer-lasting (i.e. hours) depression in cell-mediated immune function. It is proposed that during this 'open window' of immune depression athletes have an increased risk of becoming infected with a variety of pathogens. Since elite athletes often train intensively on a daily basis, the cumulative time that they are at increased risk of infection may be significant.[16,25,26] In an effort to summarize the relationship between exercise and infectious disease, it has been proposed that the apparent relationship between intensity of exercise and its predisposing effect on the risk of upper respiratory tract infections in humans fits a J-shaped curve.[16,25] This model suggests that the risk of IRD in athletes is attenuated by moderate physical activity, but is exacerbated by chronic, intensive athletic activity. While similar research in horses is not as comprehensive, the limited work that is available suggests that similar effects can be found in horses.[27–37]

This relationship between exercise and immune function is obviously not simple, and is probably modulated by several other factors such as likelihood of exposure to novel pathogens, lack of adequate rest, mental stress, transport, inappropriate nutrition or weight loss, and concurrent infectious or non-infectious disease. This is probably one of the reasons that studies directly evaluating the relationship between exercise and the occurrence of infectious disease in humans have met with equivocal results, even though the effects on various markers of immune function have been

repeatedly and convincingly demonstrated.[38] Unfortunately, almost no information is available directly examining the effects of athletic activity on the risk of IRD occurrences in horses.

How common is infectious respiratory disease in horses?

While IRD is very common among all horses there are few comprehensive estimates of the frequency of disease. There are two recent published estimates of IRD incidence in equine athletes that were obtained through prospective monitoring of race-horse populations.[2,39] A study performed at a single Canadian racetrack where investigators monitored disease occurrence during two race seasons estimated that the incidence of undifferentiated IRD was about 49 IRD cases per 1000 horse-months.[39] A prospective study of a cohort of Thoroughbred horses in Australia estimated the incidence of reported coughing and nasal discharge (infectious or non-infectious) to be approximately 1.8 cases per 1000 horse-months.[2] It is not clear if the difference in observers explains some of the difference between these estimates (reported by research investigators versus owner reported), or if the intensive nature of horse stabling at North American racetracks compared with more extensive management of race horses elsewhere is partially responsible for differences between these two estimates. The absence of influenza virus as a disease agent in Australia could also have affected these estimates. The largest population-based study estimating the frequency of undifferentiated IRD occurrence among horses was conducted by the USDA as part of the National Animal Health Monitoring System (NAHMS) Equine '98 study.[40] While the population for this study of owner-reported disease specifically excluded horses stabled at racetracks, it did include race horses that were stabled at other facilities. However, it should be noted that these data include respiratory disease occurrences from horses of all ages, including those < 1 year old. An estimated 1.5% (SE = 0.2) of horses per quarter developed IRD during this study, and the rate of reported IRD among race horses housed off-track was nearly three times greater than the average for all horses (4.3% of horses per quarter, SE = 1.9). The occurrence of IRD was reported to vary by season, and disease incidence was greatest in the spring (March through May, 2.6% of horses, SE = 0.6), and least common during the winter (December through February, 0.8% of horses, SE = 0.2). In a smaller, but similar longitudinal study, data regarding the occurrence of disease was collected from randomly selected horse operations in Michigan, and the estimated incidence of undifferentiated respiratory disease was 33 cases per 1000 horse-years.[41]

Recognizing infectious respiratory disease

Clinical signs

Horses with IRD generally develop similar clinical signs regardless of which primary or secondary agents are causing clinical disease.[8] Disease is most frequently typified by the occurrence of mucopurulent nasal discharge and sometimes coughing. In a 3-year study of respiratory disease at a Canadian racetrack, regardless of etiology, 80–95% of

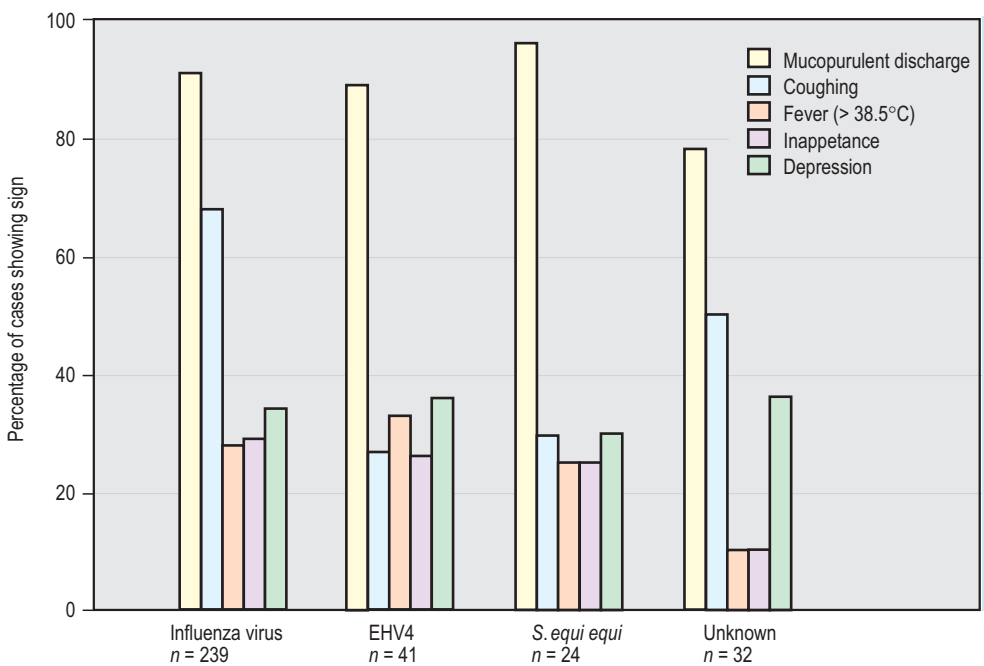


Fig. 30.2
Clinical signs, by etiology, in race horses diagnosed with IRD during a 3-year study in Canada.

affected horses developed mucopurulent nasal discharge, while the occurrence of coughing was less common and more variable (30–75% coughed depending upon the etiology; Fig. 30.2).[8] Increased serous nasal discharge may be noted prior to becoming more mucoid. Paroxysmal coughing in a majority of affected animals is suggestive of influenza virus infection, but this is not always predominant during influenza outbreaks, especially if clinical disease is mild. Fever (rectal temperature > 38.5°C or 101.5°F) is less commonly noted in affected animals (10–30%).[8] Abscessation and dramatic enlargement of submandibular lymph nodes can sometimes allow differentiation of animals infected with *Streptococcus equi* subsp. *equi*, but not all infected animals develop this pathognomonic sign.[8] Many horses infected with viral respiratory agents remain asymptomatic, especially if they are older and are more immune. Others only show vague signs such as lethargy, decreased appetite, and suboptimal performance. Evaluation of horses with mild signs and suboptimal performance may reveal evidence of lower respiratory tract infections (visible airway inflammation, inflammatory cytology, recovery of bacterial agents such as *Streptococcus zooepidemicus* subsp. *zooepidemicus*). It is not clear if viral agents play a major role in less acute lower respiratory disease. However, seroconversion to equine herpesvirus was found to be associated with occurrences of less severe lower airway inflammatory disease, in addition to the isolation of *S. equi* subsp. *zooepidemicus* and *S. pneumoniae*.[42]

While most acute viral respiratory infections have been thought to primarily or solely affect the upper respiratory tract, recent investigations suggest that the lower respiratory tract can also be significantly affected during acute viral respiratory infections.[43] Ultrasound examinations showed that horses either experimentally and naturally infected with influenza virus can develop substantial areas of pulmonary consolidation and peripheral (pleural and subpleural) irregularities.[43] However, it is not clear if these lesions are principally caused by viral damage, or if this is a result of viral–bacterial co-infection. The bacterial flora of the upper respiratory tract change dramatically after viral infections, and this is principally characterized by proliferation of beta-hemolytic streptococci (Fig. 30.3; PS Morley, KW Hinchcliff, RD Slemons, DK Gross, unpublished data).[44] However, it is not clear whether this change is simply a result of viral mucosal damage and solely coincidental with clinical disease, or whether this change contributes significantly to clinical disease in horses with IRD. Pneumonia is a well-recognized sequela to severe viral respiratory infections in humans, and has also been reported after introduction of novel influenza viruses to naïve equine populations.[28,45–48] However, this is an infrequently recognized complication of most viral respiratory infections in horses. Interestingly, the significant pulmonary consolidation that was seen after severe experimental influenza virus infections resolved uneventfully without any treatment, even in horses that continued to exercise following challenge.[43] There are few published results from objective investigations of clinical parameters in horses with viral IRD. Horses infected with influenza virus have been shown to have increased resting respiratory rates and heart rates that coincided with the occurrence of fever.[43] Pulmonary auscultation of horses experimentally and naturally infected with influenza virus showed that they often develop abnormal lung sounds, which was most frequently characterized as wheezing (DK Gross, PS Morley, KW Hinchcliff, RD Slemons, unpublished data).[43,49]

Other systemic disease signs are sometimes reported in association with viral respiratory infections. These signs are perhaps most commonly recognized in association with EHV1 infection; abortion and neurologic disease are well recognized in association with EHV1 infections. While essentially all EHV1 infections are thought to originate in the respiratory tract, signs of respiratory disease are not always evident before abortion or the onset of neurologic disease. Although equine arteritis virus is considered an infrequent cause of respiratory disease, it has also been associated with edema of the head, legs, prepuce and abdomen, and abortion. Other systemic signs including myocarditis, rhabdomyolysis, and purpura have been reported as possible sequelae of

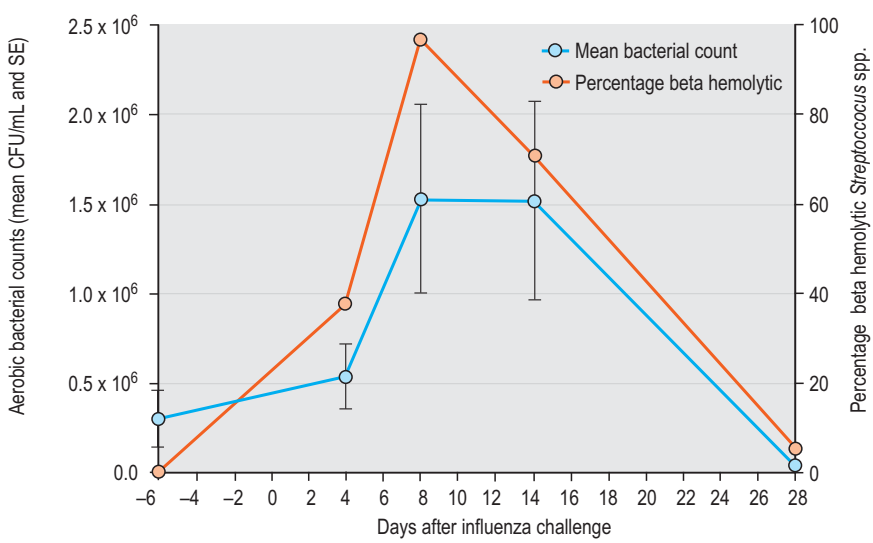


Fig. 30.3
Bacteria recovered from aerobic culture of transtracheal wash fluid following influenza challenge in naïve horses.

influenza virus infections. While it is sometimes assumed that influenza virus is a direct cause of myocarditis in horses, there is no published documentation of influenza virus infections affecting the cardiac tissues in horses. This is consistent with the fact that influenza virus is strongly epitheliotropic and that viremia is not a recognized feature of influenza virus infections.[50] Although myocarditis has been recognized in humans in association with viral infections, this condition is more likely to be identified in association with Parvo B19, enteroviruses, adenoviruses, or cytomegalovirus, and is very rarely found in association with influenza virus infections.[51] It seems likely that myocardial damage or purpura found in association with IRD would result from disseminated streptococcal infection in horses rather than viral respiratory infections.

Laboratory diagnosis

Viral IRD is often diagnosed solely upon clinical evaluation and history. However, clinical signs associated with one virus cannot be used to reliably distinguish IRD caused by other pathogens. This is important because establishing an etiologic diagnosis can be very important for targeting disease prevention efforts early in some disease outbreaks. Viral agents have been clearly shown to vary in their clinical importance as well as in their infectious and contagious nature. However, efforts to control IRD in horses can be hampered because it can be difficult to quickly establish an etiologic diagnosis for IRD.

Serology

Viral infection is most often confirmed in horses using serology, which may be the most sensitive method available. However, even when isolation and epidemiologic data point to a single etiology for outbreaks of respiratory disease, serologic investigations found that only 72% of horses with disease thought to be caused by influenza virus infection seroconverted to this virus during epidemics, and only 36% of horses with disease thought to be caused by EHV4 seroconverted to herpesvirus.[8,39] By far the most commonly recognized viral agents associated with respiratory disease in horses are influenza and EHV4. However, diagnostic laboratories do not routinely test for other types of viral infections. In addition, regardless of the etiology, most serologic tests require evaluation of multiple blood samples; the first must be obtained soon after infection and then at least 2 or more weeks later. It may not be logistically possible to obtain samples at these times or it may not be practically relevant or important to veterinarians or owners.

Virus isolation

Virus isolation is a very specific method for diagnosis of viral infection, but culture techniques need a week or more for completion and require specialized laboratory equipment and skills. Early identification and sampling of affected horses is critical for virus isolation as horses shed viruses for only a short period after infection. Isolation techniques have also been found to be quite insensitive as a diagnostic test during several field investigations.[8,39,52] Because it can take weeks to obtain results, data from serology or virus isolation is often not very useful for enacting measures to control respiratory disease. As such, it would be useful to have simple tests available for rapid diagnoses of virus infections at the onset of epidemics so that control measures could be instituted.

Rapid diagnostic tests

In recent years rapid detection assays have been developed in research laboratories for identification of several viral agents (e.g. antigen capture ELISA, PCR), but most of these tests are not widely available for use in disease prevention efforts. Rapid antigen detection kits for influenza virus are, however, commercially available throughout the world. While it would be useful to have rapid tests available for other equine respiratory pathogens, influenza virus probably causes a majority of IRD cases among athletic horse populations (where it is present in the world; Fig. 30.4), and it is one of the most contagious pathogens, which increases the importance of early intervention efforts. Most of these rapid influenza detection assays are based upon using monoclonal or polyclonal antibodies to detect highly conserved viral antigens. Most commercial assays can be completed in about 15–30 minutes and several have been shown to be useful for detection of influenza virus in horses.[53–56] Because they have been standardized and are sold in kits, they are more useful for a broad variety of diagnostic applications than are isolation techniques. Although these tests are rapid and extremely useful, they have limitations. Optimal timing of sampling is important for antigen detection assays just as it is for virus isolation. Evaluation of nasal secretions collected from horses naturally infected with influenza virus suggests that only about one-third of clinically affected horses would be positive using the Directigen assay (Becton Dickinson Microbiology Systems, Cockeysville, Maryland), which has been the most

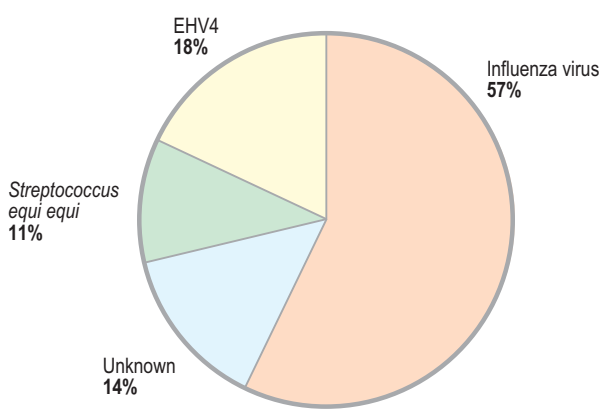


Fig. 30.4
Etiology of IRD identified in a 2-year longitudinal study at a Thoroughbred racetrack in Canada (n = 277).

widely used assay in horses.[53] Other rapid influenza tests may be more sensitive, but they may also be less specific, which can be very important when these tests are used as part of stringent disease control programs.[55,56] It is important to note that more sensitive influenza detection assays have been shown to detect viral antigen in horses recently vaccinated with modified-live intranasal products, as well as from non-vaccinated horses that were in contact with vaccinated horses.[56] This may be particularly important to consider if both vaccination and rapid detection assays are being used in disease prevention efforts during outbreaks.

Despite intensive investigative efforts, veterinarians frequently diagnose clinical IRD respiratory disease without identifying a primary etiologic agent. Potential pathogens were not identified from about 25% of IRD outbreaks investigated in England over a 6-year period.[57] Investigators in Kentucky were unable to determine the etiology of 34% (14/41) of IRD outbreaks investigated over a 5-year period.[58] Among 168 respiratory disease occurrences investigated during 1979, pathogens were identified for 44%.[59] Investigators in Canada were not able to identify an etiology for 14% (32/277) of IRD cases identified during a 2-year longitudinal study of respiratory disease among race horses (Fig. 30.4).[60] The lack of etiologic diagnosis for some IRD cases observed in these investigations is at least partially attributable to concentrating diagnostic efforts on identifying infection with agents that most frequently cause disease. It is likely that more comprehensive diagnostic efforts would identify agents in affected animals that tend to cause either less dramatic outbreaks or sporadic rather than epidemic disease (e.g. equine herpesvirus type 2 or equine rhinitis virus).

Ancillary diagnostic procedures

Although rarely utilized in most horses with viral IRD, information obtained from radiography, ultrasonography, and endoscopy may be useful for evaluating the extent and nature of guttural pouch and lower respiratory tract involvement. However, there is little published literature regarding findings of these ancillary diagnostics when applied in horses infected with various viral respiratory agents. Horses have been shown to develop marked consolidation after experimental infection with influenza virus which resolved without treatment or complication.[43] Similar findings have also been observed by these investigators in naturally infected horses. Endoscopic examination of these experimentally infected horses showed mild erythema and inflammation of the pharynx and airways, with increased amounts of mucoid respiratory secretions. Transtracheal wash fluid collected from horses infected with influenza virus was found to have increased cellularity and marked neutrophilia when compared with pre-infection values.[43] These changes were most severe for a week after infection, but changes could be detected for much longer. Intracellular bacteria were noted in about 25% of horses for up to 14 days after infection. Hemotology may also provide useful information about the general condition of horses, and horses infected with influenza virus were shown to have mild changes in white blood cell (WBC) counts and fibrinogen. However, these changes were not marked or useful in characterizing the severity of pulmonary disease.[43] Serum creatinine kinase values were not markedly affected by influenza infections. While these changes may have been useful in characterizing the general health status of horses, they were non-specific and generally did not help in establishing specific etiology.

Treatment and prognosis for viral respiratory disease in horses

Almost all viral respiratory infections are self-limiting and the primary therapeutic aim is to provide supportive care. Care should be taken to ensure that affected horses have access to clean water and adequate quantities of palatable feed as infected horses have been shown to lose weight and body condition.[43] Providing stabling in areas with minimal dust and ammonia exposure tends to lessen airway irritation and decrease the likelihood of secondary bronchitis and pharyngitis which can limit athletic performance.

Rest

It is often recommended that athletic horses with typical IRD be rested for an extended period after illness, sometimes for several weeks. This is intended to reduce the risk of serious complication such as pneumonia, pleuritis, and exercise-limiting reactive airway disease. However, there are no published reports documenting the efficacy of this practice. One investigation specifically investigated whether moderate exercise exacerbated clinical disease in horses experimentally infected with influenza virus.[43] This study found that all of the horses developed pneumonia following infection and that there was an exacerbated loss of body condition and mild differences in resting heart and respiratory rates among exercised horses. However, all of the horses fully recovered without treatment according to parameters investigated, regardless of whether they were rested. It should be noted, however, that this study evaluated a small number of horses and did not specifically evaluate performance parameters that might be important for equine athletes.

Antibacterial and antiviral agents

Horses with uncomplicated viral respiratory infections will probably recover without drug therapy; use of anti-inflammatory drugs and other non-specific treatments may reduce fever and make affected animals more comfortable, but it is not clear whether they alter the course of disease. Severely affected horses may benefit from antimicrobial therapy as the bacterial flora of the respiratory tract changes dramatically during viral infections (Fig. 30.3; PS Morley,

KW Hinchcliff, RD Slemons, DK Gross, unpublished data).[8] Bacteria can be recovered from the lower airways of horses that exhibit signs of primary viral IRD,[42,61,62] but it should be noted that there are no published studies evaluating the ability of antimicrobial (antibacterial) drugs to alter the course of IRD in horses with primary viral infections. Even horses with documented pulmonary consolidation and pneumonia secondary to experimental influenza infections were shown to recover uneventfully without the use of antimicrobial drugs.[43] Most horses affected by viral IRD show marked clinical improvement within a week of the onset of disease. Ongoing respiratory disease may reflect complications related to more severe pulmonary involvement, and these horses should be evaluated using ancillary diagnostics including pulmonary ultrasound and cytology and culture of transtracheal wash fluids.

Specific antiviral therapies for equine influenza virus and equine herpesvirus have been evaluated in equine and mouse models. However, none are licensed for this use in horses. In addition, considering the self-limiting nature of viral IRD, cost alone would preclude their use in most horses, regardless of safety or efficacy. In addition, use of antiviral drugs in humans is known to select for resistant strains. Amantadine and rimantadine have been used in humans infected with influenza virus, and both have demonstrated in vitro activity against equine influenza virus.[49,63] Oral administration of rimantadine has been evaluated in a small number of horses and administration of 30 mg/kg, by mouth, every 12 h for 4 days was associated with amelioration of clinical signs.[49] However, given the self-limiting nature of untreated influenza virus infections in horses this therapy is of questionable value. Absorption of amantadine administered orally is inconsistent and effective plasma concentrations cannot be reliably attained.[63] In addition, while intravenous administration yielded more reproducible plasma concentrations, horses have a relatively small therapeutic margin and treatment can result in seizures.[63] Use of this drug is therefore not recommended. There are a variety of reports regarding evaluation of antiviral compounds against equine herpesvirus in in vitro and mouse models, but only one published report of use in horses.[64] Respiratory disease associated with equine herpesviruses is generally mild and self-limiting, but use of these drugs in horses with other clinical disease syndromes (e.g. neurologic disease) or valuable pregnant mares may be warranted. However, caution is required as there are no reports documenting the efficacy and safety of these drugs in naturally infected horses.

Prevention of viral respiratory disease in horses

The basic features of infectious disease control programs for horse populations are similar, regardless of the type of disease or the agent that is being targeted. Specific practices employed need to be tailored to the population of horses, the facilities involved, and the diseases of greatest concern.[65,66] Consider the following basic requirements and features for effective disease prevention programs:

- Understand the mode of transmission and important biological aspects for infectious diseases of interest.
- Identify management or host factors that facilitate transmission (considering the previous item in this outline).
- Categorize animals according to risk of having or acquiring the disease of interest or infecting others. Prioritize prevention and control efforts according to those risk categories.
  - Appropriate categorization may be accomplished based upon known risk factors or history (e.g. age, history of travel, vaccination status, etc.).
  - This categorization may be facilitated by use of diagnostic procedures when appropriate (e.g. serology to help in characterizing immunity to an agent).
  - Grouping horses according to these risk categories will facilitate management and decrease the risk of transmission to animals in other risk categories. However, it is possible to manage individual horses appropriately according to their disease risk category assuming that adequate rigor is employed.
  - Prepare contingency plans for changes in disease risk when IRD is detected in the population, e.g. the need to move horses to facilitate management, or to restrict movement and access to control disease transmission.
- Monitor for evidence of disease in the population. As the adage goes, 'you cannot manage what is not measured.' Viral respiratory agents can be extremely contagious, and large portions of susceptible populations can be affected when they are introduced. Early intervention can decrease the impact of these outbreaks, but this requires active monitoring of the population and swift action when disease is detected. Employment of rapid diagnostic tests to assist in identifying viral etiologic agents is useful in providing timely, measured responses that are appropriate for the degree of contagiousness of the different agents and the significance of associated disease.
- Employ prophylactic measures that have a reasonable expectation of efficacy and are appropriate for the degree of risk aversion and the budget of the facility (e.g. vaccination, hygiene practices such as hand washing, barrier nursing precautions, foot baths, etc.).
  - Ordering available prophylactic measures based upon cost and degree of efficacy will assist in determining which should be applied first, and which should only be considered if the degree of risk aversion is high.
  - These practices vary depending upon the risk category of the animals.
  - Decisions to employ prophylactic measures often must be made far in advance of identifying IRD if they are to be of maximal benefit. For example, appropriate immunological priming is critical for vaccination to be of maximal benefit. This often requires a series of vaccinations given over several weeks.

  - Avoid wasting time, money, and effort employing prophylactic measures that do not have reasonable expectation of efficacy. More treatments are not necessarily better! Try to only use vaccines that have been adequately evaluated for efficacy. Employing non-efficacious treatments also creates a false sense of security for owners and managers, as well as increasing the likelihood that they will be dissatisfied with previous veterinary advice.
- Do not forget or underestimate the importance of optimizing the overall health and wellbeing of horses when designing disease prevention programs. Minimize stress when possible. Optimize nutrition, and provide clean, fresh water ad libitum. Maximize cleanliness, hygiene, air quality, and comfort in stabling environments. Avoid treatments and management practices that unnecessarily increase the risk of infection.

Preventing transmission

The most important aspect of preventing IRD is to minimize the likelihood of adequate direct or indirect contact that allows exposure to agents that is adequate to establish infection. As testament to this statement, it is possible to identify large, isolated horse populations in the USA and Canada that are naïve to influenza virus despite the fact that this agent is frequently recognized and considered endemic in those countries. These populations have minimal protective immunity and are highly susceptible to disease, which is a major reason that they are frequently used for experimental research on IRD.[43,67,68] These populations remain disease free because of their closed nature and the minimal likelihood of exposure to influenza virus. Given the ubiquitous nature of some IRD agents (e.g. EHV1 and EHV4), it is harder to prevent all exposure, but frequent high-risk contact increases the risk of introducing highly contagious and highly pathogenic strains. Studies of IRD in race horses have shown that horses with higher concentrations of serum antibody to influenza virus have decreased risk of disease during EHV4 epidemics, and horses with higher EVH4 concentrations have lower risk of disease during influenza epidemics.[8] This suggests that horses with increased risk of exposure to one respiratory virus are likely to have an increased risk of exposure to all respiratory viruses. This emphasizes the importance of non-specific control measures such as stringent biosecurity measures.

Indirect transmission

Direct contact among horses is obviously important for transmission of infectious respiratory agents, but the importance of indirect contact must not be overlooked. Viral IRD agents vary in their contagiousness via respiratory aerosols, and this mode of transmission seems most important in propagation of influenza epidemics. In addition, indirect transmission via contaminated surfaces and fomites can play a critical role in introduction of respiratory agents.[69–71] In many instances outbreaks in susceptible populations occur as a result of indirect transmission, and epidemics can certainly be exacerbated by this route. During a longitudinal study of respiratory disease it was noted that grooms would often wipe the face and body of affected horses with a rag, and then repeat the same procedure on unaffected horses using the same grooming tool.[39] Tattooing of young horses using the same instrument was thought to be associated with spread of infection in another outbreak.[39] Contaminated trailers, tack, waterers, and even clothing of handlers have also been implicated in introduction of respiratory agents.

Barrier nursing precautions and personal hygiene

An important concept related to care of patients with contagious diseases is the use of barrier nursing precautions. Barrier nursing precautions (e.g. gloves and water impervious gowns) can be used whenever working with high-risk patients to prevent strike-through and to minimize the potential for cross-contamination between patients. Barrier gowns are assigned for use with specific animals so that clothing most likely to be contaminated essentially stays with the patient. Disposable gloves, and separate coveralls or inexpensive disposable plastic barrier gowns (PolyWear gowns, #GEB-4250; PolyConversions Inc., Rantoul, IL 61866) could be assigned for use with specific animals. Rubber boots and disinfectant footbaths can also be used to reduce the risk of footwear serving to traffic infectious agents between stalls. In addition, limiting the number of people contacting high-risk patients and assigning specific people to care for animals in different risk categories will also reduce the risk of transmission.

Personal hygiene and cleanliness is indisputably an important cornerstone of infection control. All personnel contacting animals should be required to wear clean, appropriate attire at all times. Contaminated hands are perhaps the most frequent route of indirect nosocomial transmission in all species.[72] Frequent hand washing should be required particularly before and after handling affected animals. Alcohol-based hand sanitizing gels are available for use when it is not possible to wash hands. These hand sanitizing gels have been shown to be equal in efficacy to full surgical scrub when properly applied, but gros contamination must be removed by hand washing. I often illustrate the common-sense importance of hand hygiene as a disease control measure with students by asking them to look closely at their hands and to consider whether they would appreciate a physician with similar cleanliness performing an examination or an invasive procedure on them.

Cleaning and disinfection

Effective cleaning and disinfection are critical for breaking transmission cycles for viral agents in horse populations. Stalls should be cleaned and thoroughly disinfected between all horses, especially when they have been used to house high-risk animals. Particular attention should be paid to

disinfecting feeders, waterers, and surfaces frequently contacted by hands. Cleaning tools should not be used for animals in different risk categories unless they have been appropriately cleaned and disinfected. Bedding and feces should be removed from stalls between horses to facilitate more thorough cleaning. Dumpsters, wheelbarrows, and cleaning tools should be visibly marked for easy identification, and different sets should be assigned for use with a specific risk group. Several reviews are available regarding disinfection recommendations for livestock facilities.[73–75] Applying copious amounts of disinfectant to dirty surfaces is not effective for decontamination. Disinfectants are quickly inactivated in the presence of even small amounts of dirt and organic debris and can only be truly relied upon when applied to clean surfaces. Physical disruption is generally required to adequately remove gross contamination and surface films to ensure adequate disinfection. High pressure washing can be an efficient method for cleaning large areas but it is also possible to further disseminate surface contaminants as they may be aerosolized in the cleaning process. Some disinfectants such as phenolics are more effective in the presence of organic material, but they are also more likely to cause irritation with skin contact in horses or personnel. Bleach, chlorhexidine, and quaternary ammonium-based products are less irritating, but are easily inactivated. Recently, aerosolizing of a peroxygen compound (cold fogging) has been described as a means of inactivating airborne viruses as opposed to relying upon surface disinfection.[76] Cold fogging can also be used for dispersal of disinfectants in large buildings. However, this should only be performed with appropriate personal protection equipment for personnel and also should only be used with products that are less irritating and toxic for humans and animals.

Housing and facility design

Design of animal facilities is a critical consideration for optimal performance of disease prevention programs. Stalls and buildings should be constructed to minimize the potential for direct and indirect contact between horses. In addition, it is extremely useful to have areas that can be separated to quarantine newly introduced animals, as well as provide separation between horses in different risk categories. Care should be given to ensure that animals can receive adequate care in these different areas, preferably without trafficking animals or equipment through the environment of horses in different risk categories. At a minimum consideration should be given to separating high-risk animals from other animals with an empty stall. Cleanable surfaces should be maintained throughout practice environments wherever possible. Concrete floors are preferable to dirt, particularly for housing animals shedding contagious pathogens, as it is impossible to disinfect the latter completely. Rubber stall mats are usually quite porous, and it is very difficult to maintain effective seals at edges. This has been shown to be important in outbreaks documented in several veterinary teaching hospitals. Sealing or painting exposed wood and other porous surfaces greatly improves cleanability. However, it is important to consider quality of products and maintenance of painted surfaces when selecting sealants, as chipped and peeling paint provide a niche for bacterial contamination that is difficult to clean. Attention must also be paid to controlling wildlife (e.g. mice and birds) and insect vectors, although these are usually not considered important as a means of transmitting viral respiratory disease among horses.

Management of disease control efforts

Perhaps one of the greatest obstacles to implementing a comprehensive infection control program for all horses at large facilities is obtaining cooperation from all of the owners, managers, and veterinarians. In many training or performance facilities, athletic horses are congregated in large groups with different people responsible for care of each different group. Generally, producers only want to pay for care of their own animals and thus procedures and costs for a comprehensive control program would need to be agreed upon and shared. Even if most owners and managers wish to employ such a program, like a chain with a single weak link, it only takes one hold-out employing less optimal biosecurity practices to allow introduction of a highly contagious agent, thus placing all horses at the facility at risk. In these situations it is useful to develop a cooperative agreement among all users of a facility, and empower a single individual to direct or oversee disease control efforts. This person could also oversee surveillance efforts so that there is uniform rigor in detection and management of sick horses. This would also facilitate prompt intervention which may help decrease the severity of outbreaks when they occur. This proactive approach has been very useful for control of infectious diseases of all types among horses hospitalized at Colorado State University.

Vaccination

Vaccines can play an important role in decreasing susceptibility to infectious agents, but their use should not supersede other control efforts. The efficacy of specific influenza vaccines has been well demonstrated,[27,67,77,78] but other vaccines have limited efficacy[79,80] or published information from properly designed efficacy studies is not available. Data regarding protection provided by herpesvirus vaccines are even more equivocal.[8,80–82] Equine arteritis virus is the only other respiratory virus for which there are commercial vaccines, but their use can be restricted because of importation restrictions on seropositive stallions. Development of efficacious vaccines for respiratory viruses is complicated by the apparent short duration of immunity that follows even natural exposure, and the genetic variability and rapid genetic mutation in some viruses. While most manufacturers recommend annual boosters on vaccine labels, many equine experts recommend vaccination at much shorter intervals (e.g. every 3 months or less).[47] A vaccine that must be boosted every 3 months or more frequently is obviously performing suboptimally; managers and veterinarians should view this as strong evidence of the imperfect protection provided by some

commercial vaccines. One of the challenges that manufacturers of equine vaccines have faced is the strong aversion among owners and managers for any overtly detectable local or systemic response to vaccination. The primary concern should be whether vaccines can be used safely to evoke a protective immune response, i.e., the risk of acceptable local or systemic reaction is worth the benefit of protective immunity. Unfortunately, many managers would prefer to pay for and employ ineffective vaccines at frequent intervals rather than have any observable response to vaccination. Veterinarians have been known to be fired when vaccinations have resulted in local swelling at injection sites. This would seem to be an extremely short-sighted and inadvisable approach to selection of vaccines. Consider that vaccines are commonly used for children when they are known to cause local (swelling, pain, induration) as well as systemic responses (fever, malaise, inappetence) as long as use provides the benefit of protective immunity.

Etiology of viral respiratory disease in horses

The most important viral agents associated with respiratory disease in athletic horses are influenza virus, EHV4, EHV1, and equine arteritis virus (EAV). Influenza virus and EHV4 are the viral agents most commonly identified in association with respiratory disease (Fig. 30.4). Herpesvirus type 1 is important because of its ubiquitous nature as well as the significance of non-respiratory clinical disease that is less commonly seen in association with infection (neurologic disease and abortion). Disease associated with EAV is much less common than infection, and this agent is more important because of associated reproductive losses. Other viral agents have been isolated from horses with IRD including equine adenovirus, equine rhinitis virus, and others. While infection with these agents may be associated with the occurrence of clinical disease, particularly sporadic cases, there is very little controlled evidence documenting the significance of these agents in relation to other more common agents.

Influenza virus

Characteristics

Influenza virus is a pleomorphic orthomyxovirus with a segmented double-stranded RNA genome. The segmented RNA genome predisposes this virus to genetic reassortment and mutation, which promotes rapid viral evolution. There are three types of influenza virus (types A, B, and C) that are differentiated by their highly conserved internal proteins (matrix protein and nucleoprotein); horses are only infected by some type A influenza viruses. The more variable surface glycoproteins, hemaglutinin and neuraminidase, contain the major antigenic determinants and are used to characterize subtypes of influenza virus (e.g. H3N8). RNA viruses are more prone to genetic variation, which probably influences important variability identified in antigenically dominant surface epitopes. Three distinct subtypes of influenza virus have been isolated from horses since 1956. These are represented by the following prototype strains: influenza A/equine/Prague/56 (H7N7), which is sometimes referred to as A1 equine influenza, influenza A/equine/Miami/63 (H3N8), which is sometimes referred to as A2 equine influenza, and influenza A/equine/Jilin/89 (H3N8). Only strains that evolved from the Miami/63 isolate are currently circulating in horse populations, but this virus has evolved into two genetically and antigenically distinguishable strains:[83–85] a so-called 'Eurasian' lineage, and an 'American' lineage. The 'American' lineage viruses can be further differentiated into three evolutionary strains.[84] Contrary to geospecific strain names, 'American' lineage viruses are commonly isolated from horses in Europe and Asia, and a 'Eurasian' lineage virus was isolated from horses in Canada in 1991.[84] Tracking antigenic variation among strains of influenza virus is important because natural exposure and vaccination tend to promote strain-specific immunity. For example, while serum antibody concentrations tend to correlate well with immunity, antibody concentrations have been shown to be more strongly correlated with protection when animals were challenged with influenza virus from a homologous lineage than when they were challenged with virus from a heterologous lineage.[86]

Although some investigators have hypothesized that strains of H7N7 influenza may still circulate and that it is important to continue inclusion in vaccines, this strain of virus appears to no longer circulate as the last two reported isolations of this virus subtype occurred in Malaysia in 1977[87] and in India in 1987.[88] In 1989 a novel strain of H3N8 influenza virus emerged in horses in China and was thought to have been directly transmitted from birds,[28,89] but this strain also appears not to have been sustained in equine populations.[90]

Distribution

Equine influenza virus affects horses throughout the world, with only a few exceptions. Some member countries report to the OIE that they are free from disease,[48] but the rigor of scientific evidence to support this status varies considerably. Rigorous investigations in countries such as Australia and New Zealand have never found evidence of infection in resident horses, and there are some countries such as Singapore and Japan that have previously had infected horses but have apparently eliminated the virus through rigorous control efforts.[48]

Transmission and pathogenesis

Influenza virus is spread via aerosols, as well as by direct and indirect contact with infected horses and contaminated surfaces. As an enveloped virus, influenza virus is not particularly hardy in the environment, but epidemics have been known to result from contact with people and fomites that

have been moved from one operation to another. The incubation period is 24 to 48 hours, and clinical disease is highly variable. Virus can only be recovered from horses for about 10 days after infection at most, but viral antigen has been recovered from respiratory secretions only for as long as 21 days post-infection.[91] Influenza virus infects epithelial cells throughout the respiratory tract. Cell death and damage to mucociliary apparatus results in airway irritation and accumulation of cellular debris and respiratory secretions. Disease may be enhanced by proliferation of respiratory bacteria and secondary bacterial infections of respiratory tissues (Fig. 30.3). Disease is self-limiting in most cases.

Epidemiology and risk factors

Influenza virus is capable of being spread throughout large geographic areas and even continents when novel viruses are introduced to naïve horse populations.[70,71,88,89,92] For example, a study of sanctioned Thoroughbred and Standardbred race meetings in the USA after introduction of a novel virus in 1963 found that the outbreaks had been detected in 78% of respondent racetracks (49/63), and the virus spread throughout the USA and Canada during a 6-month period (Fig. 30.5).[70] This spread of disease highlights the importance of disease control in athletic horses which tend to be the most mobile sector of equine populations in most countries. Introduction of horses that travel from one horse population to another has been repeatedly shown to be the major inciting incident for influenza epidemics. As horses do not become persistently infected with influenza virus, animals with acute infections are critical for the introduction of virus into susceptible populations. Unfortunately horses can be infected and shed influenza virus while remaining asymptomatic, or at least only mildly affected. Considering this, some disease control programs have employed the use of rapid antigen detection tests as a screening tool for newly introduced horses.[93] Assuming that the prevalence of infection among these horses would generally be very low, the negative predictive value for this test would be quite high, and regulatory officials could be quite certain that test-negative animals were truly uninfected. However, the positive predictive value would be unavoidably very low, and positive tests would frequently be false-positive in these testing conditions.[56] However, this testing is fairly innocuous and very rapid, and the consequences of introducing influenza virus can be very significant. Some inaccuracy in testing is unavoidable and as such, this low positive predictive value may be acceptable if the managers are highly risk averse.

Just as frequent contact between populations increases the risk of introduction, frequent direct and indirect contact among horses within a population increases the risk of infection during influenza outbreaks. Care must be taken to reduce inadvertent contact, and to consider all horses in a population as being significant in the control of disease. Longitudinal studies in Canada showed exercise ponies had much greater risk of disease during influenza epidemics, which was probably attributable to their frequent contact with other horses.[94] In addition, there was less concern about their health than there was for race horses, which ironically increased the risk for all horses in the population.

Factors related to specific immunity against influenza virus are also very important in determining a horse's risk of disease. Several studies have repeatedly shown that serum antibody concentrations strongly correlate with the risk of disease, and even small increases can be associated with a dramatic decrease in disease risk. For example, horses with high antibody concentrations were shown during a series of influenza epidemics to have 2–6 times lower odds of disease

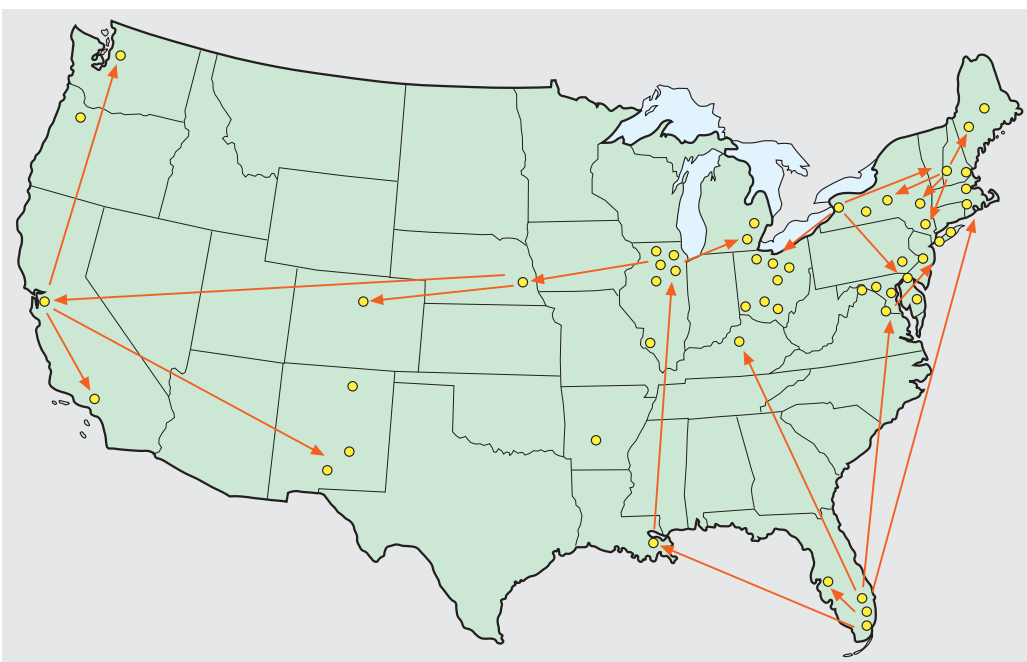


Fig. 30.5
Spread of Influenza A/equine/Miami/63 (H3N8) at racetracks in the 6-month period following introduction in 1963. Dots indicate racetracks with influenza outbreaks, arrows represent movement of horses thought to be associated with transmission. Reproduced from Scholtens et al[70] by permission of Oxford University Press.

compared with those with low antibody concentrations, and about 10–40 times lower odds of disease compared with those that were seronegative.[94] In a recent nation-wide cross-sectional study conducted by the USDA, only about one-third of all horses tested had high antibody concentrations to influenza virus; about one-third were seronegative and one-third had low antibody concentrations. Age is also associated with the risk of influenza infection, which probably is a surrogate marker of the probability of previous exposure to disease agents. This is supported by studies documenting a relationship between age and increasing antibody concentrations.[40] This age-associated disease risk is particularly important for athletic horses given the predominance of young horses in these populations.

The strength and repeatability of the association between age and measures of previous exposure demonstrate their importance as predictors of disease risk. As such, these factors can be used as important factors in categorizing horses for future disease risk, and help in targeting control measures on horses in the highest risk categories. Serum antibody concentrations could be measured as horses enter populations and more rigorous biosecurity precautions could be employed with those horses having low antibody concentrations. This information could also be used to specifically target vaccination protocols. Information collected from longitudinal studies in Canada suggested that 25% of the IRD associated with influenza virus would have been prevented during epidemics if all horses had high serum antibody concentrations prior to exposure.[94] While efficacious killed virus vaccines administered intramuscularly invoke protection by stimulating humoral immunity, it is important to note that a new modified-live intranasal vaccine has been shown to be efficacious without stimulating increases in serum antibody concentrations.[67] If vaccines are to be used in prevention efforts, it is critical to use only products with reasonable expectation of efficacy.[67,77,78] as several equine influenza vaccines that are available commercially have been shown to perform suboptimally.[79,80]

Equine herpesvirus

Characteristics

Herpesviruses are subdivided into three subfamilies based upon genetic structure: alpha, beta, and gamma. There are five herpesviruses known to infect horses, four of which have been shown to infect tissues of the respiratory tract.[95] EHV4 is an alphaherpesvirus that is thought to be a frequent cause of respiratory disease in horses. EHV1 is also an alphaherpesvirus, and while infections typically originate in the respiratory tract, it is more commonly associated with other severe systemic illness (neurologic disease and abortion) and less commonly with respiratory disease. EHV2 and EHV5 are slow-growing gammaherpesviruses that have been recovered from numerous tissues of healthy and clinically diseased horses. Their role and importance in the occurrence of clinical IRD have not been fully elucidated. All of these viruses are known to cause latent infections, that is, infection results in the viral genome being retained in host cells for long periods without transcription or translation. In practical terms, this essentially means that horses are infected for life, and that viral infections can recrudesce repeatedly throughout an animal's life. This recrudescence can result in clinical disease or be inapparent. Recent investigations suggest that essentially all foals are infected with EHV1, EHV2, EHV4, and EHV5 at very young ages.[96,97] Viruses that are homologous to EHV1, EHV2, and EHV3 have been isolated from donkeys and have been designated asinine herpesviruses (AHV3, AHV2, and AHV1, respectively). Herpesviruses are enveloped and are relatively sensitive to a variety of disinfectants and environmental conditions.

EHV4 and EHV1 were once considered the same virus (EHV1) and older descriptions of associated disease can therefore confuse readers who are not aware of the timing of this differentiation. Classically described herpesvirus rhinopneumonitis is now believed to be most commonly associated with EHV4 infections. There is extensive genetic and structural homology between these viruses especially for antigenically dominant surface glycoproteins.[95] This gives rise to apparent cross-reactivity in immunity, especially in horses that have been exposed to both viruses on multiple occasions. As such, serology is often performed against one virus or the other, and the results are assumed to reflect antibody that will react with both viruses. This cross-reactivity is also of interest relative to vaccination.

EHV2 and EHV5 were also considered the same virus until recently. The association between infections with these viruses and the occurrence of clinical IRD is less well established. EVH2 and EHV5 have been recovered from horses with non-specific signs of IRD, but they are also commonly recovered from unaffected horses. In more objective studies, virus was more likely to be recovered from foals and horses with clinical respiratory disease than from asymptomatic animals.[98–100] As methods designed to emphasize recovery of EHV2 and EHV5 have not been included in recent large-scale epidemiologic studies, it seems likely that they cause some disease currently classified as having an unknown etiology (Fig. 30.4). EHV2 and EHV5 genetically resemble Epstein–Barr virus of humans, which is also a gammaherpesvirus.[60] There appears to be significant variability among EHV5 isolates,[101] which may affect the likelihood that horses can be reinfected, as well as the ability to diagnose and investigate EHV5 using serology or polymerase chain reaction (PCR). These viruses appear to be as ubiquitous as EHV1 and EHV4, and limited studies suggest that foals are infected early in life.[97]

Distribution

EHV1 and EHV4 have been studied extensively and all available data suggest that the viruses are ubiquitous in all horse populations throughout the world. Information about the distribution of disease as recorded on the OIE website suggests that IRD associated with herpesvirus is not present among horses in some countries. However, despite the importance of these viruses and the OIE List B status of

equine rhinopneumonitis, this is undoubtedly an example of regulatory under-reporting and lack of investigative rigor. Although not extensively studied, EHV2 and EHV5 infections have been identified in horses is North America, Europe, Australia, and New Zealand, suggesting that these viruses have worldwide distribution.

Transmission and pathogenesis

It is believed that all EHV1 and EHV4 infections originate in the respiratory tract, and result in the virus genome being inserted as an episome in host cell nuclei. New infections and recrudescence both result in lymphocyte associated viremia, which allows virus to spread to tissues at distant sites. Viremia is more commonly detected with EHV1. EHV1 and EHV4 are believed to become latent in lymph nodes associated with the respiratory tract, and although not considered neurotropic, viral genome has also been identified in trigeminal ganglia. Strains vary in their tendency to cause disease, and specific strains of EHV1 are more likely to cause neurologic disease or abortion. Abortion is thought to result from both placental and neonatal infections. Unlike neurologic disease associated with herpesvirus in cattle, humans and pigs, herpesvirus myeloencephalitis in horses is not believed to be commonly associated with direct infection of neurologic tissues.[95] Diffuse vasculitis is a prominent feature of EHV1 infections, which may be the inciting factor of neurologic diseases it has also been proposed to be caused by deposition of virus–antibody complexes that create an inflammatory response in neurologic tissues.[95] Little is known about transmission and pathogenesis associated with EHV2 and EHV5. Viral infections can be detected in essentially all foals,[97] and virus has been isolated from peripheral blood leukocytes, suggesting that viremia and latency are similar to those of EHV1 and EHV4.

Epidemiology and risk factors

Repeated EHV1 and EHV4 infections are common among horses of all ages, which is also probably true for EHV2 and EHV5. Respiratory disease associated with EHV4 has also been documented to occur repeatedly in young horses. Compared with influenza virus, EHV4 is a much more common cause of IRD in horses < 1 year, and a less common cause of large IRD outbreaks among horses > 2 years old. Younger race horses have been shown to have an increased risk of IRD during outbreaks associated with EHV4. The frequency of disease associated with EHV2 and EHV5 has not been well described, but these agents may also be associated with sporadic disease or small outbreaks. Recrudescence is always a potential source of virus given the ubiquitous nature of equine herpesviruses, and this may be a common cause of sporadic IRD. However, epidemiologic data also suggests that novel disease-causing strains of EHV1 and EHV4 can be introduced into populations resulting in outbreaks of respiratory disease, neurologic disease, or abortion, suggesting that horizontal transmission is an important source of EHV1 and EHV4 during epidemics. These viruses can be transmitted by aerosols, but epidemiologic data regarding patterns of disease during outbreaks suggests that direct transmission, and indirect transmission via fomites and contaminated surfaces are more important methods of transmitting virus during outbreaks. Horses that frequently come into contact with other horses have been shown to have increased risk of IRD associated with EHV4.[8]

Because of the cell-associated nature of herpesvirus infections, it has been suggested that cell-mediated immunity is far more important than humoral immunity in protecting horses from disease. As such, the use of killed-virus vaccines and the relationship between serum antibody and protective immunity has been questioned. Cell-mediated immunity is undoubtedly important for protecting horses. However, field investigations have shown that higher serum antibody titers are associated with decreased IRD risk in association with EHV4 infections.[8,52] It is not clear if humoral immunity was protective or whether it was simply a marker of horses with stronger cell-mediated immunity against these agents. It was also shown that horses with high influenza virus antibody titers had lower risk of disease during an EHV4 outbreak, supporting the idea that antibody titers may to some degree be simple markers of previous exposure, and not entirely direct indicators of immunity.

Equine arteritis virus

Characteristics

Equine arteritis virus (EAV) is the prototype virus of the recently established genus *Arterivirus*. It is an enveloped RNA virus and is therefore relatively sensitive to drying and common disinfectants. While some variability has been demonstrated in the viral genome, there is only one recognized serotype. EAV has a limited host range and is only known to infect equids. Infections are far more common than is the occurrence of respiratory disease and EAV is primarily a concern because of associated reproductive disease. EAV is particularly problematic to the equine industries because of its ability to establish a carrier state in intact stallions. These carrier animals are important for introducing and maintaining the virus in equine populations, as well as because of their impact on trade of horses and semen. Infection is apparently more common among some breeds, especially Standardbred horses, but this is probably attributable to a higher number of carrier stallions rather than a true difference in susceptibility.

Distribution

EAV is thought to have a worldwide distribution, even though outbreaks are reported only occasionally. However, despite having OIE List B status, many countries report that they have never recognized this agent or disease.[48] Again, this is probably attributable to under-reporting and lack of investigative rigor. There has been an apparent decrease in the number of reported outbreaks, which may be attributable to increased availability of diagnostic testing as well as

increased awareness throughout the world regarding disease impact and effective disease control measures. Recent broad-based investigation of EAV infection in the USA found that about 2% of unvaccinated horses were seropositive, and another investigation based on selective sampling in the UK found that 2% or less of unvaccinated horses were seropositive.[102,103]

Transmission and pathogenesis

EAV is shed via the respiratory tract by acutely infected horses, in the semen of carrier stallions, as well as in amniotic fluid, placenta, and fetuses of aborted mares. Less important sources of virus include blood, feces, and urine of acutely infected animals. Infections in carrier stallions are inapparent even though virus is shed in their semen for their entire life, or until they are castrated. EAV infections do not apparently affect fertility of stallions. Asymptomatic infections are common, and stallions may become long-term carriers of the virus even without showing signs of disease. The incubation period in clinically affected animals is about 3 to 7 days. Clinical disease can be indistinguishable from that caused by other IRD agents, but affected horses may also develop swelling and edema that is most commonly noted in the legs, scrotum, sheath, or udder, as well as abortion in pregnant mares. Modified live and killed virus vaccines are commercially available. Control recommendations for EAV from the American Horse Council include the use of modified live vaccines,[104] and the killed virus vaccine is used in Great Britain and Ireland.[105] It should be noted that vaccination decreases the risk of disease, but does not prevent infection.[105]

Epidemiology and risk factors

Perhaps the most dominant factor affecting spread and maintenance of EAV in populations is the presence of persistently infected stallions that shed virus in semen. Further, while outbreaks of clinical disease are sometimes reported, most infections result in very mild or no clinical signs. This allows opportunity for further spread of virus without the presence of identifiable disease that might trigger enactment of more rigorous control strategies. Seroprevalence has been repeatedly shown to vary among breeds, and is highest among Standardbred horses, which may be attributable to the number of persistently infected stallions. In a broad-based cross-sectional study performed by the USDA, the seroprevalence among adult non-vaccinated Standardbreds was about 24%, compared with 4.5% among Thoroughbreds, 3.6% among Warmbloods, and about 1% among other horses.[102] Horses from operations used primarily for breeding or for boarding and training were more likely to be seropositive than horses from other operations.[102] Various countries have enacted control strategies centered on identifying persistently infected stallions, reducing the likelihood of exposure to acutely infected horses, and use of vaccines to decrease the risk of disease and decrease the risk of stallions becoming persistently infected.

Other respiratory viruses

Several other viruses have been recovered from the respiratory tract of horses showing signs of IRD, as well as from clinically normal horses. The role that these viruses play in the occurrence of respiratory disease in horses is not clear. While it is interesting that these viruses can be recovered from horses with clinical IRD, these data would be more convincing if evidence of infection was found more commonly in disease cases compared with non-cases in the same populations. A brief description of two of these agents follows.

Equine rhinitis virus

Horses are commonly infected with equine rhinitis-A virus and equine rhinitis-B virus (formerly classified as equine rhinovirus types 1 and 2, respectively). Seroprevalence has been shown to approach 100% in young and adult horses. Limited experimental challenge studies indicate that this agent can cause IRD under some conditions. Horses commonly shed virus in nasal secretions and in urine. Studies evaluating the distribution of this agent have not been performed in many countries, but infections have been documented in North America, Australia, New Zealand, UK, and Europe, suggesting a worldwide distribution.

Equine adenovirus

Equine adenovirus type 1 has been isolated from horses throughout the world, and seroprevalence can approach 100% in mature horses. In most horses infection is not believed to cause clinical disease, or it is very mild. However, adenovirus infections cause significant disease in Arabian foals with primary, severe combined immunodeficiency disease (PSCID). A limited study of experimental challenge in two immunocompetent foals showed that infection can result in pathologic changes under certain conditions.

References

1. Bailey CJ, Rose RJ, Reid SW, Hodgson DR. Wastage in the Australian thoroughbred racing industry: a survey of Sydney trainers. Aust Vet J 1997; 75(1):64–66.
2. Bailey CJ, Reid SW, Hodgson DR, Rose RJ. Impact of injuries and disease on a cohort of two- and three-year-old thoroughbreds in training. Vet Rec 1999; 145(17):487–493.
3. Hernandez J, Hawkins DL. Training failure among yearling horses. Am J Vet Res 2001; 62(9):1418–1422.
4. Ryan AJ, Dalrymple W, Dull B, et al. Round table: Upper respiratory infections in sports. Phys Sports Med 1975; 3:29–42.
5. Hanley DF. Medical care of the US Olympic Team. JAMA 1976; 236(2):147–148.
6. Weidner TG. Literature review: upper respiratory illness and sport and exercise. Int J Sports Med 1994; 15(1):1–9.
7. Weidner TG, Anderson BN, Kaminsky LA, et al. Effect of a rhinovirus-caused upper respiratory illness on pulmonary

function test and exercise responses. Med Sci Sports Exerc 1997; 29:604–609.
8. Morley PS. The epidemiology of infectious upper respiratory tract disease in horses. PhD dissertation, University of Saskatchewan, 1995.
9. NAHMS. NAHMS Equine '98: Needs Assessment Survey Results. #N207.597. 1997. Online. Available at http://www.aphis.usda.gov/vs/ceah/cahm/Equine/eq98na.pdf (accessed 11 April 2003).
10. Traub-Dargatz JL, Salman MD, Voss JL. Medical problems of adult horses, as ranked by equine practitioners. J Am Vet Med Assoc 1991; 198(10):1745–1747.
11. Peters EM, Bateman ED. Ultramarathon running and upper respiratory tract infections. S Afr Med J 1983; 64:582–584.
12. Weigl JA, Puppe W, Schmitt HJ. The incidence of influenza-associated hospitalizations in children in Germany. Epidemiol Infect 2002; 129(3):525–533.
13. Zimmerman RK, Middleton DB, Smith NJ. Vaccines for persons at high risk due to medical conditions, occupation, environment, or lifestyle, 2003. J Fam Pract 2003; 52(1 Suppl):S22–35.
14. Clarke AF, Madelin TM, Allpress RG. The relationship of air hygiene in stables to lower airway disease and pharyngeal lymphoid hyperplasia in 2 groups of thoroughbred horses. Equine Vet J 1987; 19(6):524–530.
15. Clarke AF, Madelin TM, Allpress RG. The relationship of air hygiene in stables to lower airway disease during an outbreak of equid herpesvirus-1 infection. In: Equine infectious diseases V: Proceedings of the Fifth International Conference on Equine Infectious Diseases. Lexington, KY: University Press of Kentucky; 1988; 268–271.
16. Nieman DC. Special feature for the Olympics: effects of exercise on the immune system: exercise effects on systemic immunity. Immunol Cell Biol 2000; 78(5):496–501.
17. Gleeson M, Pyne DB. Exercise effects on mucosal immunity. Immunol Cell Biol 2000; 78(5):536–544.
18. Gleeson M, Pyne DB. Special feature for the Olympics: effects of exercise on the immune system: exercise effects on mucosal immunity. Immunol Cell Biol 2000; 78(5):536–544.
19. Woods JA, Lu Q, Ceddia MA, Lowder T. Exercise-induced modulation of macrophage function. Immunol Cell Biol 2000; 78(5):545–553.
20. Woods J, Lu Q, Ceddia MA, Lowder T. Special feature for the Olympics: effects of exercise on the immune system: exercise-induced modulation of macrophage function. Immunol Cell Biol 2000; 78(5):545–553.
21. Jonsdottir IH, Hoffmann P. The significance of intensity and duration of exercise on natural immunity in rats. Med Sci Sports Exerc 2000; 32(11):1908–1912.
22. Jonsdottir IH. Exercise immunology: neuroendocrine regulation of Nk-cells. Int J Sports Med 2000; 21:S20-S23.
23. Jonsdottir IH. Special feature for the Olympics: effects of exercise on the immune system: neuropeptides and their interaction with exercise and immune function. Immunol Cell Biol 2000; 78(5):562–570.
24. Pedersen BK, Ullum H. Nk cell response to physical-activity – possible mechanisms of action. Med Sci Sports Exerc 1994; 26(2):140–146.
25. Nieman DC. Is infection risk linked to exercise workload? Med Sci Sports Exerc 2000; 32(7):S406–S411.
26. Pedersen BK, Bruunsgaard H. How physical exercise influences the establishment of infections. Sports Med 1995; 19(6):393–400.
27. Lunn DP, Hussey S, Sebring R, et al. Safety, efficacy and immunogenicity of a modified-live equine influenza virus vaccine in ponies after induction of exercise-induced immunosuppression. J Am Vet Med Assoc 2001; 218(6): 900–906.
28. Guo Y, Wang M, Kawaoka Y, et al. Characterization of a new avian-like influenza A virus from horses in China. Virology 1992; 188(1):245–255.
29. Guo Y, Wang M, Zheng GS, et al. Seroepidemiological and molecular evidence for the presence of two H3N8 equine influenza viruses in China in 1993–94. J Gen Virol 1995; 76:2009–2014.
30. Horohov DW, Keadle TL, Pourciau SS et al. Mechanism of exercise-induced augmentation of lymphokine activated killer (Lak) cell activity in the horse. Vet Immunol Immunopathol 1996; 53(3–4):221–233.
31. Horohov DW, Dimock A, Guirnalda P, et al. Effect of exercise on the immune response of young and old horses. Am J Vet Res 1999; 60(5):643–647.
32. Kurcz EV, Lawrence LM, Kelley KW, Miller PA. The effect of intense exercise on the cell-mediated immune-response of horses. J Equine Vet Sci 1988; 8:237–239.
33. Keadle TL, Pourciau SS, Melrose PA, et al. Acute exercise stress modulates immune function in unfit horses. J Equine Vet Sci 1993; 13:226–231.
34. Wong CW, Smith SE, Thong YH, et al. Effects of exercise stress on various immune functions in horses. Am J Vet Res 1992; 53:1414–1417.
35. Rose RJ. Hematological-changes associated with endurance exercise. Vet Rec 1982; 110(8):175–177.
36. Snow DH, Ricketts SW, Mason DK. Hematological response to racing and training exercise in thoroughbred horses, with particular reference to the leukocyte response. Equine Vet J 1983; 15(2):149–154.
37. Rose RJ, Hodgson DR. Hematological and plasma biochemical parameters in endurance horses during training. Equine Vet J 1982; 14(2):144–148.
38. Shephard RJ. Special feature for the Olympics: effects of exercise on the immune system: overview of the epidemiology of exercise immunology. Immunol Cell Biol 2000; 78(5):485–495.
39. Morley PS, Townsend HG, Bogdan JR, Haines DM. Descriptive epidemiologic study of disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):535–544.
40. NAHMS. Infectious upper respiratory disease in US horses: disease frequency. #N342.1001, 2001. Online. Available at http://www.aphis.usda.gov/vs/ceah/cahm/Equine/iurd98.pdf (accessed 11 April 2003).
41. Kaneene JB, Saffell M, Fedewa DJ, et al. The Michigan Equine Monitoring System.1. Design, implementation and population estimates. Prev Vet Med 1997; 29(4):263–275.
42. Burrell MH, Wood JL, Whitwell KE, et al. Respiratory disease in thoroughbred horses in training: the relationships between disease and viruses, bacteria and environment. Vet Rec 1996; 139(13):308–313.
43. Gross DK, Hinchcliff KW, French PS et al. Effect of moderate exercise on the severity of clinical signs associated with influenza virus infection in horses. Equine Vet J 1998; 30(6):489–497.
44. Morley PS, Townsend HG, Bogdan J, et al. Infectious upper respiratory tract disease caused by influenza virus in horses stabled at a racetrack. Proc Am Assoc Equine Pract 1995; 41:174–175.
45. Marois P, Pavilanis V, Boudreault A, Di Franco E. An outbreak of Type A2 influenza among horses. Can J Comp Med 1963; 27:257–260.
46. McQueen JL. Review of influenza in animals: Equine. CDC Zoonoses Surveillance. Special Report: Animal Influenza 1965; Report #5:6–13.

47. Aiello SE, Mays A, eds. The Merck Veterinary Manual – Equine Influenza. Online. Available at http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/121304.htm&word=equine%2cinfluenza (accessed 11 April 2003).
48. Handistatus II. Online. Available at http://www.oie.int/hs2/report.asp?lang=en (accessed 11 April 2003).
49. Rees WA, Harkins JD, Lu M, et al. Pharmacokinetics and therapeutic efficacy of rimantadine in horses experimentally infected with influenza virus A2. Am J Vet Res 1999; 60:888–894.
50. Mumford JA, Hannant D. Equine influenza. In: Studdert MJ, ed. Virus infections of equines. New York: Elsevier; 1996; 285–294.
51. Maisch B, Ristic AD, Portig I, Pankuweit S. Human viral cardiomyopathy. Front Biosci 2003; 8:S39–67.
52. Mumford EL, Traub-Dargatz JL, Salman MD, et al. Monitoring and detection of acute viral respiratory tract disease in horses. J Am Vet Med Assoc 1998; 213(3):385–390.
53. Morley PS, Bogdan JR, Townsend HG, Haines DM. Evaluation of Directigen Flu A assay for detection of influenza antigen in nasal secretions of horses. Equine Vet J 1995; 27(2): 131–134.
54. Chambers TM, Shortridge KF, Li PH, et al. Rapid diagnosis of equine influenza by the Directigen FLU-A enzyme immunoassay. Vet Rec 1994; 135(12):275–279.
55. Townsend HGG, Moore SL, Bogdan JR, et al. Evaluation of an optical immunoassay for the diagnosis of equine influenza. In: Salman MD, Morley PS, Ruch-Gallie R, eds. Proceedings of the 9th Symposium of the International Society for Veterinary Epidemiology and Economics. International Society for Veterinary Epidemiology and Economics, 2000; Abstract number 508.
56. Adam EN, Morley PS, Chmielewski KE, et al. Detection of cold-adapted vaccine-strain influenza virus using two commercial assays. Equine Vet J 2002; 34(4):400–404.
57. Powell DG, Burrows R, Spooner PR, et al. A study of infectious respiratory disease among horses in Great Britain, 1971–1976. In: Bryans JT, ed. Equine infectious diseases IV: Proceedings of the Fourth International Conference on Equine Infectious Diseases. Princeton, NJ: Veterinary Publications; 1978; 451–459.
58. Ostlund EN, Powell D, Bryans JT. Equine herpesvirus 1: A review. Proc Am Assoc of Equine Pract 1991; 36:387–395.
59. Burrows R, Goodridge D, Denyer M, et al. Equine influenza infections in Great Britain, 1979. Vet Rec 1982; 110:494–497.
60. Browning GF, Agius CT. Equine herpesvirus 2 and 5 infections. In: Studdert MJ, ed. Virus infections of equines. New York: Elsevier; 1996; 47–62.
61. Wood JL, Burrell MH, Roberts CA, et al. Streptococci and Pasteurella spp. associated with disease of the equine lower respiratory tract. Equine Vet J 1993; 25(4): 314–318.
62. Ward CL, Wood JL, Houghton SB, et al. Actinobacillus and Pasteurella species isolated from horses with lower airway disease. Vet Rec 1998; 143(10):277–279.
63. Rees WA, Harkins JD, Woods WE, et al. Amantadine and equine influenza: pharmacology, pharmacokinetics and neurological effects in the horse. Equine Vet J 1997; 29(2): 104–110.
64. Gibson JS, Slater JD, Field HJ. The activity of (S)-1-[(3-hydroxy-2-phosphonyl methoxy)propyl] cytosine (HPMPC) against equine herpesvirus-1 (EHV-1) in cell cultures, mice and horses. Antiviral Res 1992; 19(3):219–232.
65. Morley PS. Biosecurity of veterinary practices. Vet Clin North Am Food Anim Pract 2002; 18(1):133–155.
66. Traub-Dargatz JL, Morley PS, Dargatz DA, et al. Infection control strategies in horses for the new millennium. Proc Am Assoc Equine Pract 2000; 46:36–41.
67. Townsend HG, Penner SJ, Watts TC, et al. Efficacy of a cold-adapted, intranasal, equine influenza vaccine: challenge trials. Equine Vet J 2001; 33(7):637–643.
68. Kastner SB, Haines DM, Archer J, Townsend HG. Investigations on the ability of clenbuterol hydrochloride to reduce clinical signs and inflammation associated with equine influenza A infection. Equine Vet J 1999; 31(2): 160–168.
69. [Anon]. 1963 Equine influenza epizootic. J Am Vet Med Assoc 1963; 143(10):1108.
70. Scholtens RG, Steele JH, Dowdle WR, et al. United-States epizootic of equine influenza, 1963. Public Health Rep 1964; 79(5):393–402.
71. Guthrie AJ, Stevens KB, Bosman PP. The circumstances surrounding the outbreak and spread of equine influenza in South Africa. Rev Sci Tech 1999; 18(1):179–185.
72. Larson EL. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995; 23(4):251–269.
73. Fotheringham VJ. Disinfection of livestock production premises. Rev Sci Tech 1995; 14(1):191–205.
74. Ford WB. Disinfection procedures for personnel and vehicles entering and leaving contaminated premises. Rev Sci Tech 1995; 14(2):393–401.
75. Dwyer RM. Disinfecting equine facilities. Rev Sci Tech 1995; 14(2):403–418.
76. Antec International Ltd. Animal health: equine menu. Online. Available at http://www.antecint.co.uk/main/equine.htm (accessed 11 April 2003).
77. Mumford JA, Jessett D, Dunleavy U, et al. Antigenicity and immunogenicity of experimental equine influenza ISCOM vaccines. Vaccine 1994; 12(9):857–863.
78. Mumford JA, Wilson H, Hannant D, Jessett DM. Antigenicity and immunogenicity of equine influenza vaccines containing a Carbomer adjuvant. Epidemiol Infect 1994; 112(2): 421–437.
79. Morley PS, Townsend HG, Bogdan JR, Haines DM. Efficacy of a commercial vaccine for preventing disease caused by influenza virus infection in horses. J Am Vet Med Assoc 1999; 215(1):61–66.
80. Mumford EL, Traub-Dargatz JL, Carman J, et al. Occurrence of infectious upper respiratory tract disease and response to vaccination in horses on six sentinel premises in northern Colorado. Equine Vet J 2003; 35(1):72–77.
81. Ellis JA, Bogdan JR, Kanara EW, et al. Cellular and antibody responses to equine herpesviruses 1 and 4 following vaccination of horses with modified-live and inactivated viruses. J Am Vet Med Assoc 1995; 206(6):823–832.
82. Gerber JD, Marron AE, Bass EP, Beckenhauer WH. Effect of age and pregnancy on the antibody and cell-mediated immune responses of horses to equine herpesvirus 1. Can J Comp Med 1977; 41(4):471–478.
83. Banks J, Speidel EC, McCauley JW, Alexander DJ. Phylogenetic analysis of H7 haemagglutinin subtype influenza A viruses. Arch Virol 2000; 145(5):1047–1058.
84. Lai AC, Chambers TM, Holland RE Jr, et al. Diverged evolution of recent equine-2 influenza (H3N8) viruses in the Western Hemisphere. Arch Virol 2001; 146(6):1063–1074.
85. Daly JM, Lai ACK, Binns MM, et al. Antigenic and genetic evolution of equine H3n8 influenza a viruses. J Gen Virol 1996; 77:661–671.

86. Yates P, Mumford JA. Equine influenza vaccine efficacy: the significance of antigenic variation. Vet Microbiol 2000; 74(1–2):173–177.
87. Loke CT. Outbreak of equine influenza in Malaysia and Singapore. Singapore Vet J 1981; 5:53–54.
88. Singh G. A note on the concurrent isolation, from horses and ponies, of influenza A/EQ 1 and A/EQ 2 viruses from an epidemic of equine influenza in India. Comp Immunol Microbiol Infect Dis 1995; 18:73–74.
89. Webster RG, Guo Y. New influenza virus in horses. Nature 1991; 351:527.
90. Mumford J, Wood J. WHO/OIE meeting: consultation on newly emerging strains of equine influenza. 18–19 May 1992, Animal Health Trust, Newmarket, Suffolk, UK. Vaccine 1993; 11:1172–1175.
91. Sutton GA, Viel L, Carman PS, Boag BL. Study of the duration and distribution of equine influenza virus subtype 2 (H3N8) antigens in experimentally infected ponies in vivo. Can J Vet Res 1997; 61(2):113–120.
92. Webster RG, Kawaoka Y, Guo Y. Equine influenza in China. Foreign Animal Disease Report 1991; 19:3.
93. Powell DG, Watkins KL, Li PH, Shortridge KF. Outbreak of equine influenza among horses in Hong Kong during 1992. Vet Rec 1995; 136(21):531–536.
94. Morley PS, Townsend HG, Bogdan JR, Haines DM. Risk factors for disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):545–550.
95. Crabb BC, Studdert MJ. Equine rhinopneumonitis and equine abortion (Equine herpesviruses 4 and 1). In: Studdert MJ, ed. Virus infections of equines. New York: Elsevier; 1996; 11–38.
96. Gilkerson J, Jorm LR, Love DN, et al. Epidemiological investigation of equid herpesvirus-4 (EHV-4) excretion assessed by nasal swabs taken from thoroughbred foals. Vet Microbiol 1994; 39(3–4):275–283.
97. Dunowska M, Wilks CR, Studdert MJ, Meers J. Equine respiratory viruses in foals in New Zealand. New Zealand Vet J 2002; 50(4):140–147.
98. Murray MJ, Eichorn ES, Dubovi EJ, et al. Equine herpesvirus type 2: prevalence and seroepidemiology in foals. Equine Vet J 1996; 28(6):432–436.
99. Borchers K, Wolfinger U, Goltz M, et al. Distribution and relevance of equine herpesvirus type 2 (EHV-2) infections. Arch Virol 1997; 142(5):917–928.
100. Dunowska M, Wilks CR, Studdert MJ, Meers J. Viruses associated with outbreaks of equine respiratory disease in New Zealand. New Zealand Vet J 2002; 50(4):132–139.
101. Dunowska M, Holloway SA, Wilks CR, Meers J. Genomic variability of equine herpesvirus-5. Arch Virol 2000; 145(7):1359–1371.
102. NAHMS. Equine Viral Arteritis (EVA) and the US Horse Industry. #N312.0501. 2000. Online. Available at http://www.aphis.usda.gov/vs/ceah/cahm/Equine/eq98eva.pdf. (accessed 11 April 2003).
103. Newton JR, Wood JL, Castillo-Olivares FJ, Mumford JA. Serological surveillance of equine viral arteritis in the United Kingdom since the outbreak in 1993. Vet Rec 1999; 145(18):511–516.
104. Equine Viral Arteritis Protocol. 2000. Online. Available at http://www.horsecouncil.org/health/evaproto.html (accessed 11 April 2003).
105. De Vries AAF, Rottier PJM, Glaser AL, Horzinek MC. Equine viral arteritis. In: Studdert MJ, ed. Virus infections of equines. New York: Elsevier; 1996; 171–200.

CHAPTER 31

Bacterial infections of the respiratory tract of athletic horses

J. Richard Newton, James L. N. Wood and Kenneth W. Hinchcliff

Streptococcus equi infection ('strangles')

- Highly contagious disease of horses characterized by outbreaks of disease.
- Disease is spread by fomites and direct transmission. Inapparent carriers are important in perpetuating the disease.
- Clinical signs include fever, depression, cranial lymphadenopathy and purulent nasal discharge.
- Metastatic infection causes abscesses in thoracic and abdominal lymph nodes and in other organs.
- Treatment includes drainage of accessible abscesses, supportive care and, in some cases, administration of antibiotics.
- Prevention centers on detection of carriers and exclusion of infected horses. Vaccination is of limited efficacy in preventing the disease.

Recognition of disease

History and presenting complaint

Streptococcus equi infection is the most frequently reported infectious disease of horses worldwide, with affected horses usually having either direct or indirect contact with other infected horses or known outbreaks.[1,2] However, the sudden onset of disease may not be readily attributable to contact with horses with obvious clinical signs of strangles and in these cases transmission from an outwardly healthy carrier is usually the source of infection.[3]

Although the disease occurs commonly in non-athletic horses it occurs at least sporadically among groups of high-value equine athletes. At least in the early stages of outbreaks of strangles, pathognomonic clinical signs of lymphadenopathy may not be present and unless specific diagnostic tests are conducted, non-specific signs of respiratory disease (including nasal discharge, coughing and pyrexia) may inadvertently be attributed to infection by organisms other than *S. equi*.[4,5]

Physical examination

An early clinical sign of strangles is marked pyrexia (39.4–41.1°C/103–106°F) associated with depression and loss of appetite.[1,2] Affected horses invariably develop an initial serous nasal discharge that becomes purulent and profuse within 2 days and some cases have a soft, moist cough and/or purulent ocular discharge.

Strangles is classically characterized by a lymphadenitis associated with rapid metastasis of *S. equi* infection from buccal and nasopharyngeal mucosal surfaces to the draining

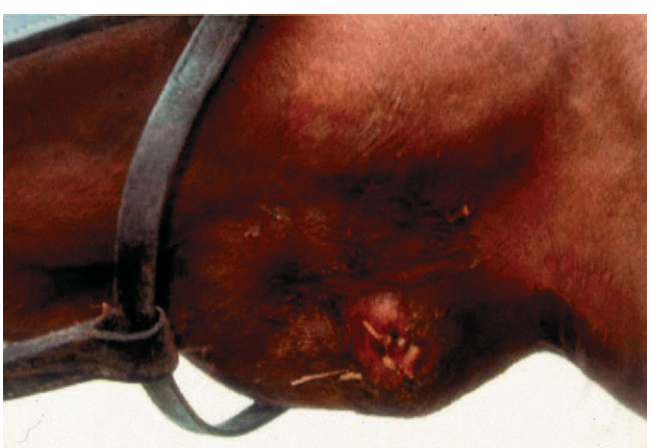


Fig. 31.1
Draining submandibular lymph node abscess in a horse with strangles.

lymph nodes of the head and neck. This spread probably occurs within hours of infection. Within several days the submandibular (Fig. 31.1) and parotid lymph nodes (Fig. 31.2) become palpably firm, swollen and painful and with abscessation of these and the retropharyngeal lymph nodes (RPLNs). The pharynx becomes obstructed, causing difficulty in breathing (hence the name 'strangles'; Fig. 31.3). One to two weeks after signs initially appear, the abscessated lymph nodes usually develop sinuses and rupture their purulent contents through either the skin (Figs 31.1, 31.2) or into the guttural pouches (Figs 31.4, 31.5).[5] At this stage of the disease horses often show a sudden and marked clinical improvement. Rupture of the RPLNs results in guttural pouch empyema that may then drain into the pharynx through the pharyngeal pouch opening (Figs 31.6, 31.7), the most dependent part of the pouch when the horse has its head lowered to the ground.[3,5–7] This purulent discharge is either swallowed or flows down the nose to appear as a profuse nasal discharge. Lymph nodes of the head may

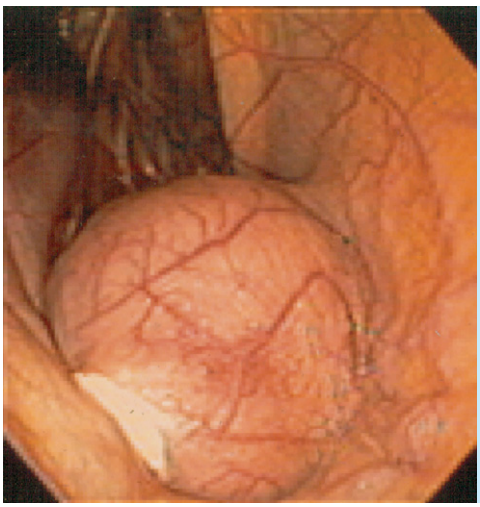


Fig. 31.4
Retropharyngeal lymph node abscess draining into the guttural pouch of a horse with strangles.

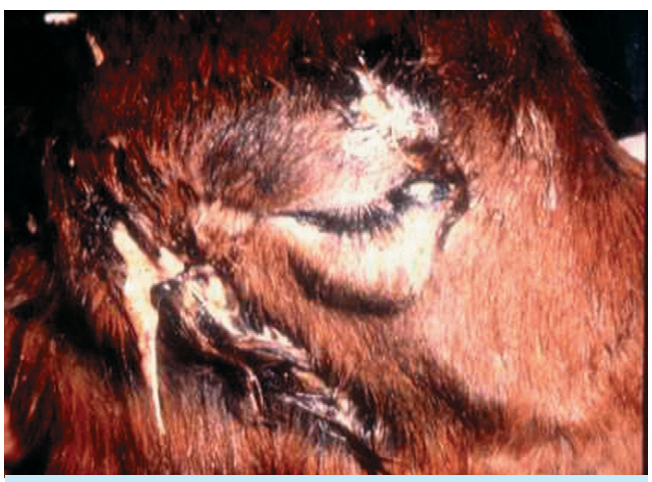


Fig. 31.2
Draining parotid lymph node abscess in a horse with strangles.

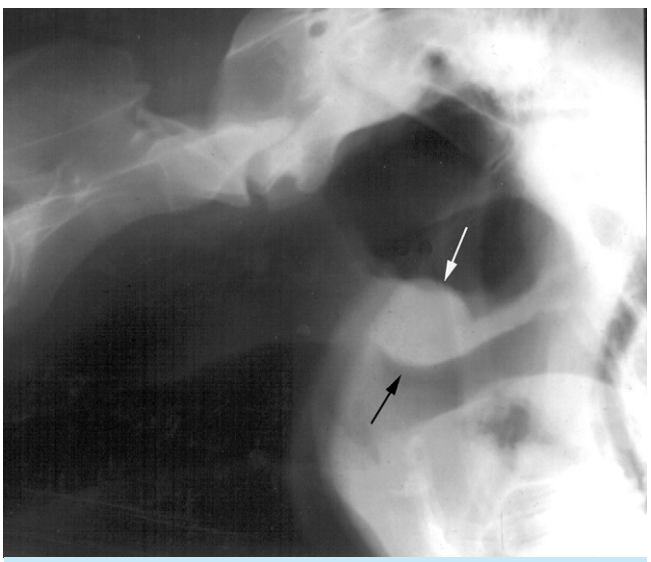


Fig. 31.5
Radiograph of the pharynx of a horse with a retropharyngeal lymph node abscess (arrows) associated with *S. equi* infection.

Fig. 31.3
Airway obstruction ('strangles') in a foal (picture courtesy of H. Townsend).

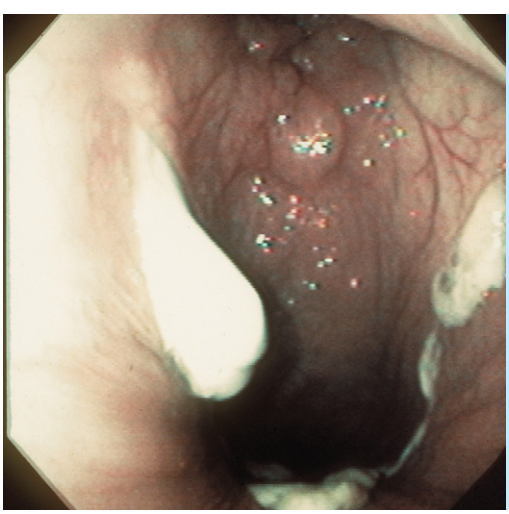


Fig. 31.6
Purulent discharge draining through the pharyngeal opening of the guttural pouches (picture courtesy of W. Beard).

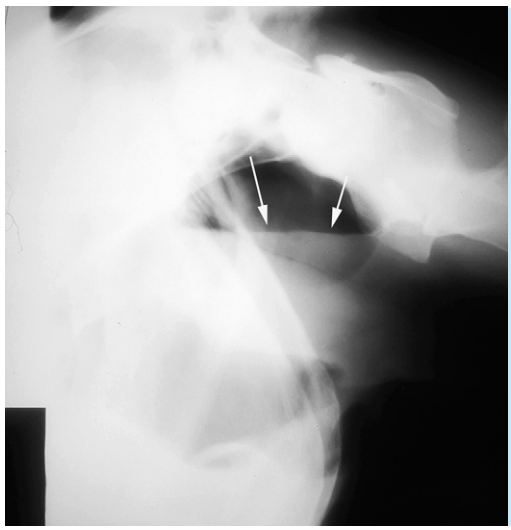


Fig. 31.7 Radiograph of the pharynx of a horse with guttural pouch empyema secondary to *S. equi* infection. The fluid level within the pouch is indicated by arrows.

abscessate sequentially so that in most cases the entire clinical course of disease lasts several weeks, although not all infected animals in outbreaks necessarily show typical signs.

A strongly presumptive diagnosis of strangles may be made on clinical grounds in horses that demonstrate lymph node abscessation, although in some outbreaks lymphadenitis may only occur in later cases or remain clinically inapparent.[4,5] However, in these apparently atypical strangles outbreaks, earlier abscessation of RPLNs in some horses may be confirmed by the detection of guttural pouch empyema on endoscopic examination.

Morbidity rates of 100% are not uncommon in some susceptible populations and mortality rates of 8–10% have been reported amongst cases,[8,9] although rates are usually much lower in well-managed animals. As well as the usual clinical signs of strangles, serious complications occur in as many as 20% of cases.

Metastatic ('bastard') strangles Metastatic strangles is the systemic spread of infection by *S. equi*, with abscessation of parts of the body other than the lymph nodes of the head. A wide range of structures may be affected, including the lungs, liver, spleen, kidneys, brain, spinal cord, joints, endocardium, and the cervical, pulmonary, prescapular, mediastinal and mesenteric lymph nodes. Abscesses also occur paravertebrally, and cutaneously, on the limbs (Fig. 31.8) and in the perianal, periorbital and facial regions.

A diagnosis of metastatic strangles should initially be suspected with the presentation of overt and unusual clinical signs in any animal that is known to be either currently suffering, or has recently recovered from or has had contact with horses with strangles. Signs of metastatic strangles may be indicative of the anatomical site(s) of infection but are often fairly non-specific and include increased respiratory effort, periodic pyrexia, depression, inappetence, intermittent colic and chronic weight loss.

Fig. 31.8 Discharging abscess on the hind quarters of a horse with metastatic strangles (picture courtesy of H. Townsend).

Fig. 31.9 Facial edema and nasal discharge in a horse with strangles-associated purpura hemorrhagica (picture courtesy of P. Dixon).

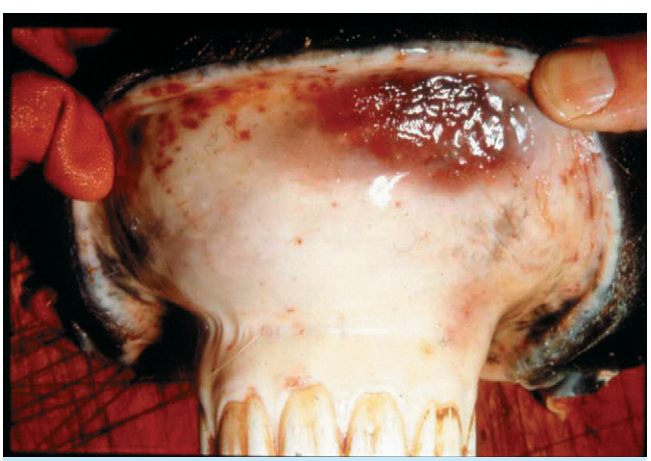


Fig. 31.10 Hemorrhage and edema on the mucosal surface of the upper lip in a horse with purpura hemorrhagica (picture courtesy of H. Townsend).

Purpura hemorrhagica Purpura hemorrhagica is a strangles-related immune-mediated condition that usually occurs suddenly in older horses. Purpura is characterized by vasculitis resulting in subcutaneous edema especially involving the head (Fig. 31.9) and limbs and petechial hemorrhages on the surfaces of the mucosae (Fig. 31.10), musculature and viscera. Immune complexes, containing the surface M-protein antigen of *S. equi*, have been shown to be involved in the pathogenesis of purpura.[10,11] The vasculitis may be widely disseminated through the body affecting many organs, including the gastrointestinal tract, kidneys, lungs, muscles and heart, and the resulting peripheral edema may be so severe as to cause circulatory collapse and death. Diagnosis of purpura hemorrhagica is generally made on the basis of typical clinical signs, which usually appear between 2 and 4 weeks after an apparent resolution of strangles or following administration of a strangles vaccine.

Special examination

Confirming a diagnosis of guttural pouch empyema with or without chondroids following strangles is achieved by direct visual assessment of both pouches using endoscopy (Figs 31.6, 31.11) or radiography (Fig. 31.7). Cytologic assessment and culture and polymerase chain reaction (PCR) of *S. equi* in lavage samples collected via a sterile disposable catheter passed through the biopsy channel of the endoscope should accompany visual examination as infection and inflammation may be present in the absence of obvious and visible pathology.[6,12]

The diagnosis of guttural pouch empyema with chondroids may also be made by radiography of the head (Fig. 31.12)[6,12] and *S. equi* may be cultured from lavages collected by direct percutaneous sampling of the pouch.[13,14]

Metastatic strangles Further diagnostic procedures may aid the confirmation of the presence and site of *S. equi* abscessation in metastatic strangles. Appropriate techniques include hematologic examination (usually showing leukocytosis with left shift and mature neutrophilia), clinical biochemistry (raised serum globulin and fibrinogen levels) and peritoneal and/or pleural fluid evaluation (raised white blood cell count, protein and fibrinogen levels, presence of intra- and extracellular cocci on a stained smear even though bacteriological culture is frequently negative). Examination per rectum (with or without transrectal or transabdominal ultrasound examination) may reveal an abnormal abdominal mass that is generally resented on palpation. Abdominal abscesses may be diagnosed by exploratory laparotomy or laparoscopy. Sometimes the diagnosis can only be made at necropsy in animals found dead or after elective euthanasia for intractable idiopathic disease. Isolation of *S. equi* from abscesses provides a definitive diagnosis of metastatic strangles.

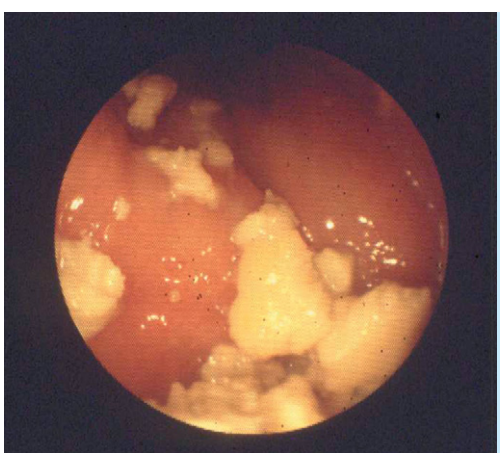


Fig. 31.11 Endoscopic appearance of a guttural pouch with chondroids forming following strangles.

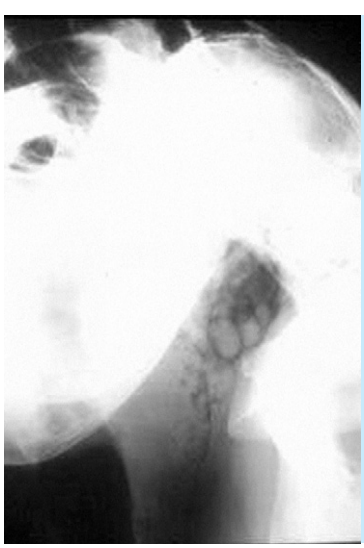


Fig. 31.12 Radiographic appearance of chondroids in the guttural pouch of a horse following strangles.

Laboratory examination

Sample submission To maximize effective containment and control of strangles outbreaks, a definitive diagnosis should be made as early as possible, especially in horses that do not have classical signs of lymphadenitis. This may be achieved by bacterial culture of *S. equi* from appropriate samples such as aspirated pus from lymph nodes (Fig. 31.13)

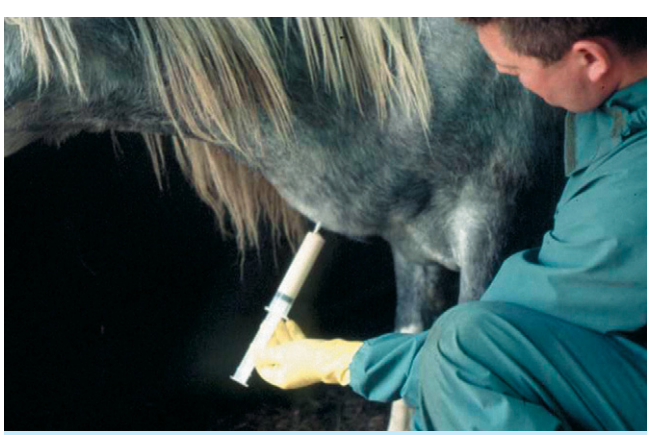


Fig. 31.13 Aspiration of pus from an infected lymph node in a case of metastatic strangles.

and swabs or washings from discharging abscesses and the nasopharynx. Samples should preferably be submitted from a large and representative sample of suspected cases, rather than a single sample from a single case. In addition, care should be taken with the interpretation of negative laboratory results, especially from horses demonstrating signs that are typical of strangles. Draining abscesses frequently become rapidly colonized by other bacteria that overgrow and mask the presence of *S. equi*. Therefore, a negative result on a single short nasal swab from one horse, for example, should not necessarily be taken as assurance that *S. equi* is not involved in an outbreak of respiratory disease in a group of horses. This is because mucosal colonization by *S. equi* may be short-lived and as with draining abscesses the background flora is complex and the presence of *S. equi* may be hidden. Consequently, it is wise always to follow the general rule of thumb that 'if it looks like strangles, then it probably is strangles'.

Bacterial culture Conventional bacterial culture and differential identification from other hemolytic bacterial species, particularly the closely related *S. zooepidemicus*, by sugar fermentation and Lancefield group typing remain the cornerstone of definitive diagnosis of *S. equi* infection. *Streptococcus equi* is conventionally identified by the inability of subcultures of its hemolytic colonies to ferment ribose, sorbitol, trehalose and lactose when inoculated into serum sugar broths and by possession of the Lancefield group C antigen in a latex agglutination test.

In chondroids formed after strangles, *S. equi* can be cultured and demonstrated histologically on the surface and lining fissures within their structure (Figs 31.14, 31.15).

Polymerase chain reaction (PCR) PCR assays are now available for diagnosis of *S. equi* infection on nasopharyngeal swabs or nasal wash samples.[15,16] PCR is used in conjunction with culture to improve the sensitivity of detection of *S. equi*, especially in outwardly healthy but potentially infectious horses that pose a risk of transmission if in close contact with susceptible animals.[4] PCRs have been developed for detection of the DNA of the hypervariable region of the M-protein gene[16] and 16S–23S RNA gene intergenic spacer,[15] which in combination are able to differentiate *S. equi* from the vast majority of subtypes of the ubiquitous but closely related *S. zooepidemicus* species.

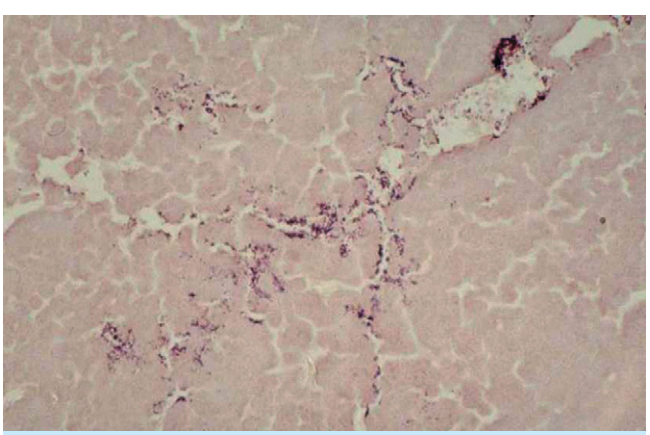


Fig. 31.14
Dark Gram-positive staining *S. equi* lining fissures within a chondroid removed from the guttural pouch of a horse following strangles.

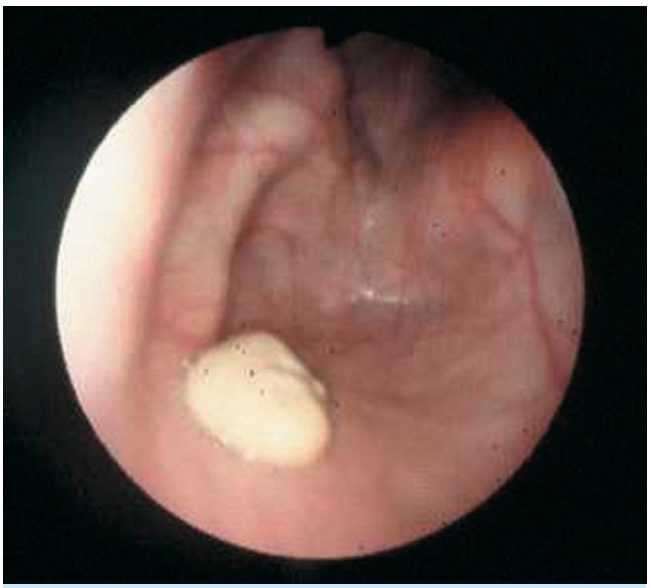


Fig. 31.15
A single chondroid within a guttural pouch.

During recent intensive outbreak investigations in the UK using repeated swabbing of the nasopharynx and endoscopy of guttural pouches, variants of *S. equi* have been isolated from a significantly higher proportion of carriers (24%) compared with clinical cases of strangles (< 1%, Fisher's exact P = 0.0002).[17] The variants lacked DNA that coded for up to 20% of the surface expressed M-protein and were shown to express truncated forms of this protein compared with non-variant *S. equi*.[17] As variants were much more prevalent in outwardly healthy horses than those with signs of strangles, they possibly represented a less virulent but immunizing subtype of *S. equi*, which may have been contributing to herd immunity by acting as a natural, live vaccine. Experimental infection in naïve Welsh mountain ponies has, however, shown that variant *S. equi* expressing a truncated M-protein are as pathogenic as subtypes with the full M-protein, producing typical clinical signs of strangles including lymph node abscessation, 'bastard' strangles (Fig. 31.13) and guttural pouch empyema. This demonstrates that at the present time all carriers should be regarded as potential sources of new strangles outbreaks.

Necropsy examination

Diagnosis of metastatic strangles can often only be made at necropsy in animals found dead or after elective euthanasia for retractable idiopathic disease, with the culture of *S. equi* from abscesses providing a definitive diagnosis of 'bastard' strangles.

Necropsy findings have confirmed that the guttural pouch is frequently the only site of carriage of *S. equi* in otherwise outwardly healthy horses that continue to harbor the organism long after initial infection.

Diagnostic confirmation

The presence of *S. equi*, identified by culture or PCR in appropriate swab, lavage or aspirate samples from horses with evidence of respiratory disease, including guttural pouch empyema or abscessation, confirms a diagnosis of strangles. However, some caution is required with results that are positive by PCR only, as this finding may reflect the persistence of killed bacteria, as was demonstrated in two horses following treatment for guttural pouch empyema and/or chondroids.[18] However, despite the disadvantage that PCR might produce such 'false positives', in the context of presumptively detecting *S. equi* carriers, PCR has the advantage of detecting DNA in the nasopharynx that might have originated from living bacteria in the guttural pouches. Large unguarded nasopharyngeal swabs[6] greatly facilitate the sampling of any material draining from the guttural pouches into the nasopharynx. Given the risk for 'false positives', however, PCR can only be regarded as a presumptive test for *S. equi* carriers until infection has been demonstrated in the guttural pouches by culture.

Treatment and prognosis

Therapeutic aims

The only treatment usually needed for the majority of cases of strangles is provision of a dry and warm environment, palatable and easily swallowed food and good quality nursing care. Maturation and discharge of abscesses should be encouraged by use of poultices and lancing. This should be followed by frequent flushing with 3–5% dilute povidone-iodine solution until discharge of pus ceases. Lancing of abscesses and emergency surgical tracheostomy may be needed when there is acute respiratory obstruction. Non-steroidal anti-inflammatory drugs (NSAIDs) may be administered as appropriate to reduce the pyrexia, pain and inflammation associated with *S. equi* infection and consequently improve the demeanor of affected horses and maintain their appetite (Table 31.1).

The use of antimicrobial therapy in strangles remains extremely controversial. Although *S. equi* is susceptible in vitro to many of the antimicrobials that are commonly used in horses, their effectiveness in vivo may be poor. This is especially true where there has been migration of infection to the lymph nodes or where there is accumulation of pus such as in guttural pouch empyema or 'bastard' strangles. Furthermore, there are frequently problems with recurrence of lymphadenitis and subsequent abscessation some time after the antimicrobial treatment ends. Although it is commonly cited that use of antimicrobials induces metastatic strangles, there is little scientific evidence to support this and this severe complication is known to occur in outbreaks where no such treatment has been used. In addition, use of antimicrobials may instill a false sense of security in owners

Table 31.1 Details of treatments commonly used for strangles and its complications

Drug name	Drug type	Indication	Dose rate	Route of administration	Duration of treatment
Procaine penicillin G	Antibiotic	Treat *S. equi* infection	10,000–20,000 IU/kg q 12–24 h	Intramuscular	5–7 days but longer for metastatic strangles
Ceftiofur	Antibiotic	Treat *S. equi* infection	2 mg/kg q 12–24 h	Intramuscular or intravenous	Up to 10 days
Trimethoprim potentiated sulfonamide	Antibiotic	Treat *S. equi* infection	15–30 mg/kg q 12 h	Oral	Up to 28 days
Phenylbutazone	NSAID	Reduce pyrexia, pain and inflammation	4.4 mg/kg q 24 h	Oral	As required
Flunixin	NSAID	Reduce pyrexia, pain and inflammation	1.1 mg/kg q 12–24 h	Intravenous	Up to 5 days
Meclofenamic acid	NSAID	Analgesia with metastatic strangles	2.2 mg/kg q 24 h	Oral	As required
Dexamethasone	Steroid	Reduce vasculitis with purpura hemorrhagica	Up to 0.20 mg/kg q 24 h	Intramuscular, intravenous or oral	As required

q, Every; NSAID, non-steroidal anti-inflammatory drug.

and veterinary surgeons that animals are no longer infectious and so strict hygiene measures are no longer necessary. Consequently, the use of antimicrobial therapy in strangles outbreaks should be very carefully considered. If antimicrobials are used (Table 31.1) it is strongly recommended there should be continued close clinical monitoring of animals for several weeks after the end of antibiotic administration, during which time the highest standards of hygiene should also be maintained. Further screening of animals during this period by bacterial culture of nasopharyngeal swab or lavage samples is strongly recommended, although false positive PCR results are possible during this time.[18]

Metastatic strangles Treatment of metastatic strangles is possible when abscesses are accessible so that they can be drained and flushed with dilute povidone-iodine. A prolonged course of large dose parenteral procaine benzylpenicillin (Table 31.1) should be initiated and administered daily for several weeks. Alternatively, oral antimicrobial treatment, such as trimethoprim potentiated sulfonamide, can be used for longer periods of treatment.

Other appropriate symptomatic treatment, such as analgesics (Table 31.1), may be administered where indicated. The diagnostic techniques described earlier may be useful in monitoring for remission of abscessation during and following treatment.

Purpura hemorrhagica Treatment of purpura hemorrhagica is aimed (i) at removing antigenic stimulation by *S. equi*, (ii) at reducing the exaggerated immune response, (iii) at reducing vasculitis and (iv) at providing supportive therapy. It has been proposed that this may be achieved by use of procaine benzylpenicillin to treat the *S. equi* infection and intravenous administration of corticosteroids such as dexamethasone (Table 31.1) to suppress the immune response and reduce vessel wall inflammation. However, penicillin treatment is controversial as it can lead to bacterial cell lysis that could increase amounts of circulating M-protein, which may potentially increase immune complex formation and consequently worsen clinical signs. Supportive care, such as leg wraps, light walking exercise, hydrotherapy, diuretics and intravenous fluid administration, should be used as necessary.

Guttural pouch empyema Appropriate approaches to treatment of guttural pouch empyema in individually affected horses depend on the volume and consistency of the material within the pouch(es).[5,12,18–20]

Repeated flushing of pus-filled pouches via rigid bovine uterine catheters or indwelling Foley catheters using saline or dilute povidone-iodine solution, followed by lowering of the head to allow drainage or use of a suction pump attached to the endoscope, have been shown to help the elimination of empyema.[12,18] Administration of both topical and systemic sodium benzylpenicillin improves the success rate of treatment.

Topical instillation of 20% (w/v) acetylcysteine solution has also been used to aid the treatment of empyema.[19] Acetylcysteine, by disrupting disulfide bonds in mucoprotein molecules, has a denaturing/solubilizing activity, thereby decreasing the viscosity of mucus and helping natural drainage from the pouch. Erythema of the guttural pouch mucous membranes has been observed though following use of acetylcysteine.[18]

In more long-standing cases there is inspissation of the purulent material, which produces a thickened empyema and leads to chondroid formation that does not readily drain into the pharynx. These cases are less straightforward to treat by topical therapy as they are usually refractory to large volume irrigation and early attempts at removal by endoscopically guided instruments have been technically difficult and time-consuming. Conventional treatment of such cases has been by the surgical technique of hyovertebrotomy and ventral drainage through Viborg's triangle. This technique, however, carries all the inherent risks of general anesthesia and surgical dissection around the major blood vessels and nerves of this region of the head and neck, as well as the possibility of *S. equi* contamination of the hospital environment and subsequent risk of transmission to susceptible horses. More recently, use of improved sedation techniques and endoscopic instruments, including use of memory-helical polyp retrieval baskets passed through the biopsy channel of the endoscope, now more easily facilitates non-surgical removal of chondroids, even if they are found in very large numbers and in conjunction with empyema. This is usually sufficient for successful treatment of even the most severe guttural pouch pathology when combined with topical and systemic antimicrobial therapy.

Therapy

Table 31.1 summarizes types of therapy with their indications, dose rates, routes of administration and duration of treatment for treatments commonly used with strangles and its complications.

Prognosis

The prognosis for most cases of uncomplicated strangles is good although airway obstruction following enlargement of abscessated lymph nodes of the head and neck may be fatal unless emergency tracheostomy is performed. 'Bastard' strangles may carry a poor prognosis, especially if abscesses are large and not readily accessible for continued external drainage. Purpura hemorrhagica may be rapidly fatal despite appropriate treatment.

Etiology and pathophysiology

Etiology

Strangles is caused by a primary infection with *Streptococcus equi*, a Gram-positive, Lancefield group C, beta-hemolytic bacterium.

Molecular characterization of *S. equi* and the closely related *S. zooepidemicus* has shown that isolates of *S. equi* are antigenically more similar and are actually derived from the antigenically more diverse *S. zooepidemicus* species. Various molecular typing techniques such as random amplified

polymorphic DNA analysis (RAPD), multilocus enzyme electrophoresis (MEE) and pulsed-field gel electrophoresis (PFGE) have been applied to different *S. equi* isolates from around the world and show that not all isolates are antigenically identical. However, to date no correlation between antigenically distinct types and clinical severity of outbreaks has been shown using these techniques.

Pathophysiology

The incubation period for strangles varies between 3 and 14 days depending on infectious dose and the host's immune status. There appears to be a very rapid (within hours of colonization) transfer of *S. equi* infection from the site of initial infection usually on the buccal or nasopharyngeal mucosal surfaces to the draining lymph nodes of the head and neck. *S. equi* is able initially to resist phagocytosis by polymorphic leukocytes but this is then followed by a massive recruitment of white blood cells with consequent abscess formation with associated fibrosis and walling off of infection. Eventually abscesses discharge through the weakest point, which is usually the skin in the case of the submandibular and parotid lymph nodes but dorsally through to the lumen of the guttural pouch for retropharyngeal lymph nodes. Horses usually make a rapid and uneventful recovery following natural drainage of abscessated lymph nodes. Metastatic strangles is believed to follow blood- or lymph-borne metastasis of *S. equi* infection to sites distal to infected lymph nodes. The signs of purpura hemorrhagica are mediated through immune complexes formed between the M-protein antigen of *S. equi* and immunoglobulins of the host's exaggerated immune response.[10,11]

Epidemiology

Active and recovering strangles cases are an extremely important and easily recognizable source of new *S. equi* infections for susceptible horses through their purulent discharges from lymph nodes, nose and eyes. Transmission of *S. equi* infection occurs when there is either direct or indirect transfer of these purulent discharges between affected and susceptible horses. Direct transmission refers to horse-to-horse contact, which occurs through normal equine social behavior involving head-to-head and nose-to-nose contact.

Indirect transmission occurs with the sharing of contaminated housing, water sources, feed or feeding utensils, twitches, tack, and other less obvious fomites such as the clothing and equipment of handlers and veterinary surgeons and, anecdotally, even via other animal species.

The organism is also able to remain viable and infectious in the environment for extended periods if maintained in moist discharges, particularly when not exposed to chemical disinfectants and/or sunlight.[21]

It is increasingly recognized that transmission originating from outwardly healthy animals may be of greater importance than from purulent discharges from sick horses because the source of infection is not obvious and appears suddenly and without warning.

Horses that are incubating the disease are outwardly healthy and potentially infectious but do themselves go on to develop signs of strangles. It is assumed that normal nasal secretions are the source of infection in these animals. The other important outwardly healthy but potentially infectious horses are those convalescent cases that continue to harbor the organism after full clinical recovery. A moderate proportion of horses continue to harbor *S. equi* for several weeks after clinical signs have disappeared, although in the majority the organism is no longer detectable 4 to 6 weeks after total recovery. It is therefore appropriate to consider all recovered horses as potentially infectious for at least 6 weeks after their purulent discharges have dried up.

In a proportion of outwardly healthy, potentially infectious horses, carriage and at least periodic shedding of *S. equi* occurs for prolonged periods after apparent full and uncomplicated recovery. These horses are commonly referred to as long-term, asymptomatic *S. equi* carriers and there is strong anecdotal evidence that they can be a source of new disease in a large proportion of outbreaks, even in well-managed groups of horses.[4,12] If strangles control measures are to be fully effective there must be recognition of the importance of carrier animals and appropriate detection and management of these animals.[4,5,18]

It appears probable that short-lived empyema of the guttural pouches is the most common outcome of uncomplicated drainage of RPLN abscessation. However, in up to 10% of horses in strangles outbreaks[4] there is apparent failure of this clearance mechanism resulting in chronic empyema of the pouch. The failure of drainage of the guttural pouch may be related to the extended periods for which some housed horses are kept with their heads elevated. In some horses, guttural pouch empyema with *S. equi* infection may persist asymptomatically for many months or even years.[6] In these long-standing cases pus in the pouches inspissates and then eventually forms into discrete, ovoid, smooth concretions known as chondroids. Chondroids may occur singly (Fig. 31.15) or as multiples (Fig. 31.16), sometimes in very large numbers, and have been shown to harbor viable *S. equi* within their core (Fig. 31.14).

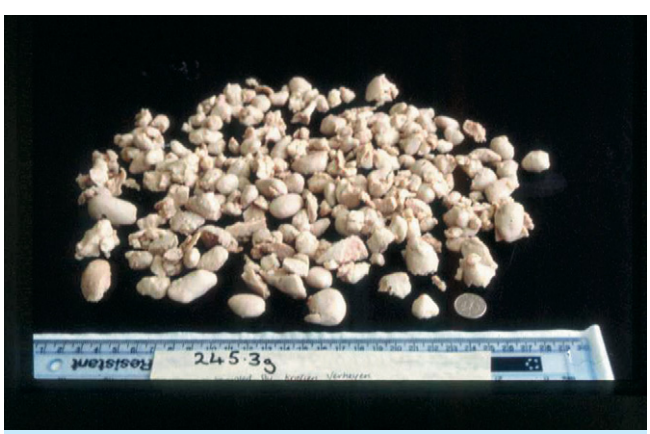


Fig. 31.16
Multiple chondroids removed non-surgically from the guttural pouch of a horse after strangles.

By the identification, segregation and treatment of these potentially infectious horses, prolonged outbreaks have been successfully controlled and further outbreaks undoubtedly prevented.[4,5,12] A systematic program of repeated nasopharyngeal swabbing or nasal washing (i.e. at least three samples taken at weekly intervals) of horses following the cessation of clinical signs or during quarantine of incoming horses, using conventional culture in conjunction with PCR, has successfully identified carrier horses.[4]

Control of outbreaks

Investigation of strangles outbreaks by veterinary surgeons should begin with a detailed history to evaluate the full extent of the potential disease problem. The review should aim to identify affected groups of horses and allow the geography of the premises and the management practices on them to be assessed for further risks and future opportunities for disease control. A practical disease control strategy should then be agreed and implemented. The general aims and measures for such a strategy are outlined in Table 31.2. However, this outline strategy will need to be adapted to the individual circumstances of each specific premises and outbreak.

In summary, all movements of horses on and off the affected premises should be stopped immediately with implementation of parallel segregation and hygiene measures. Strangles cases and their contacts should be kept in clearly marked 'dirty' (i.e. *S. equi* positive) areas of isolation. The overall aim of the control strategy, following bacteriological screening, is to move horses from the 'dirty' to 'clean' areas where non-affected and non-infectious horses are kept. Considerable care should be taken to maintain the highest standards of hygiene throughout the premises and for the duration of the investigation. Screening of all convalescing cases and their healthy contacts should be conducted using nasopharyngeal swabs or lavages, with special care taken to maintain good hygiene to avoid inadvertent transmission between horses during sampling. Repeated weekly swabs or lavages should be taken over several weeks and tested for *S. equi* by conventional culture and PCR, but because PCR can detect dead as well as living bacteria, positive PCR results should only be regarded as provisional, subject to further investigation. Most asymptomatic, long-term carriage of

Table 31.2 Aims and measures used to control transmission of *S. equi* on affected premises

	Aim	Measure
1.	To prevent the spread of *S. equi* infection to horses on other premises and to new arrivals on the affected premises	Stop all movement of horses on and off the affected premises immediately and until further notice
2.	To establish whether horses are infectious in the absence of clinical signs of strangles (i.e. asymptomatic carriers)	At least three nasopharyngeal swabs or lavages are taken at approximately weekly intervals from all recovered cases and their contacts and tested for *S. equi* by culture *and* PCR
3.	To determine if horses are likely to be free from infection with *S. equi* (i.e. non-infectious for strangles)	At least three consecutive nasopharyngeal swabs or lavages are negative for *S. equi* by culture and PCR
4.	To determine if horses are likely to be harboring *S. equi* (i.e. infectious for strangles)	*S. equi* is cultured or detected by PCR on any of the screening swabs. (Horses with only positive PCR results are considered provisionally positive subject to further tests)
5.	To prevent direct transmission of *S. equi* infection by isolation of infectious horses from those screened negative for *S. equi*	Infectious horses are maintained in so-called 'dirty' (i.e. *S. equi* positive) isolation areas that are physically cordoned from the other 'clean' areas of the premises where non-infectious horses are kept. Clustering of cases in groups should allow parts of the premises to be easily allocated as 'dirty' and 'clean' areas
6.	To prevent indirect cross-infection by *S. equi* from horses in the 'dirty' area to those in the 'clean' area of the premises	Potentially infectious horses in the 'dirty' area are preferably looked after by dedicated staff or are dealt with *after* non-infectious horses in the 'clean' area. Strict hygiene measures are introduced including provision of dedicated clothing and equipment for each area, disinfection facilities for personnel and thorough stable cleaning and disinfection methods
7.	To monitor horses in the 'dirty' areas for persistence of *S. equi* infection and to establish sites of carriage of infection	Nasopharyngeal swabbing or lavages are continued with endoscopic examination of the upper respiratory tract including guttural pouches in those horses in which *S. equi* was detected after clinical signs had disappeared. Horses that satisfy the non-infectious criteria of measure 3 above or have at least the third swab of the series negative by PCR (to allow for possible persistence of PCR-positive but dead bacteria) are returned to the 'clean' area
8.	To eliminate inflammation and *S. equi* infection from the guttural pouches and other sites	Removal of lesions through a combination of flushing and aspiration of saline and removal of chondroids using endoscopically guided instruments. Topical and systemic administration of penicillin antimicrobial treatment to eliminate *S. equi* infection (see 'Treatment and prognosis')

S. equi occurs in the guttural pouches of recovered horses. Therefore endoscopy of the upper respiratory tract, especially the guttural pouches, should be performed in all outwardly healthy horses in which *S. equi* is detected, either by culture or by PCR. Guttural pouch lavages should also be tested for *S. equi* using culture and PCR. Other sites such as the nasal sinuses or trachea should also be considered in horses that continue to harbor *S. equi* in the absence of pathology or *S. equi* infection of the guttural pouches.[3]

Prevention

Although more preferable than controlling outbreaks, prevention of strangles is extremely difficult to achieve, particularly in the absence of specific measures aimed at reducing the risk of inadvertent introduction of *S. equi* infection through asymptomatic carriers. Prevention is especially problematic where there is frequent movement and mixing of horses and where strangles outbreaks elsewhere have not been appropriately investigated and controlled or are known about. Wherever possible animals being introduced to a new population of horses should be maintained in strict isolation (quarantine) where they are screened for *S. equi* by repeated nasopharyngeal swabs or lavages. This should be performed in accordance with the protocol outlined for controlling outbreaks (i.e. three samples taken at weekly intervals), with samples tested for *S. equi* by culture and PCR and animals testing positive by either test being retained in isolation for further investigation and treatment. High standards of hygiene should also always be maintained to avoid indirect transmission between quarantined and resident horses.

Vaccination

Although strangles occurs in most countries around the world, relatively few nations currently use vaccination as a means of control or prevention and in those areas where it is used, strangles remains an endemic and extremely significant equine infectious disease. Despite there being some limited scientific evidence to show that strangles vaccines are effective in reducing the severity of disease, the protective immunity that they convey is generally poor and very short-lived. Importantly, as well as their limited effectiveness, many problems have been encountered with both local and systemic reactions to strangles vaccines. Although the original heat-inactivated whole culture vaccines (so-called bacterins) have higher rates of reaction compared with the later protein-rich extract products, both have been associated with an unacceptably high level of adverse effects. Recently a live, intranasal vaccine based on an apparently avirulent and naturally occurring strain of *S. equi* has been used in North America. Whilst this type of vaccine, if it remains truly avirulent, might have superior immunizing ability and minimal side effects compared with the intramuscularly administered inactivated or protein-based vaccines, there have also been problems reported with adverse reactions to this live mutant vaccine strain of *S. equi*. Reactions similar to those signs seen in the natural disease have been reported, albeit at a lower rate than encountered with disease. Such signs include nasal discharge, abscessation of lymph nodes and other sites, allergic reactions, systemic responses and purpura-like signs. These reactions and the occurrence of *S. equi* abscesses at the site of intramuscular injection given immediately after intranasal administration of this vaccine demonstrate the potential of this product to produce strangles-like signs in horses.

In keeping with other streptococcal pathogens, the virulence of *S. equi* is most probably determined by a complex series of multiple, genetically coded determinants. This is demonstrated by the lack of efficacy of M-protein vaccines and by the ability of a live, intranasal vaccine strain, the naturally occurring M-protein gene deletion mutants and heat-inactivated bacterin vaccines to all produce abscesses. Therefore, in order to produce a truly effective strangles vaccine with maximal efficacy and minimal side effects, it will be necessary to have knowledge and understanding of the mechanisms of the vast majority, if not all, of these determinants. To this end, the entire DNA genome of *S. equi* has recently been sequenced.

Detailed analysis of the *S. equi* genome should provide novel understanding of the mechanisms by which *S. equi* causes strangles in horses and how it manages to evade host immune responses. Further research based on the genome sequence should lead to the development of more effective and safer strangles vaccines for horses.

The role of bacteria, including *Streptococcus zooepidemicus*, in inflammatory airway disease

- Inflammatory airway disease is common in athletic horses.
- Some, but not all, cases are associated with bacterial infection, in particular *Streptococcus zooepidemicus* and *Actinobacillus*/*Pasteurella* spp.
- The role of environmental factors, such as stabling, is debated.

Recognition of disease

Clinical recognition of inflammatory airway disease (IAD) associated with bacteria follows standard patterns for the diagnosis of IAD, with the simple addition that quantitative bacteriology is needed to assess the presence of bacteria (and their clinical significance). Recognition is thus not discussed at length here, but rather, readers are referred to Chapter 29 in this book.

Etiology and pathophysiology

Etiology

There are few published studies that consider the role of either viruses or bacteria in the etiology of IAD. Most studies that do consider their role in IAD are based on disease in young race horses, although there are some that consider lower respiratory tract disease in foals.

Multidisciplinary epidemiological studies of IAD have provided strong evidence for a multifactorial etiology of IAD.[22] It is not argued here that bacteria are the only cause of IAD, merely that they are likely to be responsible for a significant proportion of the syndrome as a whole.

IAD associated with bacteria has been most extensively studied in Thoroughbred race horses in the UK; there are also several published studies of the relationship between bacteria and respiratory disease in young Thoroughbred race horses in Australia. The evidence for a role of bacteria in IAD in these young animals is reviewed below. Disease of the older horse is not considered here, not because bacteria cannot play a role in such animals, but rather because there are no published studies that objectively consider any such role.

When reviewing the evidence, the mean duration of cases of acute IAD in young race horses – around 2 months – needs to be considered.[22,23] In this respect, conclusions derived from cases seen at secondary and tertiary referral institutes are likely to be quite different in nature from those that come from population-based epidemiological investigations.

It is important that associations between disease and the presence of infections are analyzed quantitatively when considering evidence of possible causation. This is expensive and time-consuming in large-scale epidemiological studies, but nonetheless important. Evidence for epidemiological associations being causal requires careful and inclusive evaluation of all possible evidence.[24] Difficulties with experimental animal models means that *direct* evidence for causation will only be available when the impact of effective vaccination programs is studied in comparative and controlled studies. Such studies will not be possible until efficacious vaccines against the major bacterial agents implicated have been developed. In the field, it is often not possible to isolate implicated bacterial infections in pure culture from cases of disease; mixed infections are the norm, as indeed they are in cases of pneumonia in both horses and farm animals. However, this section is restricted to IAD; the presence of bacteria reported from cases of pneumonia is not considered here.

Direct evidence In young race horses, *Streptococcus pneumoniae* capsule type 3 has been recognized for some time as an important respiratory pathogen[25] – and its first reported isolation from horses dates back more than 30 years ago.[26] This is a major respiratory pathogen in humans, although the capsule type 3 isolated from horses appears genetically distinct from human strains, being deficient in pneumolysin and streptolysin, these being major pathogenic determinants.[27] Not only was the infection associated with the presence of IAD,[25] which the authors referred to as lower respiratory tract disease using a case definition that would classify it as IAD, but they were also able to reproduce signs of IAD experimentally by instilling the organism into the trachea of resting ponies.[28]

This preliminary epidemiological and experimental evidence for *S. pneumoniae* has been further supported by additional strong evidence from large-scale epidemiological studies of respiratory disease in young race horses in both Britain and Australia. In Britain, there was a close association between the organism and IAD in 2-year-old horses[29] and the infection was associated with coughing in young race horses in Australia;[30] although IAD itself was not studied, 85% of the cases of coughing in this study were suffering from IAD. This infection is relatively uncommon in cases of respiratory disease in young race horses (6%:[23]; 12%:[30]) in contrast to *Streptococcus zooepidemicus* and the *Actinobacillus/Pasteurella* group of bacteria.

Several of these studies of IAD or coughing in young race horses have reported a close association between the presence of *S. zooepidemicus*, particularly in large numbers, and IAD[22,29,31] as well as with coughing or other non-specific signs of respiratory disease.[30,32] However, there are few if any published reports of attempts to reproduce disease experimentally in equids with either organism, although septicemia can be induced with intravenous challenge[33] and disease can be reproduced in both mice and llamas with *S. zooepidemicus*.[34]

Along with *S. pneumoniae* and *S. zooepidemicus*, *Actinobacillus/Pasteurella* spp. have been found to be associated with IAD, coughing and non-specific signs of respiratory disease in young race horses in Britain and Australia.[22,23,29–32,35,36] In every published study, *S. zooepidemicus* was the bacterium associated with IAD most commonly isolated from the trachea.[22,23,29–32,36,37] As *S. zooepidemicus* was also the bacterium usually isolated in the largest numbers, it would be reasonable to conclude that this bacterial species probably plays the largest role of all conventional bacteria in the disease syndrome.

Indirect evidence All studies of IAD in young horses have found that the likelihood of disease, the prevalence and/or the incidence of IAD decrease as animals get older (Fig. 31.17)[22,23,29–32,36,37] or have spent longer in the stable environment.[30,32,36,37]

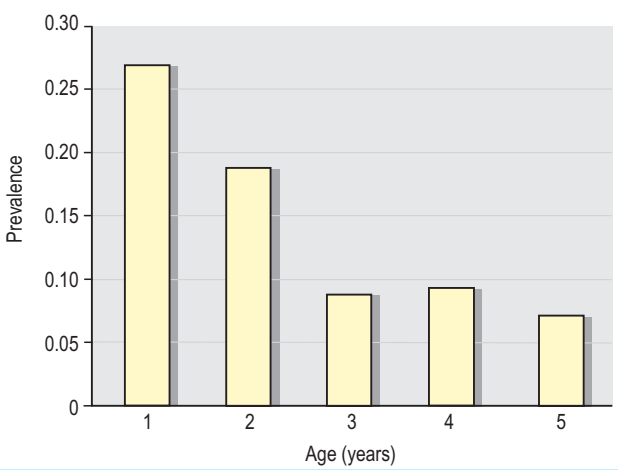


Fig. 31.17
Variation in prevalence of IAD in young race horses with age.

It is clear that a poor environment can exacerbate or prolong IAD[22] but our observations that IAD is frequently observed in weanling pony foals kept at grass[37] argue strongly against the stable environment being the only cause.

Desensitization to stable environmental contaminants could be hypothesized as a reason for a decrease in the frequency of disease in older animals, but this is most unlikely given that sensitization to them is implicated in the causal pathway of RAO in the older animal.

It is most likely that the decreases in the rates of IAD in older animals that correlate with the length of time in the stable environment and/or increasing age are due to the development of immunity to the infections that are responsible for a large part of the disease. The multidisciplinary investigations of IAD that have been undertaken have generally reported that these infections are usually bacterial rather than viral.[29]

Are the associations reported from epidemiological studies causal? Particular care needs to be taken when considering evidence of causation from epidemiological studies. Most of the studies referred to above used multivariable statistical methods, which reduces the likelihood of confounding, at least by measured variables. Furthermore, use of the nine Bradford Hill criteria[24] to assess whether the epidemiological associations between these bacteria and IAD are likely to be causal does suggest that bacteria do cause lower respiratory tract disease in horses.

Several studies have confirmed a reasonable strength of association (measured as relative risk) and a significant biological gradient for these bacteria and IAD, with increasing numbers of bacteria having a greater strength of association with disease.[22,25,29,36,38,39] Examination of tracheal wash data from young Thoroughbred race horses using a zero to nine ordinal scoring of airway inflammation demonstrates a significant biological gradient for increasing mean $\log_{10}$ colony-forming units (CFU) per milliliter of *S. zooepidemicus* and *Actinobacillus/Pasteurella* and increasing inflammation score (Fig. 31.18). There was no such gradient for *Staphylococcus*.

The associations with IAD are also specific for the three bacterial species of *S. zooepidemicus*, *Actinobacillus/Pasteurella* and *Streptococcus pneumoniae* and are consistent between different studies.[22,25,29,36,38,39] Bacterial infections as causes of IAD in young horses are biologically plausible, are coherent as the results do not conflict with current knowledge and are analogous with similar and identical bacteria being the cause of respiratory disease in other species. Furthermore, *S. equi*, a subtype of *S. zooepidemicus*,[15] causes 'strangles' in horses and is generally accepted as a primary bacterial equine pathogen. There is experimental evidence that intratracheal inoculation of *S. pneumoniae* causes IAD and pneumonia in young pony foals, with the organism being recovered from the trachea and pneumonic lesions.[28] A temporal relationship between bacterial infection and IAD is difficult to confirm due to the possibility of an earlier predisposing viral infection. However, results of a longitudinal study of IAD failed to show that the association between bacteria and IAD is dependent on prior infection with any of the known equine viruses[29] – and infection with the most common virus, equine herpesvirus 1/4, which was also the only virus statistically associated with IAD, was only detected in 7.5% of cases, despite the use of sensitive serological techniques.

Epidemiology

The results from investigations of endemic IAD in training yards,[22,23,39] as well as from outbreak investigations[35,40] have been reported. The substantial variation between years and between training yards in the prevalence of IAD (Fig. 31.19) gives the syndrome, at least in the UK, the appearance of occurring in outbreaks,[23] suggesting an infectious etiology.

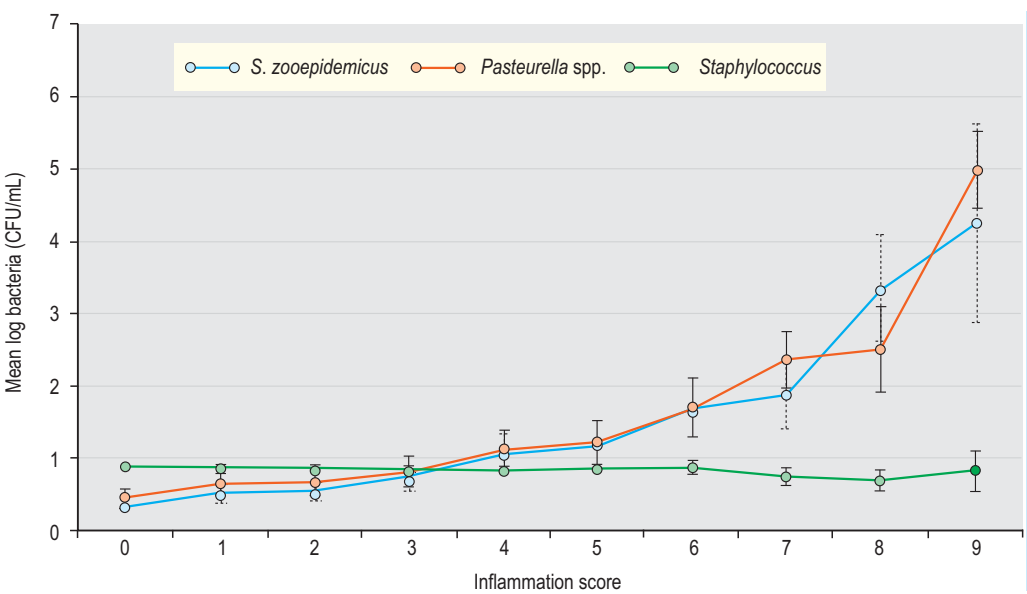


Fig. 31.18 Variation in mean $\log_{10}$ CFU/mL of three bacterial species with inflammation score in young race horses.

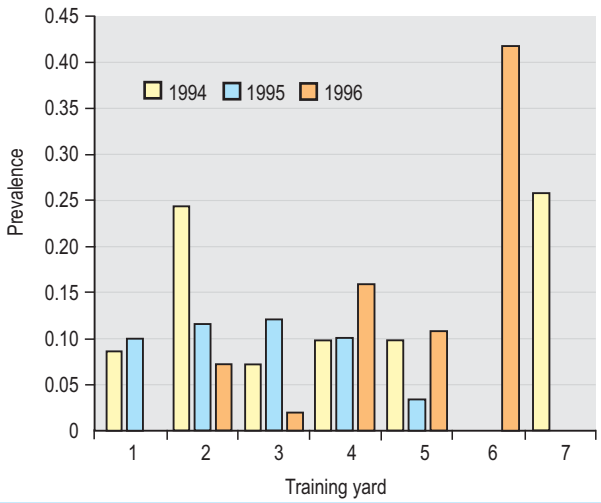


Fig. 31.19
Variation in prevalence of IAD in young race horses with year and trainer.

The disease in Britain is generally much more common in the winter and early spring, declining in prevalence through the year until the annual recruitment of young susceptible yearling animals into training yards in the autumn (Fig. 31.20). This is again consistent with the acquisition of immunity in individual animals and the progressive development of herd immunity in relatively stable groups through the year.

We have studied the molecular epidemiology of *S. zooepidemicus* in both horses in training and young ponies at grass;[37] workers from Kentucky have also reported results from similar investigations based on bacterial genotype and phenotype.[16,41] The molecular results have shown that, within a background of apparently constant *S. zooepidemicus* challenge, different strains of the bacterium are spreading or declining through different groups of animals.[37] All of the studies undertaken thus far have been too small to reliably detect small differences in pathogenicity between different strains; no large differences have yet been reported. The results, along with those from detailed evaluation of *Pasteurella* spp. subtypes,[42] indicate that great care needs to be taken when interpreting results from studies that have not used detailed molecular tools that identify differences between otherwise identical strains of these bacteria. Much more dynamic spread of different, non-cross-reactive strains is likely to be occurring between and amongst groups of horses than is apparent when using traditional microbiological methods.

Much work is necessary to clarify the role of bacteria in IAD, particularly in the older horse, but there is increasing acceptance that, at least in the acute disease in the young equine athlete, bacterial infections play an important role in the etiology.

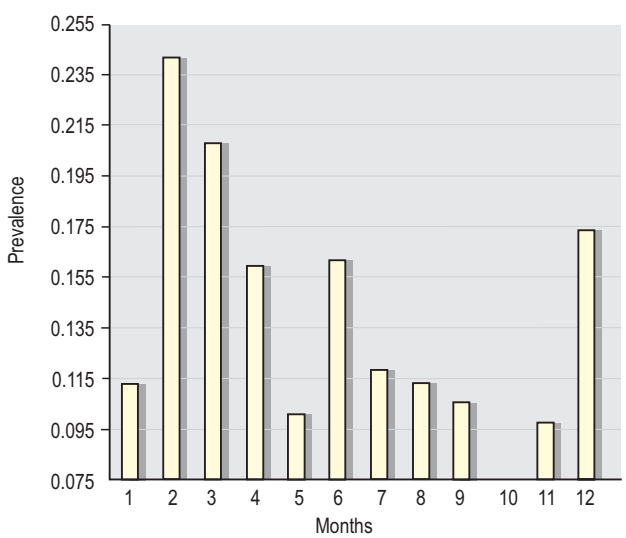


Fig. 31.20
Variation in prevalence of IAD in young race horses with month of the year.

Equine pleuropneumonia (pleuritis, pleurisy)

- Combination of pneumonia and accumulation of inflammatory exudate in pleural space is referred to as pleuropneumonia.
- Risk factors for development of the disease include transportation, viral respiratory disease, general anesthesia, esophageal obstruction, and penetrating chest wound.
- Clinical signs include combinations of fever, depression, anorexia, exercise intolerance, nasal discharge, mucopurulent nasal discharge and cough.
- Identification of pneumonia and inflammatory, septic pleural fluid confirms the diagnosis.
- Tracheal aspirate fluid and pleural fluid should be cultured and the results used to direct treatment.
- Treatment involves prolonged administration of antimicrobials and drainage of pleural fluid.
- Prognosis for life is good with aggressive treatment. Prognosis for return to racing is fair.

Recognition of disease

History and presenting complaint

Horses with pleuropneumonia frequently have a history of transportation over long distances (> 800 km), recent viral respiratory disease or contact with horses with evidence of infectious respiratory disease, recent general anesthesia, choke (esophageal obstruction), rupture of the esophagus or penetrating chest wound.[43,44] While spontaneous disease does occur, most cases in athletic horses are associated with one of these risk factors. The presence of pleural effusion in a horse lacking one of these risk factors should raise the index of suspicion of unusual underlying disease, such as neoplasia or congestive heart failure.

Physical examination

Acute pleuropneumonia is characterized by the sudden onset of combinations of fever, depression, inappetence, cough, exercise intolerance, respiratory distress, shallow respirations, respiratory distress and nasal discharge. Horses with chronic disease have exercise intolerance, weight loss, mild depression, intermittent fever, cough and mucopurulent nasal discharge.

Acutely affected horses are usually pyrexic, tachycardic and tachypneic. Pyrexia, while an expected finding, is not always detected, especially in horses administered non-steroidal anti-inflammatory drugs. Inappetence and depression are common clinical signs. Spontaneous coughing is unusual although manipulation of the trachea or pharynx will usually induce a soft cough. The horse may be reluctant to move or may exhibit signs of chest pain, including reluctance to move, pawing and anxious expression, that may be mistaken for colic, laminitis or rhabdomyolysis. Affected horses often stand with the elbows abducted and walk with a stiff, stilted gait taking small steps. Thoracic excursions during breathing are shallow. Nasal discharge ranges from serosanguineous to mucopurulent and occurs from both nostrils. The breath may be malodorous.

Horses with chronic pleuropneumonia have intermittent fever, mild tachycardia and tachypnea. Inappetence and weight loss are usual. Exercise intolerance is marked and exercise may be associated with coughing, subsequent fever and mucopurulent nasal discharge. Nasal discharge ranges from serosanguineous to mucopurulent, is usually present in both nares and is exacerbated when the horse lowers its head. The breath may be malodorous, although this is a more common finding in horses with subacute to chronic disease. Ventral edema occurs in approximately 50% of horses with pleuropneumonia.[44]

Auscultation Auscultation of the thorax reveals attenuation of normal breath sounds in the ventral thorax in horses with significant accumulation of pleural fluid. However, the attenuation of normal breath sounds may be mild and difficult to detect, especially in large or fat horses or in horses in which there is only slight accumulation of pleural fluid. Auscultation of the thorax with the horse's respiratory rate and tidal volume increased by having it breathe with a large airtight bag over its nostrils may reveal crackles and wheezes in the dorsal lung fields and attenuation of the breath sounds ventrally. However, this procedure is unnecessary and not recommended if there is clear evidence of pulmonary disease or pleural effusion is detected on routine auscultation or other examination. There is often fluid in the trachea detectable as a tracheal rattle.

Percussion Use of percussion to detect accumulation of pleural fluid requires knowledge of the boundaries of the lung fields in a normal horse. The boundaries of the lung fields are the 17th intercostal space at the level of the tuber coxae, 16th space at the level of the tuber ischii, 13th space at the level of the midthorax, 11th space at the level of the shoulder and 6th space at the olecranon (Fig. 31.21). Percussion of the chest wall in horses with excessive pleural fluid or pulmonary consolidation will reveal a clear line of demarcation below which the normal resonant sounds are muffled. This line of demarcation represents the dorsal limit of the pleural fluid. Both lung fields should be examined to identify localized areas of consolidation. Careful percussion of the thorax is a cheap and effective means of identifying the presence and extent of pleural fluid accumulation.

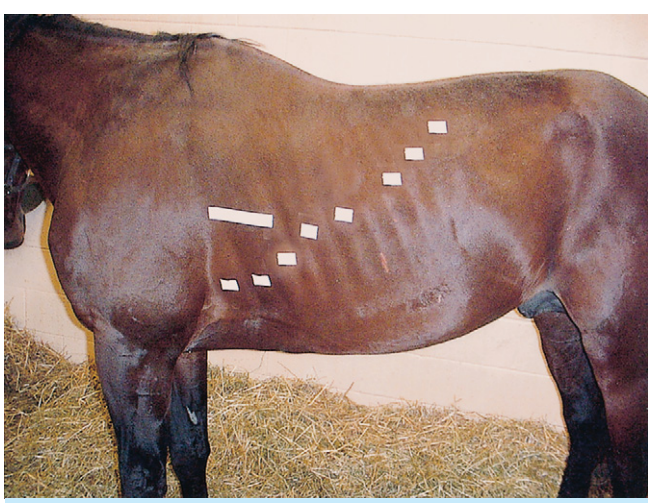


Fig. 31.21
Lung fields as detected by percussion. Short white marks indicate normal lung fields. Long white mark indicates level of fluid accumulation in a horse with pleuropneumonia.

Special examination

Ultrasonography Ultrasonographic examination of horses suspected of having pleural effusion provides definitive identification of presence of fluid. Thorough

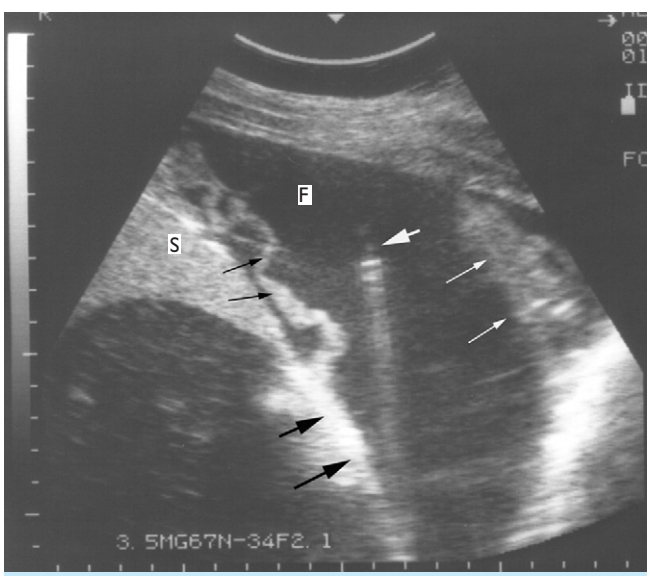


Fig. 31.22
Ultrasonogram of the left hemithorax of a horse with acute pleuropneumonia demonstrating accumulation of fluid (F) within the pleural space, an atelectic lung lobe (small white arrows) and free gas within the pleural fluid (large white arrow). The spleen (S), diaphragm (large black arrows) and pericardial-diaphragmatic ligament (small black arrows) are evident. Dorsal is to the right of the photograph.

ultrasonographic examination of both hemithoraces invariably reveals the presence of excessive pleural fluid in horses in which it is present (Fig. 31.22). It is a very sensitive technique with which to detect accumulation of pleural fluid, determine the character of the fluid, identify localized areas of fluid accumulation or pulmonary consolidation, identify sites for thoracocentesis and to monitor response to treatment.[45,46] Pleural fluid initially accumulates ventrally in acute cases, but may become localized dorsally in chronic cases with septation of the pleural space and trapping of fluid. Ultrasonographic examination is much more sensitive in detecting the presence of pleural effusion than is thoracic radiography.[45]

The examination is best performed using a 3.5 to 5.0 sector scanner. Linear probes, such as those used for routine reproductive examination, are adequate to identify fluid but do not allow good examination of all areas of the chest accessible with sector scanners. The entire thorax should be examined in a systematic fashion. The presence of and characteristics of fluid within the pleural space, presence and location of pulmonary consolidation or abscessation and potential sites for diagnostic and therapeutic thoracocentesis should be identified. For horses with long-standing disease, the area cranial to the heart should be examined for the presence of cranial thoracic masses (abscesses). This examination requires that the horse's ipsilateral forelimb be placed well forward, usually with the aid of an assistant, to allow adequate visualization of the cranial thorax.

The ultrasonographic characteristics of the pleural fluid should be noted. Pleural fluid may contain small gas echoes, an indication of infection with anaerobic bacteria and a poor prognosis,[46] strands of fibrin, or echogenic material consistent with cellular debris (Fig. 31.22). Sterile pleural effusion, such as may be present during the earliest stages of the disease, is clear and homogeneous without fibrin strands. With increasing chronicity the amount of fibrin increases, the parietal and visceral pleura become thickened, and the pleural fluid becomes echogenic consistent with the presence of cellular debris. Regions of consolidated or atelectic lung adjacent to the visceral pleura may be evident on ultrasonographic examination (Fig. 31.22), but lung consolidation deeper in the lung cannot be visualized on ultrasonographic examination.

Radiography Radiographic examination of horses with excessive pleural fluid reveals ventral opacity which obscures the ventral diaphragmatic and cardiac silhouettes (Fig. 31.23). It is not possible on radiographic examination to differentiate accumulation of pleural fluid from consolidation of the ventral lung lobes.[45] Radiographic examination may be useful in demonstrating lesions, such as pulmonary abscesses or consolidation, that are not confluent with the visceral pleura and therefore not able to be detected by ultrasonographic examination (Fig. 31.24). The dorsal lung regions, visible above the line of fluid and consolidation, often have a severe interstitial opacity and evidence of bronchopneumonia. Pneumothorax may be present in horses in which thoracocentesis has been performed or chest tubes have been placed, or that have developed bronchopleural fistulae.

Thoracocentesis and tracheal aspiration Pleural fluid should be collected by thoracocentesis of both hemithoraces and submitted for cytologic and bacteriologic examination.

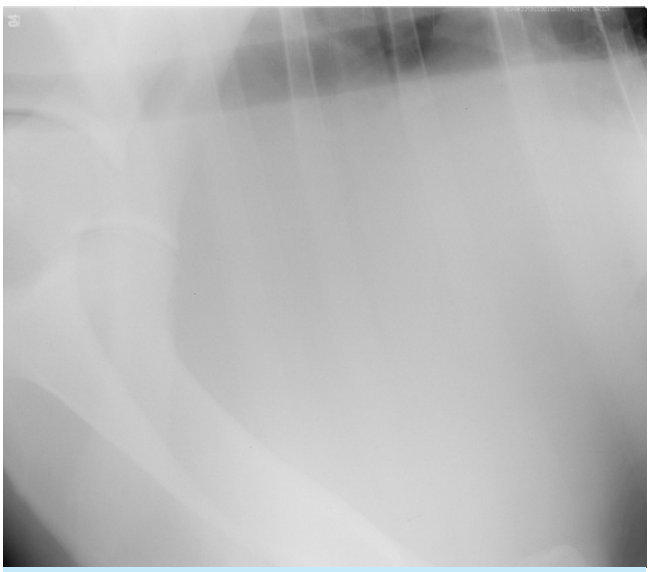


Fig. 31.23
Lateral thoracic radiograph of a horse with acute pleuropneumonia. Accumulation of fluid in the pleural space obscures the cardiac and ventral diaphragmatic silhouette.

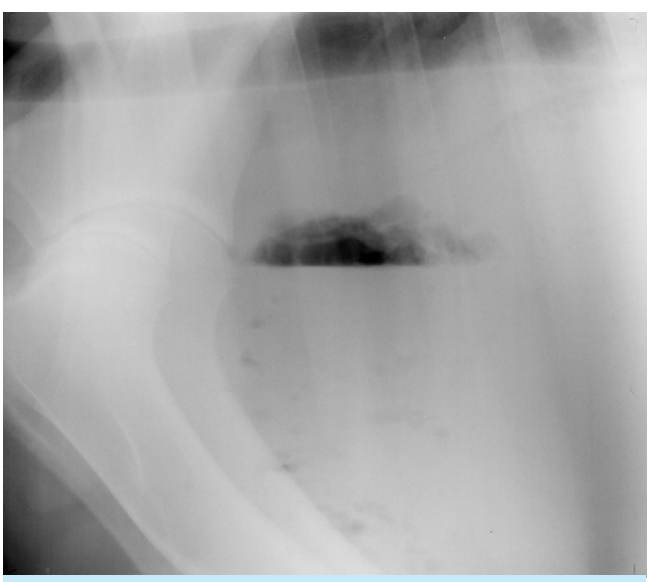


Fig. 31.24
Lateral thoracic radiograph of a horse with pleuropneumonia. Abscessation within the cranial thorax is evident.

Collection of pleural fluid is essential in confirming the diagnosis, allowing culture of the causative bacteria, and providing a baseline cell count and protein concentration by which to judge the success of treatment.

A tracheal aspirate should be collected and submitted for bacteriologic and cytologic examination. Both tracheal aspirates and pleural fluid should be examined in any horse with pleuropneumonia as bacteria may be recovered from one, but not the other, sample.[47] Examination of bronchoalveolar lavage fluid is not useful in diagnosing pleuropneumonia in horses.[48]

Laboratory examination

Hematology and serum biochemistry Acute pleuropneumonia is characterized by leukocytosis with a mature neutrophilia, mild to moderate anemia, hyperfibrinogenemia, and hypoalbuminemia.[49] There are similar findings in horses with chronic disease and hyperglobulinemia is also usually present. Severely affected horses with acute disease often have hemoconcentration and azotemia.

Pleural fluid and tracheal aspirates

Pleural fluid in acute cases is usually cloudy and red to yellow. It has an increased leukocyte number ($> 10.0 \times 10^9$ cells/L) composed principally of degenerative neutrophils, and an abnormally high protein concentration (> 2.5 g/dL, 25 g/L), and may contain intracellular and extracellular bacteria.[50] A Gram stain of the fluid should be examined. The pleural fluid should be cultured for aerobic and anaerobic bacteria. A putrid odor suggests infection by anaerobic bacteria. Sterile pleural fluid has pH, Po_2 and Pco_2 and lactate, glucose and bicarbonate concentration similar to that of venous blood.[51] Infected pleural fluid is acidic, hypercarbic and has an increased concentration of lactate and decreased concentrations of bicarbonate and glucose compared with venous blood.[51]

Tracheal aspirates have a leukocytosis comprised of degenerate neutrophils with intra- and extracellular bacteria. Cultures of tracheal aspirates more frequently yield growth than do cultures of pleural fluid (90% versus 66%).[47]

Isolation of bacteria from tracheal aspirates or pleural fluid may be affected by prior antimicrobial treatment. The chances of culturing bacteria from tracheal aspirate or pleural fluid samples may be increased by collection of samples after withholding antimicrobials from the horse for 24 hours. While briefly withholding antimicrobials may not be contraindicated in horses with chronic disease, it is not recommended for horses with acute disease.

Necropsy examination

The pneumonia involves all areas of the lungs but is most severe in the cranial and ventral regions. The pleura are thickened and have adherent fibrin tags and there is excessive pleural fluid. The pleural fluid contains strands of fibrin and is usually cloudy and serosanguineous to yellow. Histologically, there is a purulent, fibrinonecrotic pneumonia and pleuritis.

Diagnostic confirmation

The presence of excessive pleural fluid containing bacteria and degenerate neutrophils in combination with clinical signs of respiratory disease provides confirmation of the disease.

Diseases that cause respiratory distress and pleural effusion in horses are listed in Table 31.3.

Table 31.3 Diseases causing pleural effusion in horses

Pleuropneumonia
Intrathoracic neoplasia including extension of gastric squamous cell carcinoma
Penetrating chest wounds
Esophageal perforation
Diaphragmatic hernia
Congestive heart failure
Hemangiosarcoma (causing hemothorax)
Pulmonary hydatidosis
Pulmonary infarction
African horse sickness

Treatment and prognosis

Therapeutic aims

The therapeutic aims are prompt institution of broad-spectrum antimicrobial therapy, removal of infected pleural fluid and cellular debris including necrotic lung, relief of pain, correction of fluid and electrolyte abnormalities, relief of respiratory distress, prevention and treatment of complications including laminitis (for discussion of complications, see 'Prognosis').

Therapy

Antimicrobial therapy The prompt institution of systemic, broad-spectrum antimicrobial therapy is the single most important component of treatment of horses with pleuropneumonia (Table 31.4). Antimicrobial therapy is almost always started before the results of bacterial culture of pleural fluid or tracheal aspirate are available and antimicrobial sensitivity of isolated bacteria determined. Use of antibiotics or combinations of antibiotics with a broad spectrum of antimicrobial activity is important because of the polymicrobial nature of most infections. The wide range of Gram-positive and Gram-negative bacteria associated with the disease (see 'Etiology') makes prediction of the susceptibility of the causative organisms difficult. Furthermore, superinfection with bacteria, especially Enterobacteriaceae and obligate anaerobes, commonly occurs in horses with disease initially caused by a single bacterial species. Administration of drugs that are effective in the treatment of penicillin-resistant obligate anaerobes is also important.

Antimicrobial therapy should be broad spectrum to include coverage of the likely bacteria involved in the disease. It should therefore provide coverage against *Streptococcus* spp., *Actinobacillus*/*Pasteurella* spp., Enterobacteriaceae and anaerobes including *Bacteroides* spp. A combination of penicillin G, an aminoglycoside and metronidazole provides broad-spectrum coverage and is a frequently used empirical therapy until the results of bacterial culture are known. Results of bacterial culture and subsequent antimicrobial susceptibility testing may aid selection of further antimicrobials. However, superinfection with Gram-negative and anaerobic bacteria is common and there is a sound rationale for continued use of a combination of antimicrobials providing broad-spectrum coverage throughout treatment of the disease.

Antimicrobial therapy will be prolonged in most cases, usually being required for at least one month and often several months. As the disease resolves it may be possible to

Table 31.4 Antimicrobial agents and recommended doses for treatment of pleuropneumonia in horses

Drug	Dose, route and interval	Comments
Procaine penicillin G	22 000–44 000 IU/kg, i.m. q 12 h	Effective against *Streptococcus* spp. and most anaerobes with the exception of *Bacteroides fragilis*. Achieves low plasma concentrations but has prolonged duration of action. Cheap. Synergistic with aminoglycosides. Should not be used as sole treatment
Sodium or potassium penicillin G	22 000–44 000 IU/kg, i.v. q 6 h	Effective against Gram-positive organisms (except penicillinase producing bacteria such as *Staphylococcus* spp.) and most anaerobes. Achieves high plasma concentrations. Synergistic with aminoglycosides. Expensive
Ampicillin sodium	11–22 mg/kg, i.v. or i.m., q 6 h	Wider spectrum than penicillin G. Achieves high plasma concentrations. Synergistic with aminoglycosides
Ceftiofur sodium	2.2 mg/kg, i.m. or i.v. q 12 h	Wide spectrum of action against Gram-positive and -negative organisms and most anaerobes. Can be used as sole treatment, though not recommended. Clinical results sometimes disappointing
Chloramphenicol	50 mg/kg, p.o. q 6 h	Good spectrum of action including anaerobic bacteria. Poor oral bioavailability and disappointing clinical efficacy. Use prohibited in some countries. Potential human health hazard
Gentamicin sulfate	7 mg/kg, i.v. or i.m. q 24 h	Active against *Staphylococcus* spp. and many Gram-negative organisms. Inactive against anaerobes. Poor activity against *Streptococcus* spp. Synergistic with penicillin
Amikacin sulfate	21 mg/kg, i.v. or i.m. q 24 h	Wider spectrum of Gram-negative activity than gentamicin. Expensive
Trimethoprim-sulfonamides	15–30 mg/kg, p.o. q 12 h	Theoretical wide spectrum of action. Disappointing clinical efficacy
Rifampin	5–10 mg/kg, p.o. q 12 h	Penetrates abscesses well. Active against Gram-positive bacteria and some Gram-negative. Must be used in conjunction with another antibiotic (not an aminoglycoside)
Ticarcillin-clavulanic acid	50 mg/kg, i.v. q 6 h	Broader spectrum of Gram-negative activity than penicillin G. Expensive
Metronidazole	15–25 mg/kg, p.o. q 6–8 h	Active against anaerobes only. Used in conjunction with other antimicrobials (especially penicillin and aminoglycosides). Neurotoxicity rare

i.v., intravenous; p.o., orally; i.m., intramuscular; q, every.
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change from parenteral antibiotics to orally administered antibiotics such as a combination of trimethoprim and a sulfonamide, although the clinical response to this combination is sometimes disappointing.

Cessation of antimicrobial therapy should be based on lack of fever, nasal discharge, respiratory distress or cough, lack of evidence of intrathoracic abscesses on ultrasonographic and radiographic examination of the thorax, and resolution of neutrophilia and hyperfibrinogenemia. There should be no appreciable pleural fluid on ultrasonographic examination.

Drainage of pleural fluid Chronic, effective drainage of the pleural cavity and intrathoracic abscesses is critical for successful treatment of horses with pleuropneumonia.[52] Horses with sterile pleural fluid may require only a single drainage of pleural fluid. More severely affected horses may require intermittent drainage on each of several days, and most cases will require insertion of a tube into the pleural space to provide continuous drainage for several days to several weeks. Horses with chronic disease may benefit from a thoracotomy that provides continuous drainage and the ability to lavage the chest. Ultrasonographic examination of the chest is very useful in identifying the presence of pleural fluid, the optimal sites for drainage, and the efficacy of drainage.

Intermittent drainage can be achieved by inserting a bovine teat cannula or similar blunt cannula into the pleural

space. This should be done aseptically and under local anesthesia. If ultrasonographic examination is not available, the cannula should be placed in the 6–8th intercostal space on the right side or the 7–9th on the left side just above the level of the olecranon. Pleural fluid that does not contain large fibrin clots (which clog the cannula) can be drained and the cannula removed. However, the process is slow if large quantities of fluid must be removed. Intermittent drainage is indicated when the quantities of pleural fluid are small (< 5 L), relatively cell free, or localized. This situation is most likely to occur in horses with acute disease.

Insertion of large bore trocars (20–30-French, 6–10 mm outside diameter) facilitates rapid fluid removal, allows drainage of viscid fluid and provides continuous drainage (Fig. 31.25). The chest tube should be inserted in an aseptic fashion under local anesthesia at sites indicated by ultrasonographic examination or as described above. A one-way valve should be attached to the external end of the tube to prevent aspiration of air and development of a pneumothorax. A balloon or condom with the end removed is an effective one-way valve. The presence of an intact, functional one-way valve is critical in preventing development of a pneumothorax. The chest tube is secured to the chest wall with a purse-string suture. The tube may be retained for several days to a week, but should be monitored frequently (every few hours) and cleared of fibrin clots as needed.

Complications of drainage of pleural fluid include: collapse of the animal if the fluid is removed too rapidly; pneumothorax; sudden death due to cardiac puncture or laceration of a coronary vessel; and perforation of abdominal viscera. Collapse can be prevented by administering fluids intravenously during pleural fluid drainage and by removing the fluid gradually (over a period of 30 minutes). Some horses develop a cellulitis around the chest tube that requires the tube be removed.

Thoracotomy or resection of a rib may be required in chronic cases to provide drainage of intrathoracic abscesses or chronic pleural effusion that is refractory to treatment with antimicrobials (Fig. 31.26).[52] Thoracotomy is an effective intervention in many horses with advanced pleuropneumonia and should not be considered an emergency or heroic procedure. Dangers of thoracotomy include the development of bilateral pneumothorax with subsequent death, persistent drainage of pleural fluid through a chronic fistula, and diminished athletic performance. Horses in which a thoracotomy, and especially that involving resection of a rib, has been performed are unlikely to return to active racing or similar strenuous athletic endeavors.

Pleural lavage Infusion and subsequent removal of 5–10 L of warm saline or balanced polyionic electrolyte solution into the affected pleural space may be beneficial in the treatment of cases with viscid fluid or fluid containing large

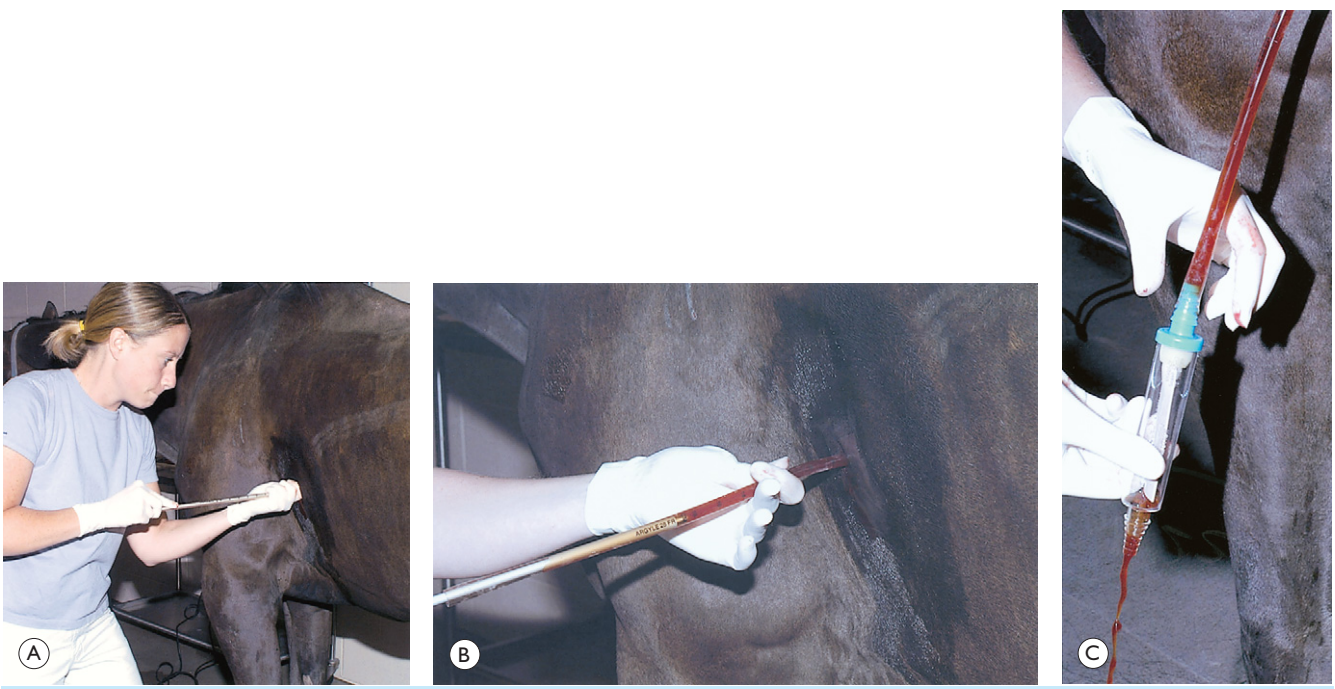


Fig. 31.25
(A) Insertion of a chest tube into a horse with pleuropneumonia. Considerable force is necessary to advance the thick trocar into the horse's chest. The hand of the operator against the chest is used to control the rate at which the trocar is advanced. Once the trocar has penetrated the parietal pleura, evident as a reduction in force needed to advance the trocar, the chest tube is advanced over the trocar into the pleural space. (B) Pleural fluid begins to drain as the trocar is removed from the chest tube. If fluid is not immediately apparent, the chest tube should be repositioned. (C) Attachment of a Heimlich valve or similar one-way valve will permit free drainage of fluid from the pleural space while preventing aspiration of air.

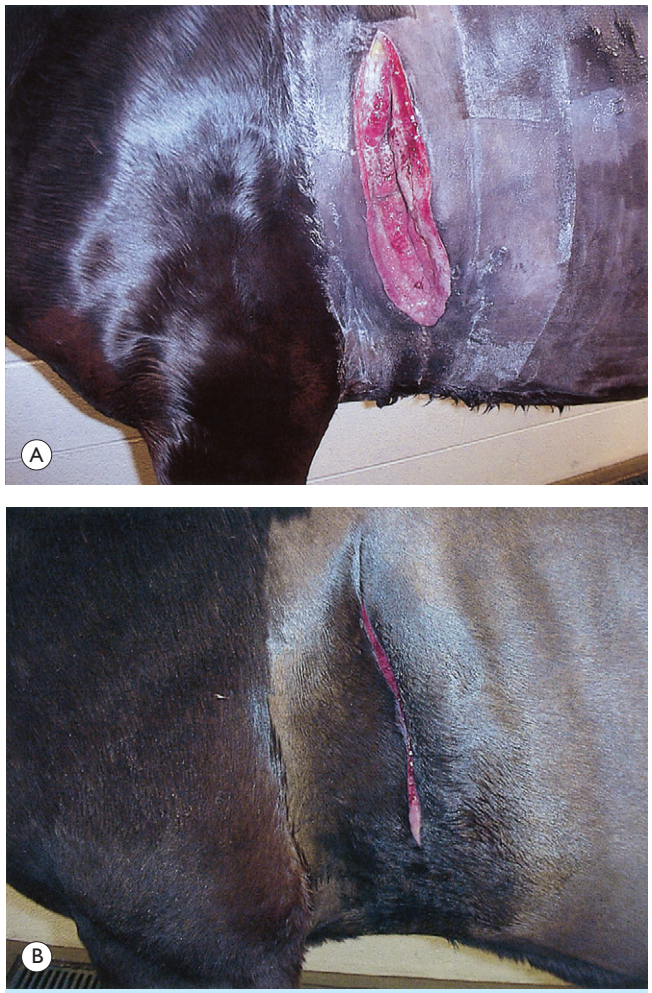


Fig. 31.26
(A) Thoracotomy in a horse with extensive pleural disease. Most thoracotomy incisions will be smaller, but large incisions are sometimes required if there is extensive loculation of fluid. (B) Healed thoracotomy of horse pictured in (A).

amounts of fibrin and cell debris. The fluid can be infused through the chest tube that is used to drain the pleural space. Care should be taken not to introduce bacteria with the infusion.

Supportive therapy Acutely or severely ill horses may be dehydrated, azotemic and have acid–base disturbances. These horses should be treated with appropriate fluids administered intravenously.

Pleuropneumonia is a painful disease and every attempt should be made to relieve the horse's chest pain. Non-steroidal anti-inflammatory drugs including flunixin meglumine (1 mg/kg, by mouth, i.m. or i.v., every 8 hours) or phenylbutazone (2.2 mg/kg, by mouth or i.v., every 12 hours) often provide effective analgesia and presumably reduce inflammation in the pleural space.

Horses should be provided with good nursing care including a comfortable stall, free access to palatable water, and a good diet. Affected horses will often not eat adequately and should be tempted with fresh and nutritious fodder.

Attention should be paid to the horse's feet to detect early signs of laminitis and allow appropriate measures to be taken.

Prognosis

The clinical course of the acute form of the disease may be less than 10 days if effective therapy is instituted before the pleural effusion becomes infected or there is substantial deposition of fibrin in the pleural space. The prognosis for a return to previous function is good in horses that respond to treatment. However, in most cases, even if appropriate therapy is instituted, the disease becomes chronic. The prognosis for life for horses able to be treated aggressively is very good (60–95%) and the prognosis for return to previous function if the horse survives is reasonable (60%).[44,53] The prognosis for return to previous function for horses that developed chronic disease and complications is poor (31%).[53]

Complications

Complications of pleuropneumonia include development of jugular thrombophlebitis (25% of cases), pulmonary, mediastinal or pleural abscesses (10–20% of cases), cranial thoracic mass (5–10% of cases), bronchopleural fistula (5%), pericarditis (2%), and laminitis (1–14%).[44,49,54] Intrathoracic abscesses are evident as chronic disease, weight loss, cough, and fever, and are readily detected by a combination of ultrasonographic and radiographic examination. Cranial thoracic masses are evident as an elevation in heart rate, prominent jugular pulse, spontaneous jugular thrombosis and forelimb pointing. The signs are referable to a mass in the cranial thorax displacing the heart caudally and to the left and impairing venous return to the heart in the cranial vena cava.[54] Ultrasonographic and radiographic examination reveals the presence of the mass. Bronchopleural fistulae develop when a section of pulmonary parenchyma sloughs leaving an open bronchiole that communicates with the pleural space.[55] The bronchopleural fistula can be diagnosed

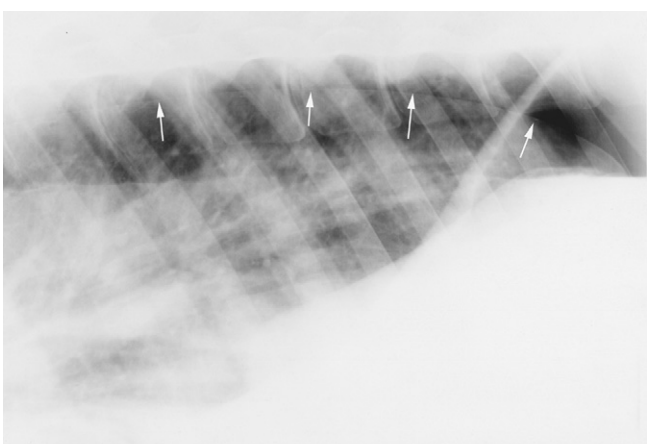


Fig. 31.27
Pneumothorax in a horse with pleuropneumonia. Partially collapsed lung is evident in the dorsal thorax (arrows).

by infusion of fluorescein dye into the pleural space and detecting its presence at the nares, or by pleuroscopic examination.[49] Mild pneumothorax develops in horses with chest tubes that permit aspiration of air into the chest, bronchopulmonary fistulae or thoracotomy (Fig. 31.27).

Etiology

Pleuropneumonia of horses is almost always associated with bacterial infection of the lungs, pleura and pleural fluid. The most common bacterial isolates from tracheal aspirates or pleural fluid of horses with pleuropneumonia are aerobes or facultative anaerobes including: *Streptococcus zooepidemicus*, *Pasteurella* spp., *Actinobacillus* spp., Enterobacteriaceae (particularly *E. coli*, *Klebsiella* spp. and *Enterobacter* spp.), *Pseudomonas* spp., *Staphylococcus* spp. and *Bordetella* spp.[44,47,56] *S. zooepidemicus* is isolated from over 60%, *Pasteurella*/*Actinobacillus* spp. from approximately one-third, and Enterobacteriaceae spp. from approximately 40% of cases.[44,47,56]

Obligate anaerobes isolated include *Bacteroides* spp. (including *B. fragilis*), *Clostridium* spp., *Eubacterium* and *Fusobacterium* spp.[44,47,56] *Bacteroides* spp. are isolated from approximately 20%, *Clostridium* spp. from 10%, and *Eubacterium* spp. from 6% of horses with pleuropneumonia.[47] *Mycoplasma felis* is an unusual cause of pleuritis in horses.[57]

Equine pleuropneumonia is associated with polymicrobial infections of the lungs and pleura in 50–80% of cases, although disease caused by infections of a single bacterial species occurs.[47,56] Infections by single bacterial species are usually by *S. zooepidemicus*, *Pasteurella*/*Actinobacillus* spp., or Enterobacteriaceae whereas almost all infections by anaerobes are polymicrobial.[47] Infection by obligate anaerobic bacteria is associated with disease of greater than 5–7 days' duration.[58]

Pleuritis is also caused by penetrating chest wounds, perforated esophagus, thoracic neoplasia and pulmonary hydatidosis.[44,59–61] Other diseases, such as congestive heart failure, may cause pleural effusion without inflammation.

Pathogenesis

Bacterial pleuropneumonia develops following bacterial colonization of the lungs with subsequent extension of infection to the visceral pleura and pleural space. Organisms initially colonizing the pulmonary parenchyma and pleural space are those normally present in the upper airway, oral cavity and pharynx, with subsequent infection by Enterobacteriaceae and obligate anaerobic bacteria.[58] Bacterial colonization and infection of the lower airway is attributable to either massive challenge or a reduction in the efficacy of normal pulmonary defense mechanisms or a combination of these factors.[58] Factors that increase bacterial contamination of the lower respiratory tract include prolonged head elevation, such as may occur during transportation, impaired pulmonary defense mechanisms secondary to viral respiratory tract disease, aspiration of feed material in dysphagic horses, and aspiration of dirt and grass during high intensity exercise.[58,62–64] Transportation may also impair the activity of pulmonary defense mechanisms allowing otherwise innocuous bacterial contamination to cause disease.[62]

Bacterial multiplication in pulmonary parenchyma is associated with the influx of inflammatory cells, principally neutrophils, tissue destruction and accumulation of cell debris in alveoli and airways. Infection spreads both through tissue and via airways. Extension of inflammation, and later infection, to the visceral pleura and subsequently pleural space causes accumulation of excess fluid within the pleural space. Pleural fluid accumulates because of a combination of excessive production of fluid by damaged pleural capillaries (exudation) and impaired reabsorption of pleural fluid by thoracic lymphatics.

Accumulation of parapneumonic pleural effusions has been arbitrarily divided into three stages: (1) exudative, (2) fibrinopurulent, and (3) organizational.[65] The exudative stage is characterized by the accumulation of sterile, protein-rich fluid in the pleural space as a result of increased pleural capillary permeability. Bacterial invasion and proliferation, further accumulation of fluid, and deposition of fibrin in pleural fluid and on pleural surfaces occurs if the disease does not resolve rapidly and is referred to as the fibrinopurulent stage. The organizational stage is associated with continued fibrin deposition, restriction of lung expansion and persistence of bacteria. The pleural fluid contains much cellular debris and bronchopleural fistulae may develop.

Epidemiology

Pleuropneumonia occurs worldwide in horses of all ages and both sexes, although most cases occur in horses > 1 and < 5 years of age.[47] Estimates of the incidence or prevalence of the disease are not available. The case fatality rate varies between 5 and 65%, with the higher rate reported in earlier studies.[53,66]

Risk factors

The risk of a horse developing pleuropneumonia is increased by 4 if the horse is a Thoroughbred race horse, 14 if the horse was transported more than 500 miles in the previous week, 10 if the horse has a recent (< 2 week) history of viral respiratory tract disease or exposure to a horse with such disease, and 4 if the horse has raced within the previous 48 hours.[43] Other suggested risk factors include general anesthesia, surgery, disorders of the upper airway, exercise-induced pulmonary hemorrhage, esophageal obstruction and dysphagia.

Prevention

Prevention of pleuropneumonia involves reduction of risk factors associated with the disease. The main risk factors are other infectious respiratory disease and transportation. Every effort should be made to prevent and treat respiratory disease in athletic horses, including institution of effective

vaccination programs. Horses with infectious respiratory disease should not be vigorously exercised until signs of disease have resolved.

Transportation of athletic horses is common and essential for their participation in competitive events. It cannot, therefore, be eliminated. Every effort should be made to minimize the adverse effects of transportation on airway health. Recommendations for transport of horses first made in 1917 are still relevant.[67,68] Updated, these recommendations include the following:

- Not transporting a horse unless it is healthy. Horses with fever should not be transported.
- Knowledgeable staff familiar with the horse should accompany the horse.
- Suitable periods of rest and acclimation should be provided before recently transported or raced horses are transported.
- The time during which horses are confined for transportation should be kept to a minimum. Horses should be loaded last and unloaded first in flights with mixed cargo.
- The route taken should be the most direct and briefest available.
- Horses should be permitted adequate time to rest at scheduled breaks. If possible, on long journeys horses should be unloaded and allowed exercise (walking) and access to hay and water.
- Horses should have frequent, preferably continuous, access to feed and water during transportation.
- Horses should not be exercised after arrival until they are free of fever, cough or nasal discharge.
- Horses should not be restrained during transportation such that they are unable or unwilling to lower their head.
- Air quality should be optimal in the vehicle used to transport the horse.

References

1. Timoney JF. Strangles. Vet Clin North Am Equine Pract 1993; 9:365–374.
2. Sweeney CR. Strangles: *Streptococcus equi* infection in horses. Equine Vet Educ 1996; 8:317–322.
3. Newton JR, Wood JLN, Chanter N. Strangles: long term carriage of *Streptococcus equi* in horses. Equine Vet Educ 1997; 9:98–102.
4. Newton JR, Verheyen K, Talbot NC, et al. Control of strangles outbreaks by isolation of guttural pouch carriers identified using PCR and culture of *Streptococcus equi*. Equine Vet J 2000; 32:515–526.
5. Fintl C, Dixon PM, Brazil TJ, et al. Endoscopic and bacteriological findings in a chronic outbreak of strangles. Vet Rec 2000; 147:480–484.
6. Newton JR, Wood JLN, Dunn KA, et al. Naturally occurring persistent and asymptomatic infection of the guttural pouches of horses with *Streptococcus equi*. Vet Rec 1997; 140:84–90.
7. Knight AP, Voss JL, McChesney AE, Bigbee HG. Experimentally-induced *Streptococcus equi* infection in horses with resultant guttural pouch empyema. Vet Med Small Animal Clinician 1975; 70:10, 1194–1195, 1198–1199.
8. Ford J, Lokai MD. Complications of *Streptococcus equi* infection. Equine Pract 1980; 2:41–44.
9. Sweeney CR, Whitlock RH, Meirs DA, et al. Complications associated with *Streptococcus equi* infection on a horse farm. J Am Vet Med Assoc 1987; 191:1446–1448.
10. Galan JE, Timoney JF. *Streptococcus equi* associated immune complexes in the sera of horses with purpura haemorrhagica. Abstracts of papers presented at the 65th Annual Meeting of the Conference of Research Workers in Animal Disease 1984; 98.
11. Galan JE, Timoney JF. Immune complexes in purpura hemorrhagica of the horse contain IgA and M antigen of *Streptococcus equi*. J Immunol 1985; 135:3134–3137.
12. Newton JR, Wood JLN, DeBrauwere MN, et al. Detection and treatment of asymptomatic carriers of *Streptococcus equi* following strangles outbreaks in the UK. In: Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, UAE. Newmarket: R and W Publications; 1998.
13. Chiesa OA, Garcia F, Domingo M, Cuenca R. Cytological and microbiological results from equine guttural pouch lavages obtained percutaneously: correlation with histopathological findings. Vet Rec 1999; 144:618–621.
14. Chiesa OA, Vidal D, Domingo M, Cuenca R. Cytological and bacteriological findings in guttural pouch lavages of clinically normal horses. Vet Rec 1999; 144:346–349.
15. Chanter N, Collin N, Holmes N, et al. Characterization of the Lancefield group C streptococcus 16S–23S RNA gene intergenic spacer and its potential for identification and sub-specific typing. Epidemiol Infect 1997; 118:125–135.
16. Walker JA, Timoney JF. Molecular basis of variation in protective SzP proteins of *Streptococcus zooepidemicus*. Am J Vet Res 1998; 59:1129–1133.
17. Chanter N, Talbot NC, Newton JR, et al. *Streptococcus equi* with truncated M-proteins isolated from outwardly healthy horses. Microbiology 2000; 146:1361–1369.
18. Verheyen K, Newton JR, Talbot NC, et al. Elimination of guttural pouch infection and inflammation in asymptomatic carriers of *Streptococcus equi*. Equine Vet J 2000; 32:527–532.
19. Bentz BG, Dowd AL, Freeman DE. Treatment of guttural pouch empyema with acetylcysteine irrigation. Equine Pract 1996; 18:33–35.
20. Adkins AR, Yovich JV, Colbourne CM. Nonsurgical treatment of chondroids of the guttural pouch in a horse. Aust Vet J 1997; 75:332–333.
21. Jorm LR, Plowright W, Rossdale PD, Wade JF. Laboratory studies on the survival of *Streptococcus equi* subspecies *equi* on surfaces. In: Equine infectious diseases VI: Proceedings of the Sixth International Conference, Cambridge, UK. Newmarket: R and W Publications; 1991.
22. Burrell MH, Wood JLN, Whitwell KE, et al. Respiratory-disease in thoroughbred horses in-training – the relationships between disease and viruses, bacteria and environment. Vet Rec 1996; 139:308–313.
23. Wood JLN, Newton JR, Chanter N, et al. A longitudinal epidemiological study of respiratory disease in racehorses: disease definitions, prevalence and incidence. In: Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, UAE. Newmarket: R and W Publications; 1998.
24. Hill AB. The environment and disease: association or causation? Proc Roy Soc Med 1965; 58:295–300.
25. Burrell MH, Mackintosh ME, Taylor CED. Isolation of *Streptococcus pneumoniae* from the respiratory tract of horses. Equine Vet J 1986; 18:183–186.
26. Gerber H. Clinical features, sequelae and epidemiology of equine influenza. Equine infectious diseases II: Proceedings

of the Second International Conference, Paris, 1969; 63–80.
27. Whatmore AM, King SJ, Doherty NC, et al. Molecular characterization of equine isolates of *Streptococcus pneumoniae*: natural disruption of genes encoding the virulence factors pneumolysin and autolysin. Infect Immun 1999; 67:2776–2782.
28. Blunden AS, Hannant D, Livesay G, Mumford JA. Susceptibility of ponies to infection with *Streptococcus pneumoniae* (capsular type 3). Equine Vet J 1994; 26:22–28.
29. Wood J. An epidemiological investigation of respiratory disease in racehorses. Milton Keynes: Life Sciences: Open University; 1999.
30. Christley RM, Hodgson DR, Rose RJ, et al. A case-control study of respiratory disease in Thoroughbred racehorses in Sydney, Australia. Equine Vet J 2001; 33:256–264.
31. Wood JL, Burrell MH, Roberts CA, et al. *Streptococci* and *Pasteurella* spp. associated with disease of the equine lower respiratory tract [see comments]. Equine Vet J 1993; 25:314–318.
32. Newton JR, Wood JLN, Chanter N. A case control study of factors and infections associated with clinically apparent respiratory disease in UK racehorses. In: Proceedings of the Society for Veterinary Epidemiology and Preventive Medicine, Noordwijkerhout, Holland, 2001.
33. Varma KJ, Powers TE, Powers JD, Spurlock SL. Standardization of an experimental disease model of *Streptococcus zooepidemicus* in the equine. J Vet Pharmacol Ther 1984; 7:183–188.
34. Cebra CK, Heidel JR, Cebra ML, et al. Pathogenesis of *Streptococcus zooepidemicus* infection after intratracheal inoculation in llamas. Am J Vet Res 2000; 61:1525–1529.
35. Wood JLN, Chanter N, Sinclair R, Mumford JA. The epidemiology of outbreaks of respiratory disease and poor performance in racing Thoroughbred horses. In: Equine infectious diseases VII: Proceedings of the Seventh International Conference, Tokyo, Japan. Newmarket: R and W Publications; 1994.
36. Chapman PS, Green C, Main JPM, et al. Retrospective study of the relationships between age, inflammation and the isolation of bacteria from the lower respiratory tract of Thoroughbred horses. Vet Rec 2000; 146:91–95.
37. Newton JR. Epidemiological studies of inflammatory airway disease in horses. Milton Keynes: Life Sciences: Open University, 2002.
38. Wood JLN, Chanter N. Can washing keep the lungs clean? Equine Vet Educ 1994; 6:220–222.
39. Wood JLN, Burrell MH, Roberts CA, et al. *Streptococci* and *Pasteurella* spp. associated with disease of the equine lower respiratory-tract. Equine Vet J 1993; 25:314–318.
40. Wood JL, Chanter N, Newton JR, et al. An outbreak of respiratory disease in horses associated with *Mycoplasma felis* infection. Vet Rec 1997; 140:388–391.
41. Anzai T, Walker JA, Blair MB, et al. Comparison of the phenotypes of *Streptococcus zooepidemicus* isolated from tonsils of healthy horses and specimens obtained from foals and donkeys with pneumonia. Am J Vet Res 2000; 143:277–279.
42. Ward CL, Wood JLN, Houghton SB, et al. *Actinobacillus* and *Pasteurella* species isolated from horses with lower airway disease. Vet Rec 1998; 143:277–279.
43. Austin SM, Foreman JH, Hungerford LL. Case-control study of risk-factors for development of pleuropneumonia in horses. J Am Vet Med Assoc 1995; 207:325–328.
44. Collins MB, Hodgson DR, Hutchins DR. Pleural effusion associated with acute and chronic pleuropneumonia and pleuritis secondary to thoracic wounds in horses – 43 Cases (1982–1992). J Am Vet Med Assoc 1994; 205:1753–1758.
45. Reef VB, Boy MG, Reid CF, Elser A. Comparison between diagnostic ultrasonography and radiography in the evaluation of horses and cattle with thoracic disease: 56 cases (1984–1985). J Am Vet Med Assoc 1991; 198:2112–2118.
46. Reimer JM, Reef VB, Spencer PA. Ultrasonography as a diagnostic aid in horses with anaerobic bacterial pleuropneumonia and/or pulmonary abscessation: 27 cases (1984–1986). J Am Vet Med Assoc 1989; 194:278–282.
47. Sweeney CR, Holcombe SJ, Barningham SC, Beech J. Aerobic anaerobic bacterial isolates from horses with pneumonia or pleuropneumonia and antimicrobial susceptibility patterns of the aerobes. J Am Vet Med Assoc 1991; 198:839–842.
48. Rossier Y, Sweeney CR, Zeimer EL. Bronchoalveolar lavage fluid cytologic findings in horses with pneumonia or pleuropneumonia. J Am Vet Med Assoc 1991; 198:1001–1004.
49. Byars TD, Becht JL. Pleuropneumonia. Vet Clin North Am: Equine Pract 1991; 7:63–78.
50. Cowell RL, Tyler RD, Clinkenread KD, Macallister CG. Collection and evaluation of equine peritoneal and pleural effusions. Vet Clin North Am: Equine Pract 1987; 3:543–561.
51. Brumbaugh GW, Benson PA. Partial pressures of oxygen and carbon dioxide, pH, and concentrations of bicarbonate, lactate and glucose on pleural fluid from horses. Am J Vet Res 1990; 51:1032–1037.
52. Schott HC, Mansmann RA. Thoracic drainage in horses. Compend Cont Educ Pract Vet 1990; 12:251–261.
53. Seltzer KL, Byars TD. Prognosis for return to racing after recovery from infectious pleuropneumonia in thoroughbred racehorses – 70 Cases (1984–1989). J Am Vet Med Assoc 1996; 208:1300.
54. Byars TD, Dainis CM, Seltzer KL, Rantanen ND. Cranial thoracic masses in the horse: a sequel to pleuropneumonia. Equine Vet J 1991; 23:22–24.
55. Boy MG, Sweeney CR. Pneumothorax in horses: 40 cases (1980–1997). J Am Vet Med Assoc 2000; 216:1955–1959.
56. Sweeney CR, Divers TJ, Benson CE. Anaerobic bacteria in 21 horses with pleuropneumonia. J Am Vet Med Assoc 1985; 187:721–724.
57. Morley PS, Chirino-Trejo M, Petrie L, et al. Pericarditis and pleuritis caused by *Mycoplasma felis* in a horse. Equine Vet J 1996; 28:237–240.
58. Raidal SL. Equine pleuropneumonia. Br Vet J 1995; 151:233–262.
59. McGorum BC, Railton DI, Clarke CJ, et al. Pleuropnuemonia associated with pulmonary hydatidosis in a horse. Equine Vet J 1994; 26:249–250.
60. Dechant JE, MacDonald DG, Crawford WH, O'Connor BP. Pleuritis associated with perforation of an isolated oesophageal ulcer in a horse. Equine Vet J 1998;30:170–172.
61. Mair TS, Brown PJ. Clinical and pathological features of thoracic neoplasia in the horse. Equine Vet J 1993; 25:220–223.
62. Raidal SL, Bailey GD, Love DN. Effect of transportation on lower respiratory-tract contamination and peripheral-blood neutrophil function. Aust Vet J 1997; 75:433–438.
63. Raidal SL, Love DN, Bailey GD. Inflammation and increased numbers of bacteria in the lower respiratory-tract of horses within 6 to 12 hours of confinement with the head elevated. Aust Vet J 1995; 72:45–50.
64. Raidal SL, Love DN, Bailey GD. Effect of a single bout of high-intensity exercise on lower respiratory-tract contamination in the horse. Aust Vet J 1997; 75:293–295.

65. Chaffin MK, Carter GK. Equine bacterial pleuropneumonia. Epidemiology, pathophysiology, and bacterial isolates. Compendium on Continuing Education for the Practicing Veterinarian 1993; 15:1642–1650.
66. Raphel C, Beech J. Pleuritis secondary to pneumonia or lung abscessation in 90 horses. J Am Vet Med Assoc 1982; 181:805–810.
67. Watkins-Pitchford H. An enquiry into the horse disease known as septic or contagious pneumonia. Vet Rec 1917; 73:345–362.
68. Racklyeft DJ, Raidal S, Love DN. Towards an understanding of equine pleuropneumonia: factors relevant for control. Aust Vet J 2000; 78:334–338.

CHAPTER 32

Heart and vessels: function during exercise and response to training

David C. Poole and Howard H. Erickson

The horse is often considered one of, if not the, premier athletic mammalian species. However, depending upon the criterion used there are other distinct (and sometimes surprising) contenders for that title. For example, as seen in Fig. 32.1, compared with the Thoroughbred race horse (65 km/h, 40 miles/h), the cheetah can achieve speeds in excess of 70 miles/h (120 km/h) and several species of antelope as well as the blackbuck, gnu and ostrich are all faster than the horse (fastest human ~27 miles/h, 43 km/h). The fastest horses ever clocked are Quarter Horses which may reach speeds of 50–55 miles/h (90 km/h).[1] Because body length determines the distance that individual muscles shorten, it might be more appropriate to judge athletic ability in terms of speed relative to body length.[2] From this perspective, the Merriam kangaroo rat is superlative, achieving 110

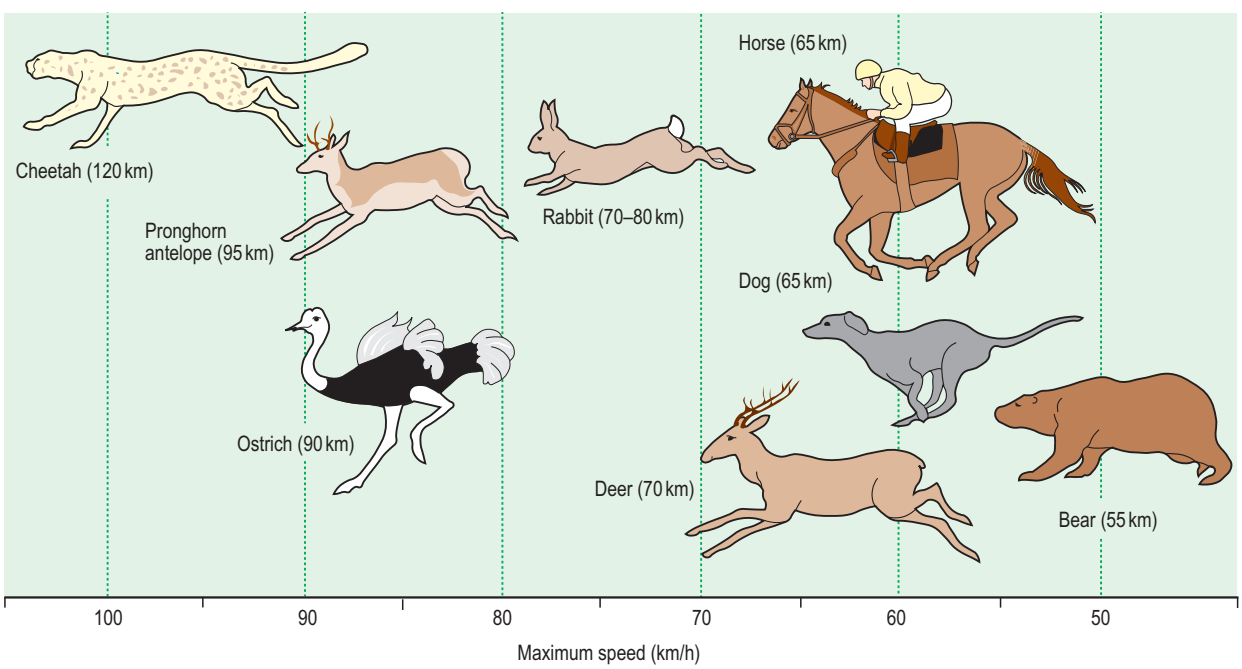


Fig. 32.1
Approximate maximum speeds for a variety of terrestrial mammalian species and the ostrich. Please note that the Quarter Horse has been clocked close to 90 km/hr (55 miles/h)[1] whereas maximal speeds for the Thoroughbred as seen in this figure with rider are somewhat lower. For converting to other commonly used units: 10 km/h = 6.2 miles/h or 2.8 m/s.

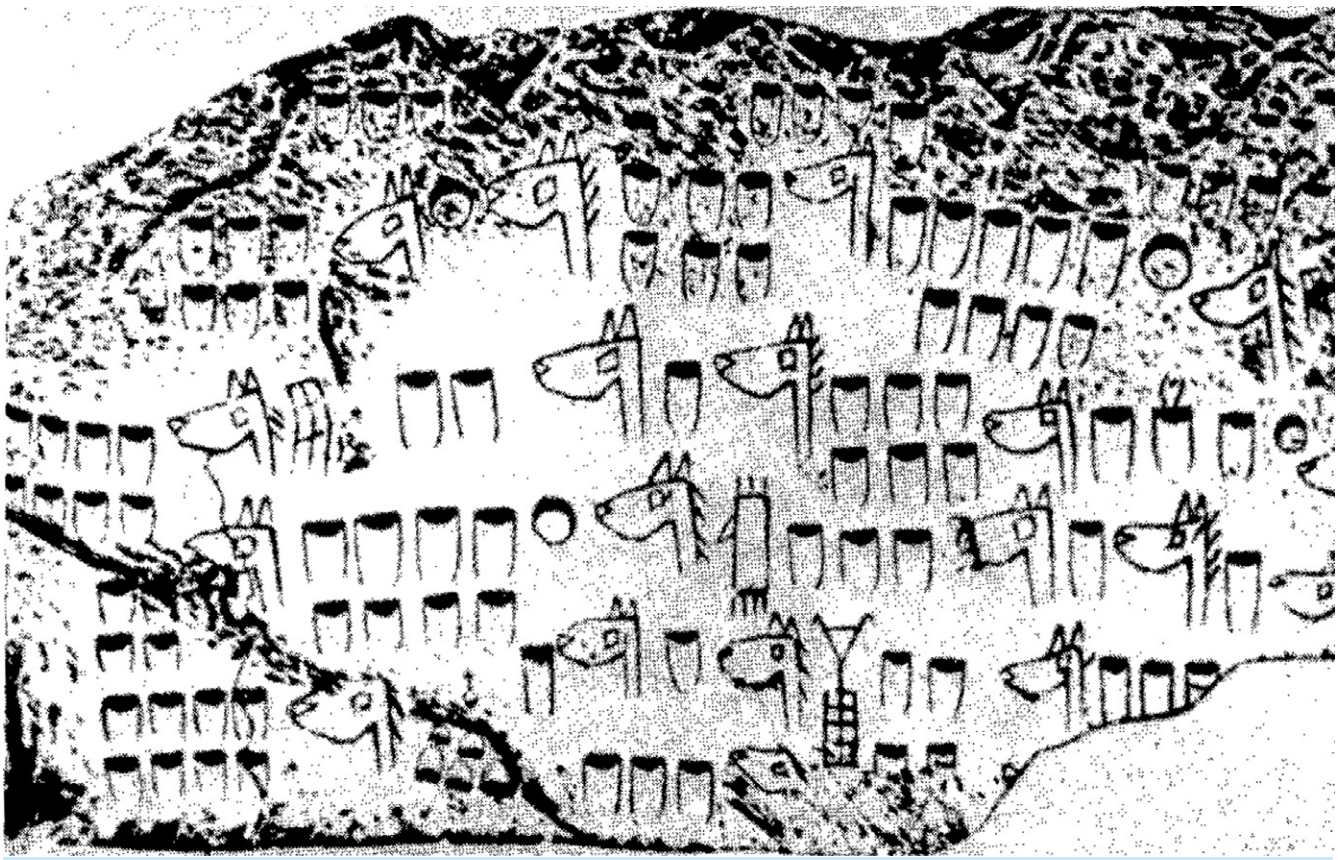


Fig. 32.2
Chaldean pedigree chart (circa 4000 BC) demonstrating that selective breeding of horses was practiced at least 6000 years ago. (Reproduced with kind permission from Lyons and Petrucelli[6] and the World Health Organization, Geneva.)

body lengths per second which is three times faster than the cheetah (32 length/s) and an order of magnitude faster than the horse (~10 length/s).

Within humans, the aerobic capacity or maximal oxygen uptake ($\dot{V}O_{2max}$) is considered an excellent (though by no means the sole) indicator of performance for running events over 1 minute in duration. Across the spectrum of terrestrial mammalian species, aerobic capacity increases over five orders of magnitude as a function of body size from approximately 0.001 L/min in the 2-g Etruscan shrew (world's smallest mammal) to in excess of 80 L/min in the elite Thoroughbred race horse. Whereas it is possible that a large rapidly walking elephant may have a higher total $\dot{V}O_2$, this remains to be demonstrated. When aerobic capacity is expressed relative to body mass, the diminutive Etruscan shrew (~ 400 mL O_2/kg/min)[2,3] reigns supreme as this measure of performance decreases systematically with increasing body mass. Amongst the larger animals, the pronghorn antelope (~ 300 mL O_2/kg/min)[4] and the horse (> 200 mL O_2/kg/min)[2,5] are outstanding and each can consume more O_2 in toto and per unit body mass than any other mammal of their respective sizes.

This chapter addresses the structural and functional capacities of the cardiovascular system that permit the horse to achieve such prodigious O_2 flows and athletic performances. As we shall see, a large, high-capacity heart is requisite. Whereas animals such as the shrew and pronghorn antelope have evolved in accordance with the laws of nature, the horse has been subjected to several thousand years of selective breeding (Fig. 32.2)[6] based upon athletic performance. As detailed below, this practice has produced a disproportionate increase in the horse's heart size and pumping capacity (cardiac output, $\dot{Q}$) compared to lung capacity; the consequence of this is a structural and functional failure of the respiratory system during maximal exercise.

The purpose of this chapter is to present those features of the equine heart and cardiovascular system that facilitate this animal's extraordinary performance. Those mechanisms underlying respiratory system failure will be discussed as they relate intimately to the cardiovascular system. Particular attention will be afforded to the plasticity of the equine cardiovascular system to exercise training and although such changes are important, compared with the magnitude of inherited interanimal variations, they are relatively modest. Throughout this chapter and contingent upon available data, reference will be made to several other species including the human, dog, ox, and camel as a basis for comparison (Fig. 32.3).[7]

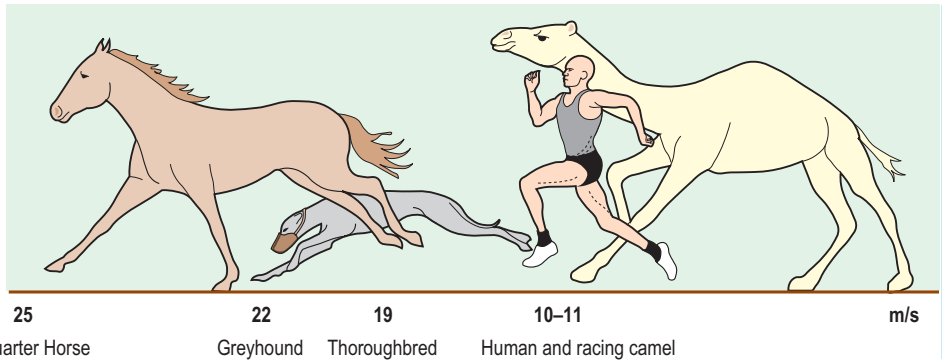


Fig. 32.3
Relative maximum speed in m/s of the four main athletic species. For converting to other commonly used units: 10 m/s = 36 km/h or 22 miles/h. (Revised from Derman & Noakes.[7])

Role of the heart and cardiovascular system in setting aerobic capacity $\dot{V}O_{2max}$

The energetic capability of skeletal muscle is so high that it far surpasses the capacity of the respiratory and cardiovascular systems to deliver O_2. In Thoroughbreds skeletal muscle comprises over 50% of body mass[8] and aerobic capacity ($\dot{V}O_{2max}$) (at least of Standardbreds) increases as a function of fat-free mass.[9] Moreover, under many conditions $\dot{V}O_{2max}$ is considered to be O_2-supply limited because the mitochondrial oxidative enzyme capacity for utilizing O_2 exceeds that of the cardiorespiratory systems to deliver O_2. In support of this notion, there is strong evidence that increasing muscle O_2 delivery during intense exercise will elevate $\dot{V}O_{2max}$. Specifically:

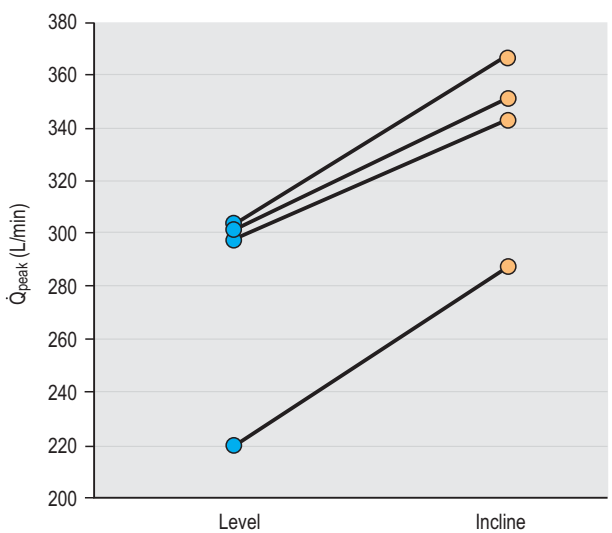


Fig. 32.4
Running on an incline (6°) significantly increases cardiac output at maximal exercise ($\dot{Q}_{peak}$) and also elevates $\dot{V}O_{2max}$. (Redrawn from McDonough et al.[12])

1. Breathing high O_2 mixtures elevates arterial O_2 content and $\dot{V}O_{2max}$ in horses[10] and humans.[11]
2. With respect to equine $\dot{V}O_{2max}$, there is recent evidence that horses run to maximal speeds on an incline (6°) exhibit higher cardiac output ($\dot{Q}$) (Fig. 32.4) and $\dot{V}O_{2max}$ values than on the flat. This increased $\dot{Q}$ and $\dot{V}O_{2max}$ results from an elevated stroke volume[12] and may relate to greater hindlimb muscle recruitment, greater swings in intrapleural pressures (higher tidal volume) aiding heart function, and/or increased hydrostatic pressures improving muscle blood flow.
3. Pericardectomy elevates stroke volume, cardiac output and $\dot{V}O_{2max}$ in dogs[13] and pigs.[14]
4. Restricting the exercising muscle mass in humans to 2–3 kg (knee extensors) rather than the 15–20 kg recruited during running or cycling elevates mass specific $\dot{V}O_2$.[15,16]
5. Blood doping (reinfusion of autologous red cells) elevates $\dot{V}O_{2max}$ in humans.[17]

Several steps in the pathway of O_2 from the atmosphere to its site of utilization within muscle mitochondria may limit the achievable $\dot{V}O_{2max}$.[18,19] These include O_2 diffusion across the blood–gas barrier in the lungs, conductive transport of O_2 in the blood (cardiac output, $\dot{Q}$, and O_2 concentration, Cao_2) and diffusion of O_2 from the skeletal muscle capillary into the myocyte. The coordinated function of respiratory, cardiovascular and muscular systems provides for rapid changes in O_2 flux from lungs to mitochondria (Fig. 32.5) and in most species, including the horse, human, and dog, the strongest determinant of $\dot{V}O_{2max}$ is the capacity of the cardiovascular system to transport O_2 (i.e. $\dot{Q}o_2$, Fig. 32.6). However, during maximal exercise in the horse other steps in the O_2 pathway also become limiting in large part because of the disproportionality between the cardiovascular and respiratory systems. For example, O_2 loading in the lung is impaired and arterial hypoxemia becomes manifested (see 'Cardiovascular physiology and responses to exercise' below). In addition, the ability to offload O_2 in the muscle capillary is limited by the finite O_2 diffusing capacity of skeletal muscle which is determined by the capillary bed and blood flow within those capillaries. Fig. 32.7 integrates the conductive and diffusive elements of O_2 transport to demonstrate how the horse achieves its very high $\dot{V}O_{2max}$.

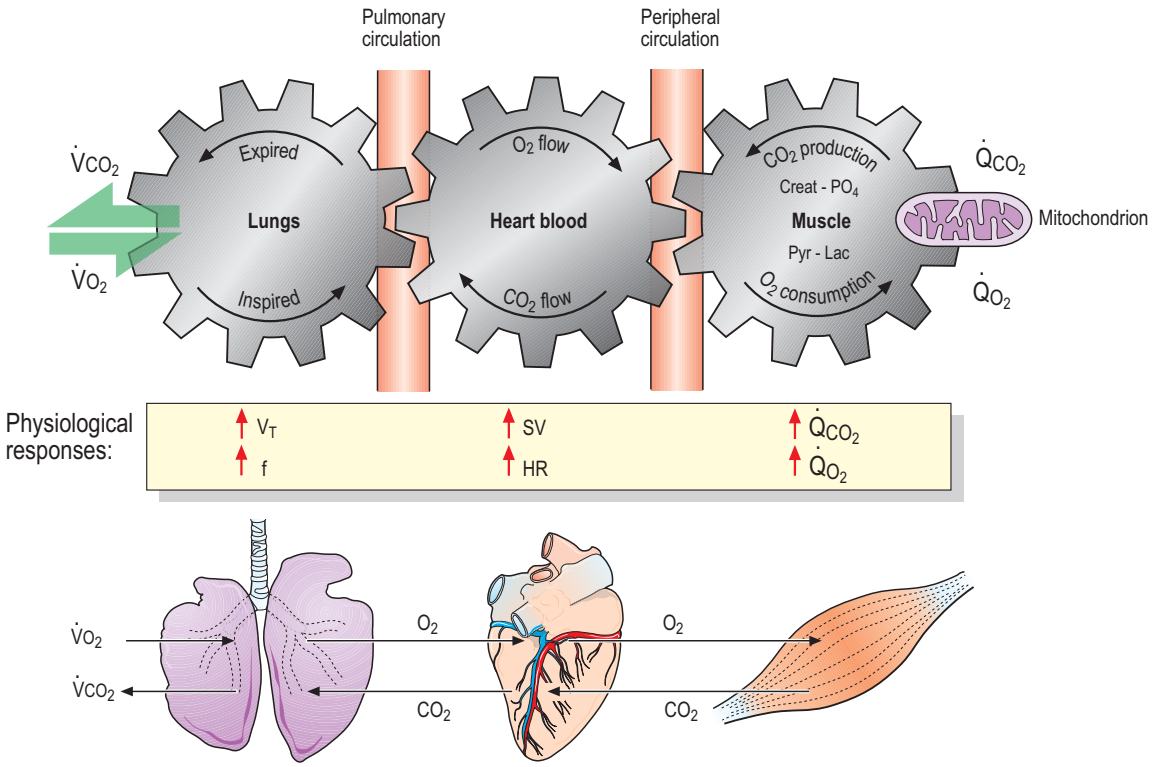


Fig. 32.5
Illustration of the pathway for oxygen (O_2) from the atmosphere to its site of utilization within muscle mitochondria. The cogs demonstrate that the respiratory (lungs), cardiovascular (heart and blood vessels), and muscle systems must increase O_2 flux in a tightly coordinated fashion to effectively deliver adequate O_2 to facilitate muscular performance. $\dot{Q}O_2$, mitochondrial O_2 delivery; $\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, CO_2 output, SV, stroke volume; HR, heart rate; V_T, tidal volume; *f*, breathing frequency; CO_2, carbon dioxide; Creat, creatine; Pyr, pyruvate; Lac, lactate; $\dot{Q}CO_2$, mitrochondrial carbon dioxide production. (Upper panel redrawn from Wasserman et al 1994.[20])

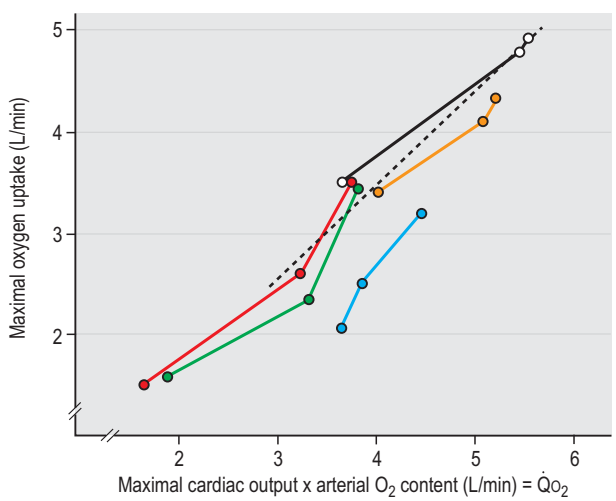


Fig. 32.6
Relationship between increased O_2 delivery ($\dot{Q}O_2$) and maximal oxygen uptake ($\dot{V}O_2$) after bedrest and exercise training in five humans (Redrawn from Saltin et al.[21])

Conductive O_2 transport (lungs to muscle) Given that high rates of O_2 delivery ($\dot{Q}O_2$) are of paramount importance for achieving this high $\dot{V}O_{2max}$, it is instructive to break down the components of $\dot{Q}O_2$:

O_2 delivery = cardiac output × arterial O_2 content

$$\dot{Q}O_2 = \dot{Q} \times CaO_2$$

$$\dot{Q} = HR \times SV$$

Therefore,

$$CaO_2 = ([Hb] \times 1.34 \times \%Sat) + \sim 0.3 \text{ mL/100 mL dissolved } O_2$$

$$\dot{Q}O_2 = HR \times SV \times [Hb] \times 1.34 \times \%Sat$$

$\dot{Q}O_2$ = Heart rate × stroke volume × hemoglobin concentration × O_2 binding capacity of Hb × % of O_2 binding sites filled

In the horse during maximal exercise, SV is determined principally by heart size and HR may approach 240 beats/min which is unusually high for such a large animal. Circulating hemoglobin concentration ([Hb]) increases nearly twofold above rest as red blood cells are released from the large muscular spleen in response to increased sympathetic activity. Table 32.1 demonstrates that the size of the heart and spleen is relatively larger in the horse than in either the ox or man. Relative heart size in the athletic dog approaches that found in the horse, but the horse is unusual in that the spleen is so large. Note that in the horse, the proportion of skeletal muscle is very high (close to 50%) and the lungs are relatively small (particularly with respect to heart size, see 'Cardiovascular physiology and responses to exercise' below). A comparison between actual heart size and $\dot{V}O_{2max}$ in the athletic horse and human is shown in Fig. 32.8.

Diffusive O_2 transport within muscle $\dot{V}O_{2max}$ is the product of $\dot{Q}_{max}$ and the extraction of O_2 primarily by the muscles as described by the Fick equation:

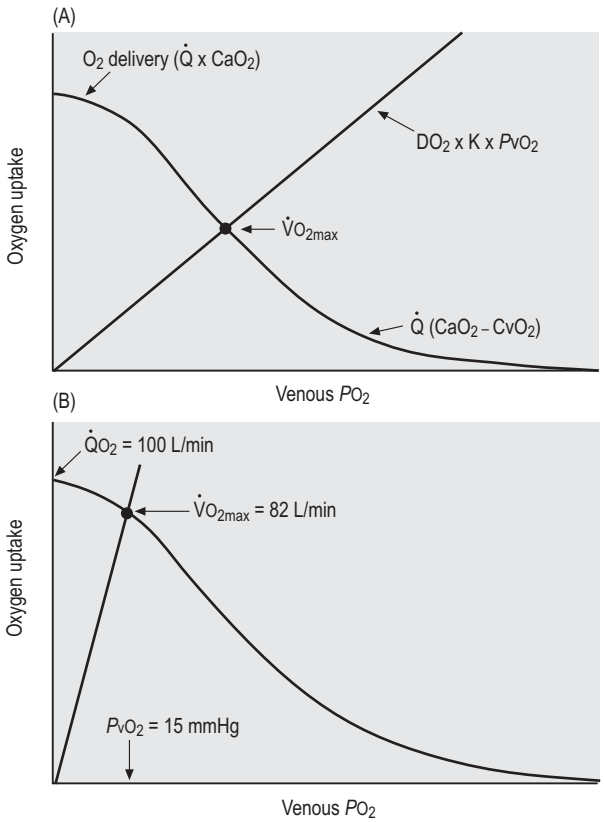


Fig. 32.7
Determination of maximal O_2 uptake ($\dot{V}O_{2max}$) by conductive ($\dot{Q}O_2$) and diffusive movement of O_2 by the cardiovascular and muscle microcirculatory systems ("Wagner" diagram[18]). The curved line denotes mass balance according to the Fick principle and the straight line from the origin represents Fick's law of diffusion. DO_2 is effective diffusing capacity and K is a constant that relates venous PO_2 to mean capillary PO_2. PvO_2, CaO_2, and CvO_2 are the partial pressure of venous O_2 and the concentrations of O_2 in arterial and venous blood, respectively. $\dot{V}O_{2max}$ occurs at the intersection of the two relationships. (A) is a general schematic whereas (B) presents actual values for a very fit Thoroughbred at maximal exercise. Understanding the conductive and diffusive determinants of $\dot{V}O_{2max}$ is essential for interpreting the structural and functional mechanisms that increase $\dot{V}O_{2max}$ with exercise training (see p. 720). See text for additional details.
((A) redrawn from Wagner et al.[18])

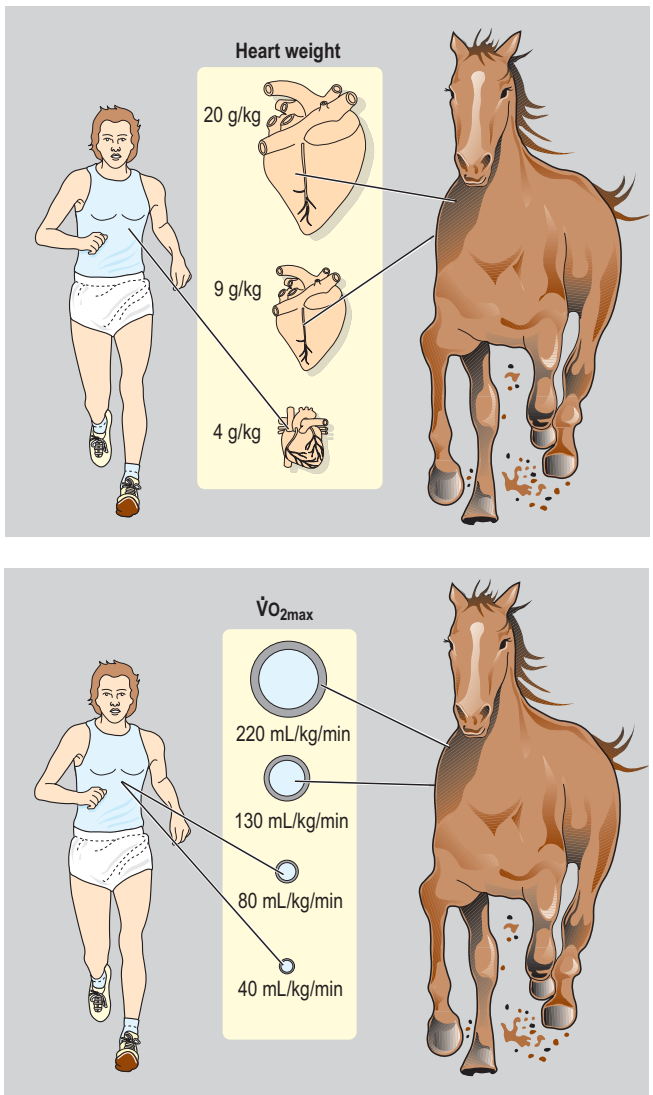


Fig. 32.8
Comparison of heart size (per kg body weight) and $\dot{V}O_{2max}$ ranges within healthy human and equine populations. Note that exercise training increases heart size and weight and also $\dot{V}O_{2max}$ (see Table 32.7 for references).

Table 32.1 Relative comparison of the weight of organs key to the loading and transport of O_2 as a % of body weight. (Data from Webb & Weaver[22])

	Horse	Dog	Ox	Man
Spleen	0.2–1.1	0.3	0.2	0.3
Heart	0.7–1.1	0.8	0.4	0.5
Lungs	0.9–1.5	0.9	0.7	1.4

$$\dot{V}O_{2max} = \dot{Q}_{max} \times (CaO_2 - CvO_2)$$

where CaO_2 and CvO_2 denote arterial and mixed venous O_2 contents. Figure 32.7 demonstrates that the effective muscle diffusing capacity (estimated by the slope of the line projecting from the origin) determines the level to which CvO_2 will fall at maximal exercise (i.e. extraction) and also the $\dot{V}O_{2max}$. The section 'Cardiovascular physiology and responses to exercise' details the determinants of muscle diffusing capacity.

This chapter deals primarily with horses in their athletic prime and considers their maximal capacities irrespective of age per se. In this respect, horses increase their cardiovascular (Fig. 32.9) and muscle oxidative enzyme (Table 32.2) capacities substantially during their first 3 years. Thus, 3- to 4-year-old horses have larger hearts,[23,25] and a lower HR[23] (larger stroke volume) at a given running speed, as well as a reduced blood lactate response to submaximal running

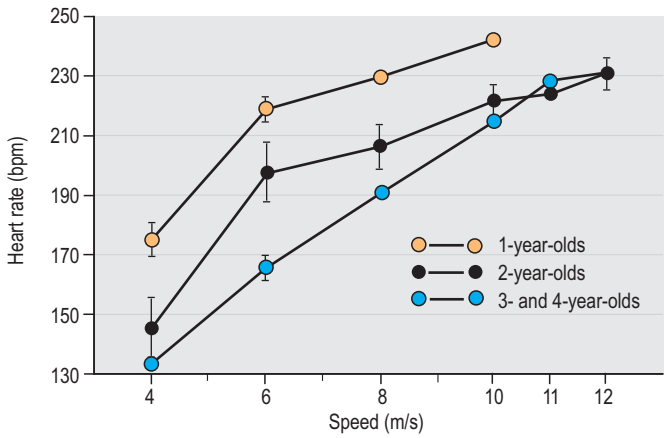


Fig. 32.9.
Reduction in heart rate response to running as a function of age which reflects increased heart size and stroke volume at 2–4 years of age in comparison with 1 year olds. (Redrawn from Rose et al.[23])

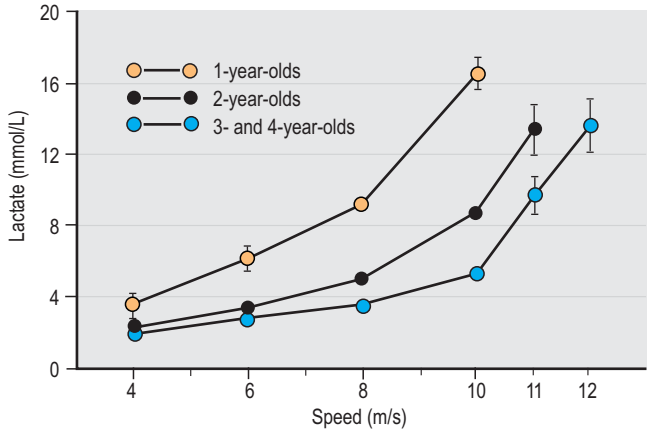


Fig. 32.10
Decreased blood lactate response to submaximal running speeds as horses age from 1 to 3 and 4 years. (Redrawn from Rose et al.[23])

speeds (Fig. 32.10).[23] The mechanistic bases for these last two alterations as they relate to increased heart size and vascular adaptations which improve muscle O_2 delivery and exchange are encompassed within the training section of this chapter ('Exercise training').

Anatomy of the cardiovascular system

Heart size

The size of the heart is a key determinant of maximum stroke volume, cardiac output, and hence aerobic capacity and exercise performance (Figs 32.11–13). This relationship has been documented in humans by examination of the electrocardiogram (ECG), ultrasound, radiographs, and post-mortem examination of heart size. For example, Paavo Nurmi, multiple Olympic champion distance runner reportedly had a heart mass nearly three times larger than predicted for his body size. At post-mortem, the heart of the seven-time Boston Marathon winner Clarence DeMar, who died of a nonmyocardial cancer, was substantially larger than normal and his coronary arteries were threefold larger than found in his nonathletic counterparts.[27]

In horses, heart mass approximates 0.9–1% of body mass, which is greater than that for other nonathletic species (Fig. 32.14) and may be as much as 1.1% of body mass in trained horses.[22] Amongst different horse breeds, racing horses have proportionally larger hearts (Fig. 32.14) and Table 32.3 lists some famous horses and their heart weights. The heaviest horse heart actually weighed was that of Sham at 18 lb (8.2 kg), who was consistently runner-up to Secretariat. Secretariat was a Triple Crown winner and holds the track record at Belmont Park (2 min 24.4 s for 1.5 miles on turf).

Table 32.2 Citrate synthase (CS), 3-hydroxy-Acyl CoA dehydrogenase (HAD), and lactate dehydrogenase (LDH) activities in the middle gluteal muscle of Thoroughbreds and Standardbreds of different ages. (Reproduced with kind permission from Snow & Valberg[24])

		Enzyme activities (mmol/kg/min)							
		Thoroughbreds				Standardbreds			
Age	Sex	No.	CS	HAD	LDH	No.	CS	HAD	LDH
1	M	20	31	20	1793	10	29	29	1936
1	S	21	32	18	1714	15	30	23	1927
2	M	23	44	22	1558	11	35	31	1938
2	S	20	42	22	1458	14	42	25	1639
3	M	21	64	31	1549	12	55	31	1362
3	S	17	58	31	1515	15	54	33	1317
4–6	M	17	67	31	1490	15	56	33	1669
4–6	S	24	67	38	1397	15	68	34	1460
Age			XXX	XXX	XX		XXX	NS	XXX
Sex			NS	NS	NS		NS	NS	NS

Note: Significance over the four age groups: XX, $P < 0.01$; XXX, $P < 0.001$; M, mare (filly); S, stallion (colt).

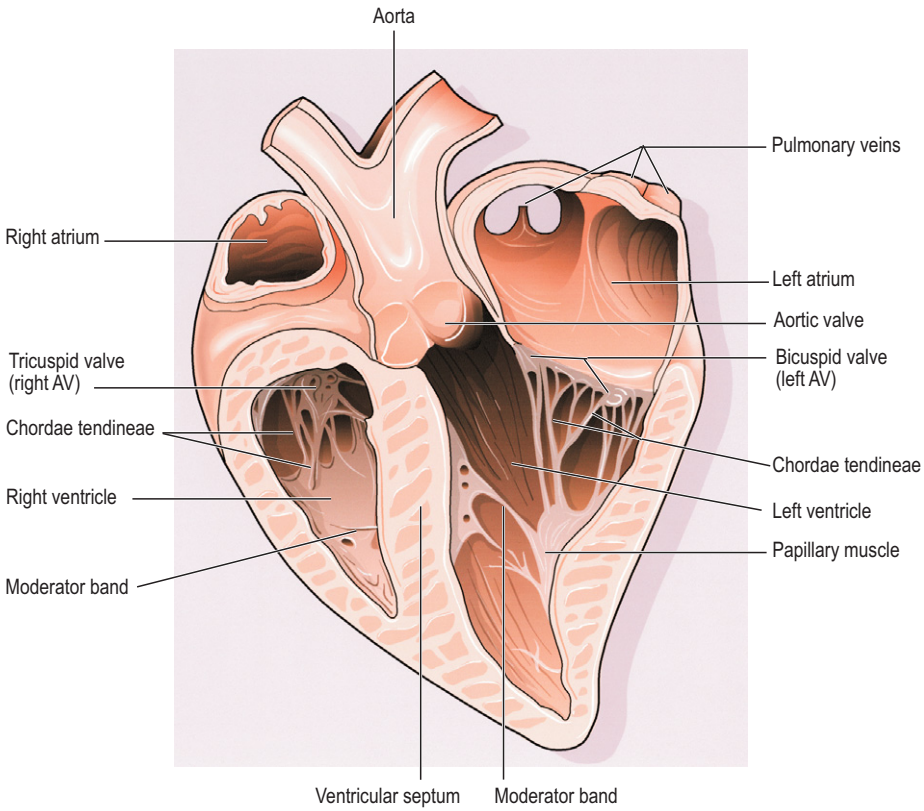


Fig. 32.11
Cross-section of the equine heart showing principal anatomic structures. AV, atrioventricular valve (see Fig. 32.12).

Tragically, Secretariat's heart was never weighed. However, the same pathologist, Dr Thomas Swerczek, who weighed Sham's heart estimated that Secretariat's heart weighed 22 lb (10 kg) and he considered it to be in perfect condition.[27] If that weight is correct, Fig. 32.13A predicts that Secretariat may have achieved a cardiac output in excess of 500 L/min and Fig. 32.13B a $\dot{V}o_{2max}$ over 120 L/min! To place heart size in visual perspective, Fig. 32.15 compares Key to the Mint's 15.8 lb (7.2 kg) heart to that of an unexceptional stallion.

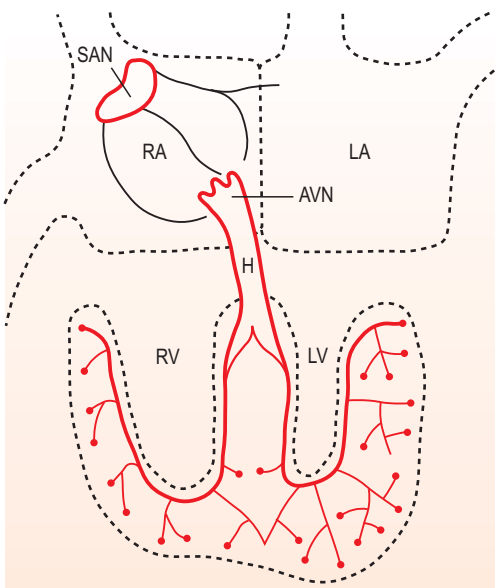


Fig. 32.12
Conduction system of the equine heart which is composed of specialized cardiac muscle fibers rather than nerves. Note the extensive arborization of the Purkinje fibres across the ventricular walls that is characteristic of the horse heart and which results in effective depolarization from multiple points. SAN, sinoatrial node; RA, right atrium; LA, left atrium; AVN, atrioventricular node; H, bundle of His; RV, right ventricle; LV, left ventricle. (Courtesy of R. Hamlin).

Given the crucial importance of heart size in setting athletic potential, there has been great interest in establishing a convenient and accurate noninvasive method of estimating this variable in horses. The mean/average duration of the QRS complex (in ECG leads I, II, and III, Fig. 32.16) has been shown to correlate with heart mass at autopsy and also racing performance.[28] Thus, larger hearts have a wider QRS complex and the so-called 'heart score' measured in milliseconds has been related to heart mass and subsequently predicted stroke volume and cardiac output as shown in Tables 32.4 and 32.5. It should be noted, however, that other studies have not been able to confirm the relationship between heart score and heart mass.[29–33] Based upon the inheritance of heart scores in race horses,[34] there is currently great interest in identifying the gene, located on the X-chromosome, that codes for heart mass.[27]

An important feature of the equine heart that may contribute to exercise-induced pulmonary hypertension concerns the disparity in size of the right and left atrioventricular (AV) valves. Specifically, at Kansas State University Professors M. Roger Fedde and Howard H. Erickson (unpublished findings) have determined that the cross-sectional area of the left AV valve is only 63% that of the right AV valve (i.e. 38.1

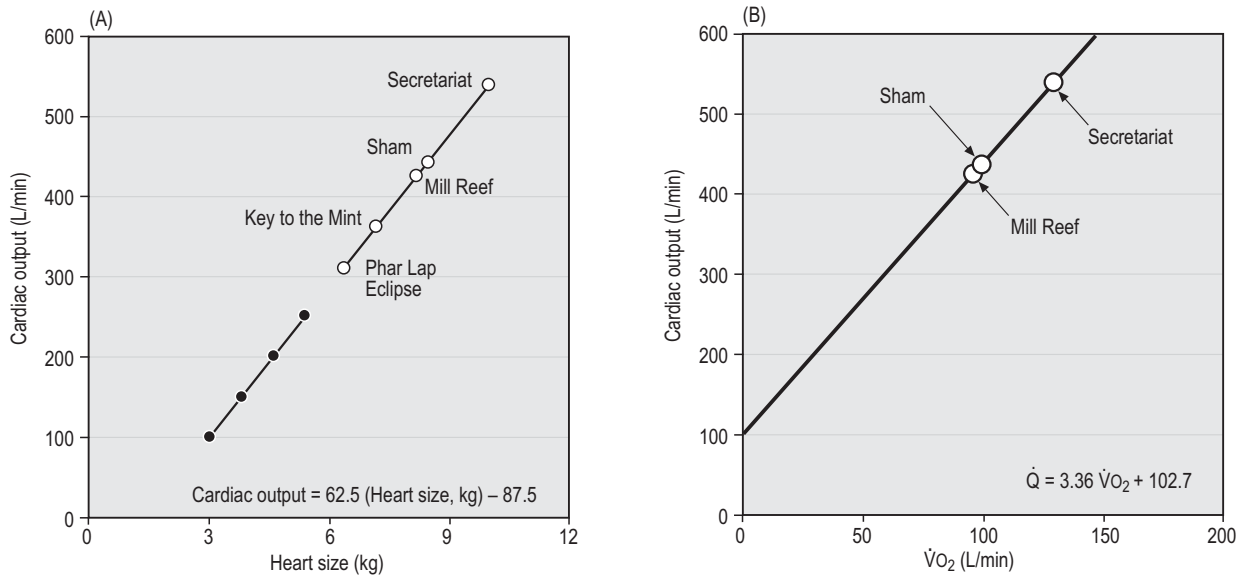


Fig. 32.13
Relationship between heart size and cardiac output ($\dot{Q}$) (A) and $\dot{V}O_2$ and cardiac output at maximum exercise (B). (A) The solid symbols are determined from the data of Evans & Rose (1988),[26] the hollow symbols are determined from that relationship and the measured or estimated (Secretariat) heart weights published for each named horse.[27] (B) An arterial–venous O_2 difference of 22.8 mL/100 mL of blood is assumed to estimate $\dot{V}O_{2max}$ values for Secretariat and Sham. The echocardiographic data of Young et al[5] are consistent with this relationship. Note Secretariat's extraordinary cardiac output (~ 540 L/min) and $\dot{V}O_{2max}$ (over 120 L/min which would be 240 mL O_2/kg/min at 500 kg bodyweight).

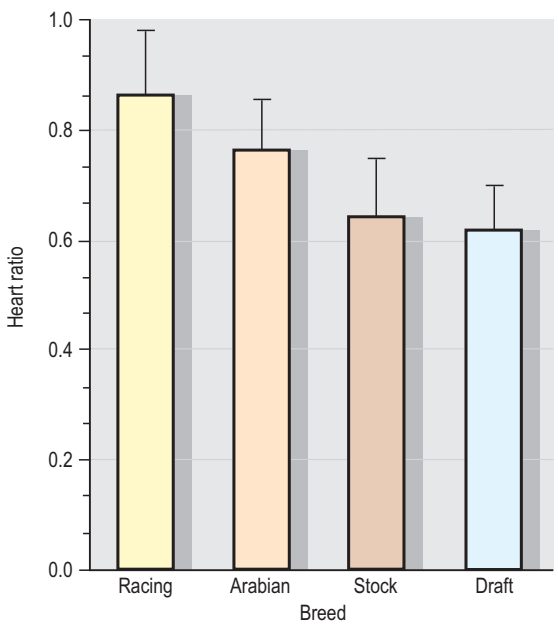


Fig. 32.14
Heart ratio (heart weight as a percentage of bodyweight) with standard deviations for racing, Arabian, stock and draft horses. Note that after training, heart ratio may reach 1.1% or higher.[22] (Revised from Kline and Foreman.[28])

Table 32.3 Heart weights and heart scores of famous race horses. (Reproduced with kind permission from Haun[27])

Name of horse (color, sex, year of birth)	Heart weight		Heart score (m/s)
	lb	kg	
Secretariat (ch.s. 1970)	22	10	
Sham [a] (ch.s. 1970)	18	8.2	
Mill Reef [a] (b.s. 1968)	16.9	7.7	
Key to the Mint (b.s. 1969)	15.8	7.2	157
Easy Goer (ch.s. 1986)	15	6.8	
Althea (ch.m. 1981)	15	6.8	
Eclipse (ch.s. 1764)	14	6.4	
Phar Lap (ch.g. 1926)	14	6.4	
Star Kingdom (ch.s. 1946)	14	6.4	
Tulloch (b.s. 1954)	13.5	6.2	136
Killaloe (b.m. 1970)	12.9	5.9	
Northern Dancer (b.s. 1961)			150
Soviet Problem (ch.m. 1990)			150
Moscow Ballet (b.s. 1982)			147
The Last Red (ch.m. 1993–twin)			140
Desert Secret (b.s. 1990)			140
Hyperion (ch.s. 1930)			133
Vo Rouge (b.g. 1983)			130

[a] Same pathologic enlargement (may add 2–3 lbs to heart weight).
b, bay; ch, chestnut; g, gelding; m, mare; s, stallion.

vs. 60.8 cm^2). As the smaller cross-sectional area will substantially elevate resistance to blood flow, this is expected to raise left atrial, pulmonary venous, pulmonary capillary, and, ultimately, pulmonary arterial pressures.

Spleen

As shown above, O_2 delivery depends not only upon cardiac output ($\dot{Q}$) but also upon arterial O_2 content (Ca_{O_2}), and the

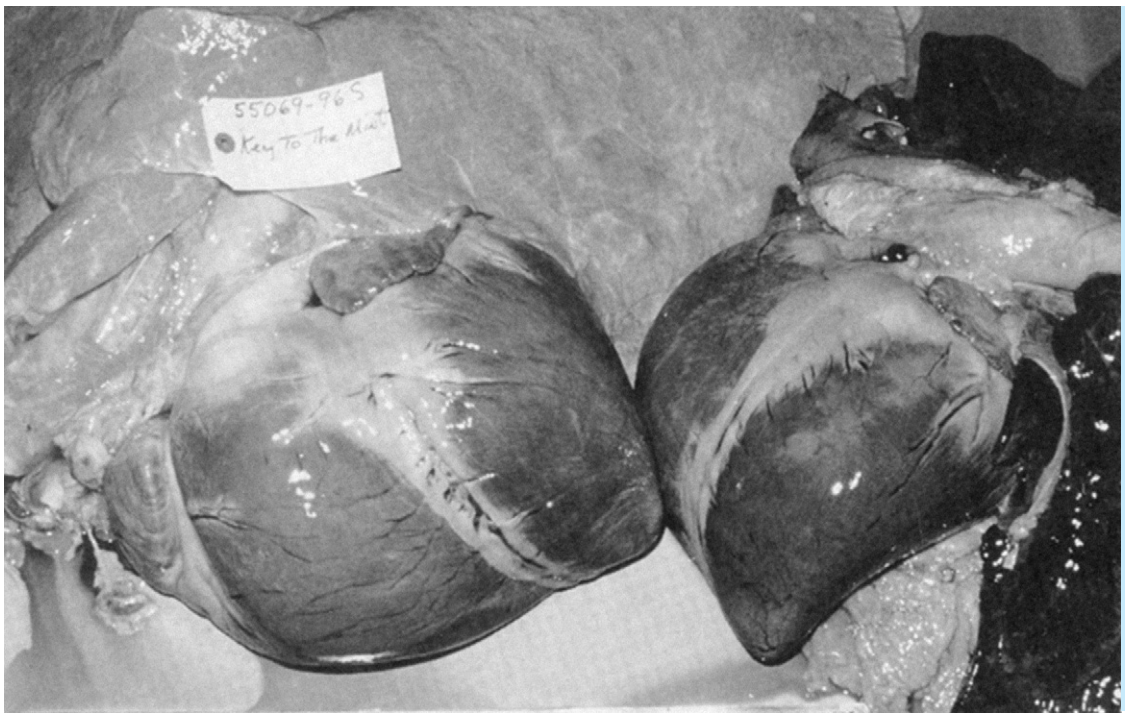


Fig. 32.15 Comparison of Key to the Mint's heart on the left (15.8 lb (7.2 kg), heart score, 157) compared with that of an unremarkable stallion on the right (12 lb (5.5 kg)). (Reproduced with kind permission from Haun[27] and Dr Thomas Swerczek)

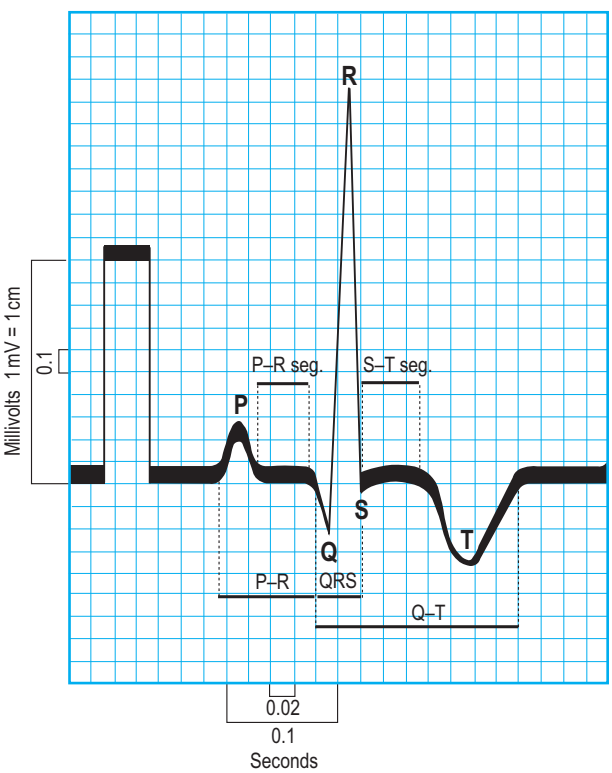


Fig. 32.16 The heart score is calculated from the width of the QRS complex (in milliseconds) on the electrocardiogram shown above. In general, the larger the heart the wider the QRS complex and the greater the heart score. See text for further details. (Reproduced with kind permission from Haun.[27])

Table 32.4 Relationship derived between heart weight and heart score. (Reproduced with kind permission from Haun[27])

Heart score (m/s)	Heart weight	
	lb	kg
100	6.6	3.0
110	7.36	3.35
120	10.12	4.6
130	11.88	5.4
140	13.64	6.2
150	15.4	7.0
160	17.16	7.8

Table 32.5 Relationships derived among heart score, heart weight, and stroke volume and cardiac output at maximal exercise

Heart score (m/s)	Heart weight (kg)[a]	Stroke volume (L)[a]	Cardiac output (L/min at max exercise)[b]
100	3.0	0.5	100
110	3.8	0.75	150
120	4.6	1.0	200
130	5.4	1.25	250

[a] Estimated by Steel (unpublished data 1977).
[b] Assuming a heart rate of 200 beats/min.

equine spleen is of paramount importance for setting the horses high exercising blood hemoglobin concentration ([Hb]) and thus Cao_2. Splenic contraction may dump 12 L or

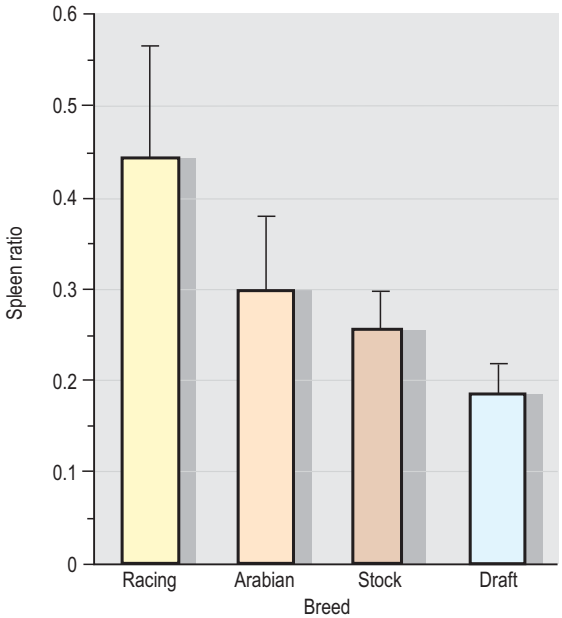


Fig. 32.17
Spleen ratio (spleen weight as a percentage of body weight) with standard deviations for racing, Arabian, stock and draft horses. (Revised from Kline & Foreman.[28])

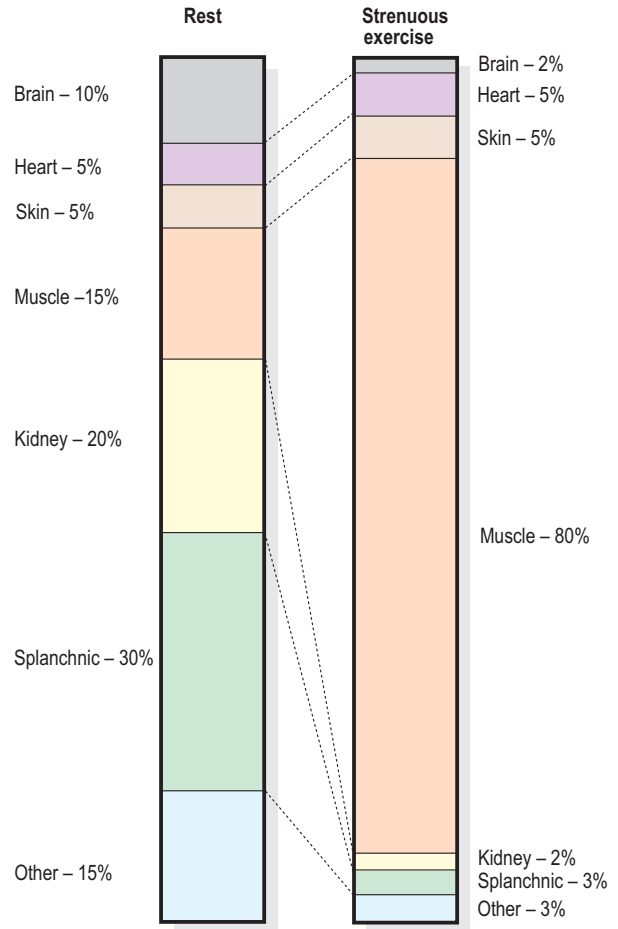
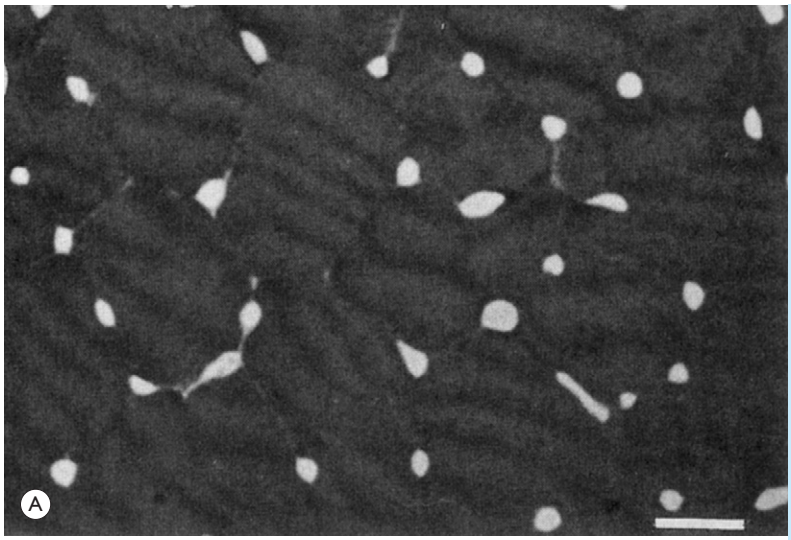


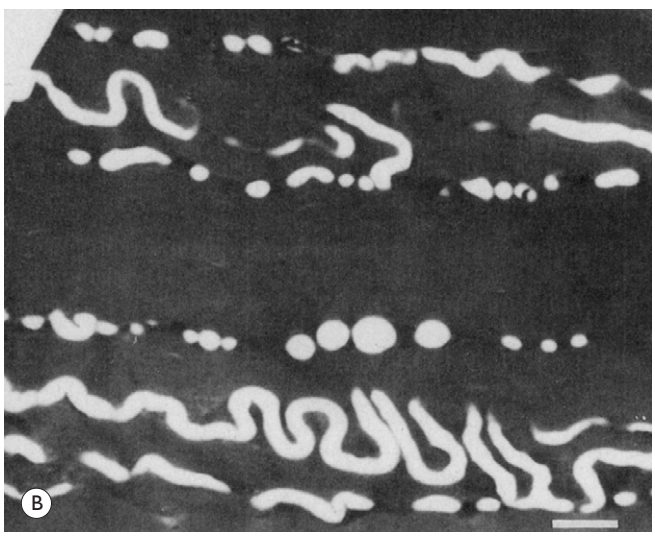
Fig. 32.18
Distribution of cardiac output ($\dot{Q}$) at rest and during maximal exercise. In the highly trained, very fit Thoroughbred, it is possible that skeletal muscle blood flow may reach as much as 90% of cardiac output. (Values from Erickson.[41])

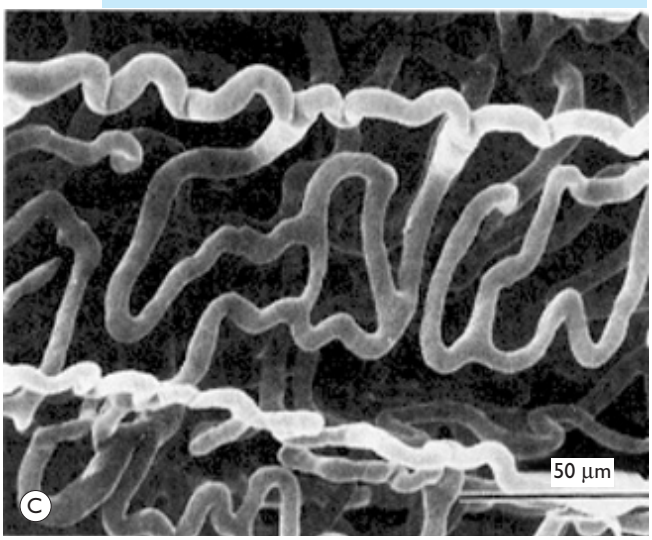
more of red cells into the circulation, thereby doubling the number of circulating red blood cells.[35–38] In keeping with the importance of $\dot{Q}o_2$ in determining racing performance, splenectomy reduces $\dot{V}o_{2max}$ by over 30% in the Thoroughbred.[37] Splenic reserve is correlated with spleen weight and total blood volume but not body mass per se.[32,35,38] Racing horses have a significantly greater splenic mass than non-racing breeds, i.e. Arabian, stock, draft[28] (Fig. 32.17).

Systemic circulation and microcirculation

In the Thoroughbred, total blood volume approximates 10% of body mass[39,40] and of this approximately 50 L of blood, 75% resides in the systemic circulation of which 60% is in the highly distensible venous system and only 15% in the arteries. Depending upon the activity undertaken (e.g. digestion, thermal stress, exercise) the cardiovascular system must redistribute $\dot{Q}$ amongst the appropriate organs. Physical exercise produces the most profound physiological stress to the horse and as shown in Fig. 32.18, the percentage of $\dot{Q}$ that perfuses the splanchnic region and kidneys is reduced from ~ 50% at rest to only 5% at maximal exercise. By contrast, exercising skeletal muscle may receive 80–90% of $\dot{Q}$ compared with only 10–20% at rest. Such flexible and precise control over blood flow distribution demands a network of powerful muscular arterioles that provide the principal resistance to flow in the systemic circulation and which can dilate or constrict rapidly in response to the vasoactive effects of muscle metabolites, prostacyclins, and nitric oxide (dilation) or sympathetic stimulation, angiotensin and endothelin (constriction). From rest to maximal exercise, skeletal muscle blood flow may increase over 60–70-fold. Although the perfusion pressure does increase substantially, elevated muscle vascular conductance (dilation) constitutes the primary mechanism by which the increased muscle blood flow ($\dot{Q}$m) is achieved and this response is detailed in the section 'Cardiovascular physiology and responses to exercise' below. Following a systematic series of bifurcations through several orders of progressively narrower arterioles, the vascular tree ramifies into a series of capillaries which form the principal site for blood–tissue exchange (Fig. 32.19). The capillary wall is devoid of smooth muscle and presents a barrier typically less than 1 μm thick between the capillary blood and the myocyte sarcolemma. The density, volume, and surface area of the skeletal muscle capillary bed is correlated closely with oxidative capacity and thus muscle fiber type.[44,45] In equine muscle (transverse section across fibers), there may be between 400 and 800 capillaries per square millimeter with







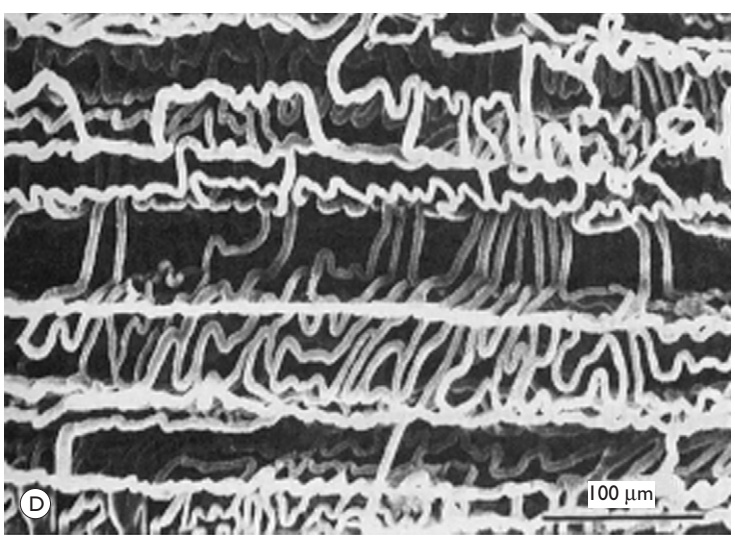


Fig. 32.19
The capillary bed of skeletal muscle possesses a complex three-dimensional geometry with extensive branching and capillaries that become extremely tortuous at short muscle sarcomere lengths forming a convoluted network around the fibers. (A, B) Light micrographs of pony vastus medialis muscle perfusion-fixed at 1.90 μm sarcomere length and cut transverse (A) and longitudinal (B) to the fiber longitudinal axis. Capillaries have been flushed clear of red cells and appear white surrounding the perimeter of the individual muscle fibers (A). A, B scale bar = 25 μm. (C, D) Corrosion casts (muscle fibers have been corroded away) of the mouse soleus muscle that demonstrates superbly the three-dimensional geometry of the muscle capillary bed. (A and B reproduced with kind permission from Mathieu-Costello et al;[42] C and D reproduced with kind permission from Ishikawa.[43])

a mean diameter of 4–6 μm[42,46] and these contain over 80% of the intramuscular blood volume. As we shall see in the Section 'Cardiovascular physiology and responses to exercise' below, the capillary volume is crucial for setting red blood cell transit time in the capillary and facilitating O_2 offloading during exercise (or loading in the pulmonary capillary).

Pulmonary circulation and microcirculation

At rest, the pulmonary circulation holds about 20% of total blood volume (mostly in larger compliant vessels rather than the capillaries) which decreases at exercise onset. Because the pulmonary circulation has to accept the whole output of the right ventricle, it is a low-pressure, high-conductance system with arteries and arterioles that are far less muscular than seen for the systemic circulation. Approximately half of the pulmonary vascular resistance is precapillary and the capillaries themselves constitute an important site of resistance particularly at high lung volumes and when alveolar pressure is positive during breathhold or forced exhalation.

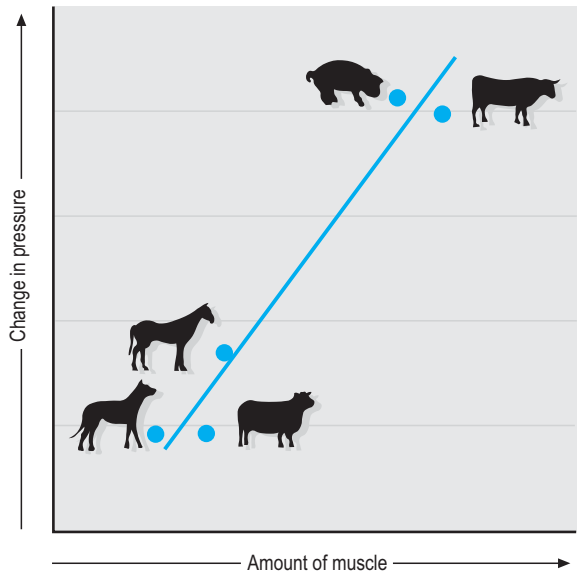


Fig. 32.20
Species variation in the muscle thickness in the walls of small pulmonary arteries and the change in pulmonary arterial pressure evidenced during hypoxic exposure. Note that the horse has far less muscle (and thus change in pulmonary arterial pressure) than the cow and the pig when exposed to hypoxia. (Redrawn from Robinson.[47])

The pulmonary vasomotor tone can be influenced by a variety of neural and humoral factors. Specifically, pulmonary arteries have both sympathetic and parasympathetic innervation and respond to serotonin, epinephrine, norepinephrine, isoproterenol, acetylcholine, angiotensin II, leukotrienes, prostacyclins, histamine, thromboxane, bradykinin, and arachidonic acid. However, as seen in Fig. 32.20, the horse has relatively little pulmonary vascular smooth muscle compared with cattle and pigs.[47] Thus, the horse exhibits only a weak vasoconstrictive response which is most evident in the low susceptibility of the horse to pulmonary hypoxic vasoconstriction but which causes a profound pulmonary hypertension in cattle and pigs at altitude. During exercise, the elevated pulmonary arterial pressures induce recruitment and distension of the vascular bed which reduces vascular resistance, elevates vascular conductance, and increases pulmonary capillary volume (Fig. 32.21). Despite this elevated conductance, pulmonary vascular pressures do become extraordinarily high during maximal exercise (see 'Cardiovascular physiology and responses to exercise' below).

The pulmonary capillaries form a dense plexus around each alveolus and, unlike their systemic counterparts, are not embedded within a supporting tissue matrix and thus are subject to collapse at positive alveolar pressures particularly when perfusion pressure is low. In the horse, these vessels are about 6–7 μm in diameter[49] (which is narrower than found in dog or rabbit lungs) and have a total wall thickness

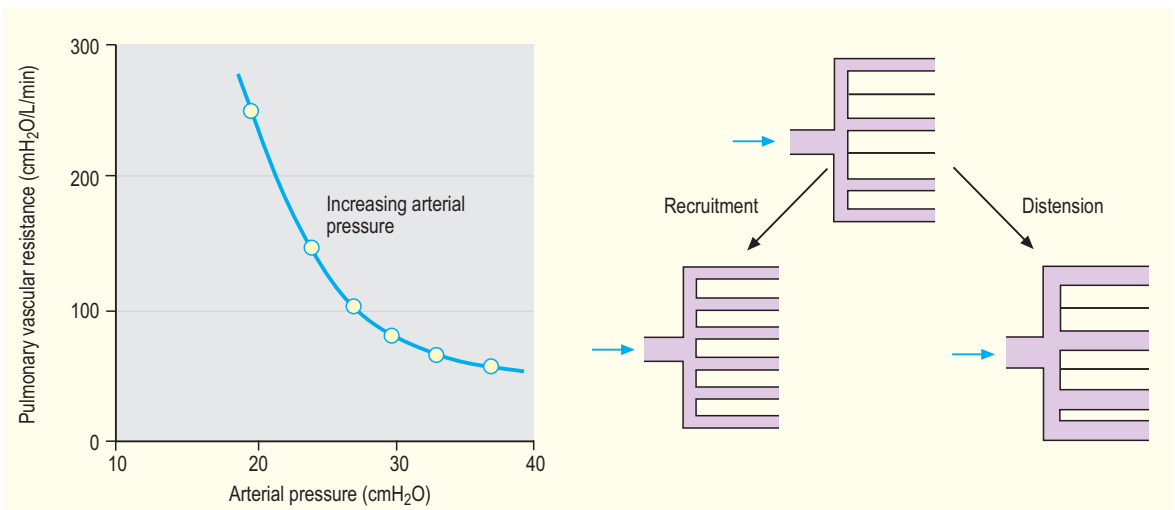


Fig. 32.21
Elevated pulmonary arterial pressure reduces pulmonary vascular resistance because it forces a recruitment of previously non-perfused vessels and distends those vessels recruited. (Revised from West.[48])

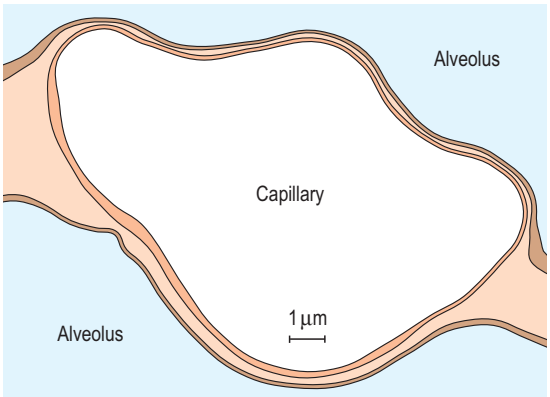


Fig. 32.22
Pulmonary capillary interposed between two alveoli. Note the exquisitely thin blood gas barrier. (Redrawn from Birks.[49])

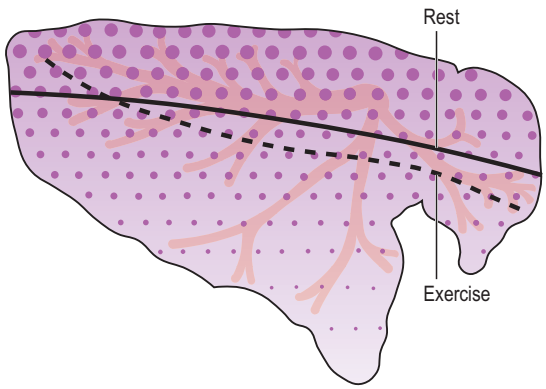


Fig. 32.23
Distribution of pulmonary blood flow in the lung at rest. The shading indicates relative blood flow (the darker the area, the greater the blood flow) and the solid and broken lines indicate relative dorsal–caudal blood flow at rest and during exercise, respectively. Note that pulmonary blood flow is not regulated by gravity, as once thought. (Data from Hlastala and colleagues;[51] redrawn from Robinson.[47])

(capillary endothelium, basement membrane, alveolar epithelium) which averages only 0.9 µm (Fig. 32.22). Consequently, even at relatively low transmural pressures (positive luminal plus negative alveolar) these vessels bulge into the alveolar space and may rupture during exercise (exercise-induced pulmonary hemorrhage). Pulmonary capillary blood volume constitutes only a very small fraction of that present in the pulmonary circulation, which confers the advantage of maximizing blood-gas spatial contact but has the consequence of limiting red blood cell transit time in the capillary. Pulmonary capillary blood volume in the horse is 60–80% greater than that of a steer of the same mass.[50]

In healthy animals, active vasomotor control is thought to play a relatively minor role (compared with the effects of hydrostatic pressure gradients, lung volume, and alveolar pressure) in setting the distribution of blood flow within the pulmonary circulation. However, recent investigations have demonstrated that there is a gravity-independent distribution of $\dot{Q}$ toward the dorsal aspect of the lung (Fig. 32.23).[51] This effect may be explained by a regionally dependent arteriolar reponsiveness. For example, arterioles in the upper lung regions exhibit a pronounced vasodilation to methacholine (an endothelium-dependent vasodilator) whereas those at the bottom do not.[52]

Cardiovascular physiology and responses to exercise

Cardiac output

Cardiac output ($\dot{Q}$) is defined as the volume of blood ejected from the right or left ventricle and is usually expressed per minute. As illustrated in Table 32.6, cardiac output is the most important means of increasing muscle O_2 delivery during exercise and is the principal determinant of $\dot{V}O_{2max}$,

Table 32.6 Cardiovascular responses to maximal exercise in a 500-kg horse. (Data from Erickson[41])

Variable	Rest	Exercise	Exercise/rest ratio
Heart rate (beats/min)	30	210–250	7–8
Cardiac output			
L/min	30	240–>450	8–13
SV (mL)	1000	1700	1.7
Systolic/diastolic arterial blood pressure (mmHg)	130/80	230/110	1.6
Pulse pressure (mmHg)	50	120+	3–4
Pulmonary artery pressure (mmHg)	20–30	90–140	3–4
Hemoglobin concentration (g/dL)	13	17–24	1.3–1.6
O_2 consumption (mL/min/kg)	2–4	160–220	40–110
L/min	1.5–20	80–110	40–75
$a - v\ O_2$ difference (mL/100mL)	5	20–25	4–5

which can vary from 90 to 220 mL/kg/min.[5,53] Very fit Thoroughbreds have had $\dot{Q}$ values measured in excess of 350 L/min and as mentioned above, based upon estimated heart size, it is likely that superlative athletes have achieved $\dot{Q}$ values between 400 and 540 L/min (Figs 32.13A, B, 32.14). During submaximal exercise, $\dot{Q}$ (and body O_2 delivery, $\dot{Q}O_2$) increase linearly with running speed and also $\dot{V}O_2$.[54–56] Increased $\dot{Q}$ in combination with the splenic-induced polycythemia may elevate $\dot{Q}O_2$ over 20-fold in a very fit Thoroughbred race horse from rest to maximal exercise. Increases in $\dot{Q}$ are driven most powerfully by heart rate with a smaller contribution from elevated stroke volume (Table 32.6).

Heart rate

At exercise onset, heart rate increases rapidly from approximately 30 beats/min at rest to approximately 110 beats/min via parasympathetic withdrawal, with the consequence that at low running speeds heart rate may elicit an early overshoot (Fig. 32.24).[26,57,58] At faster speeds, further heart rate elevations are achieved less rapidly and are driven by the sympathetic nervous system and circulating catecholamines. Maximum heart rate varies between 204 and 241 beats/min and a reduction with age has been described recently in horses.[59] In human populations a decrease of 1 beat/min/yr has been well established.[60,61] Maximum heart rate is not considered to be an important measure of fitness and as seen in the section 'Exercise training' below, does not change with training. The speed or velocity a horse can achieve or sustain at a submaximal heart rate of 140, 170 or 200 beats/min (i.e. V_{140}, V_{170}, and V_{200}) provides information about stroke volume and cardiovascular capacity and pertains directly to fitness and racing potential.[53] Both heart rate[26,57] and $\dot{V}O_2$[62] increase faster after a warm-up, although as cardiac output does not appear to limit $\dot{V}O_2$ kinetics at exercise onset,[63,64] the

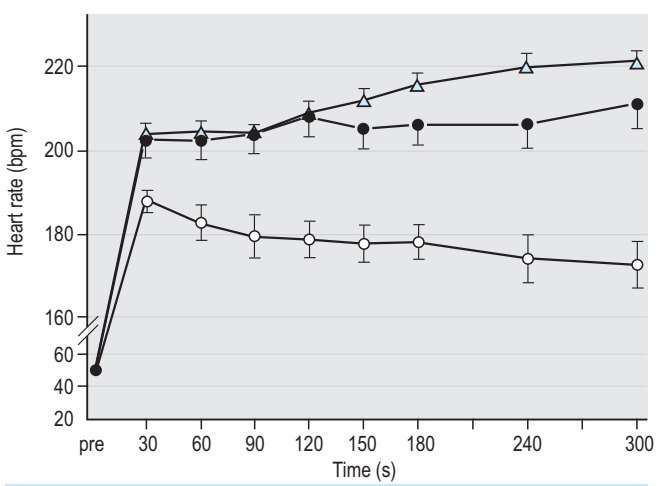


Fig. 32.24
Heart rate response following the onset of exercise at 50% (hollow circles), 75% (solid circles), and 100% (triangles) $\dot{V}O_{2max}$ in Standardbred race horses. Note the pronounced early overshoot at 50% $\dot{V}O_{2max}$. (Redrawn from Evans & Rose.[57])

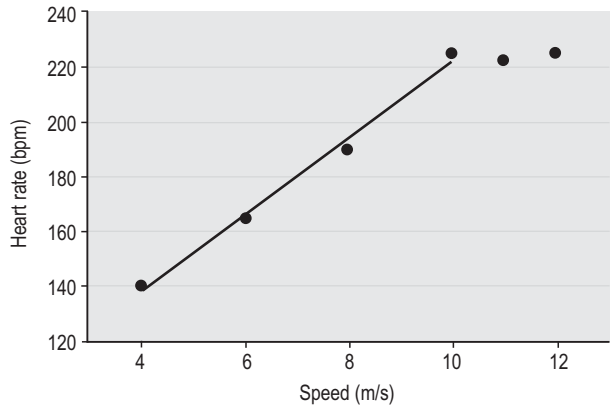


Fig. 32.25
Relationship between running speed and heart rate from 4 m/s to maximal speed (12 m/s) in a race-fit Thoroughbred race horse. (Redrawn from Evans.[53])

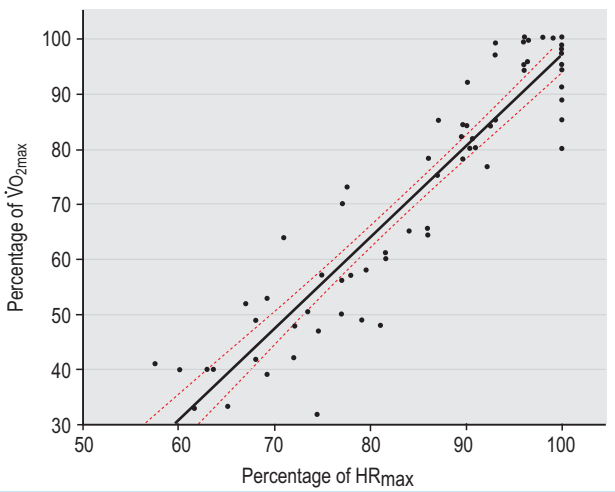


Fig. 32.26
Relationship between %maximum heart rate and $\%\dot{V}O_{2max}$ in horses of varying fitness levels. (Redrawn from Evans & Rose.[67])

two are probably not linked mechanistically. There is a linear relationship between heart rate and running speed and between $\%HR_{max}$ and $\%\dot{V}O_{2max}$ (Figs 32.25, 32.26).[53,65–67] However, at a constant running speed in the heavy intensity domain, heart rate may continue to rise and this is accompanied by rising ventilation, $\dot{V}O_2$, and $\dot{Q}$.[68] This 'slow component' of the cardiorespiratory response is driven by elevated metabolic requirements within the exercising muscles,[69] a progressive fall in blood volume, and also thermoregulatory responses to the rising body temperature.

Stroke volume

Stroke volume refers to the volume of blood ejected per beat from the left or right ventricle and increases from approximately 1000 mL (2–2.5 mL/kg) at rest up to 1700 mL (3–4 mL/kg) or higher at maximal exercise (Table 32.6).[12,53,54,56,66] If a maximum heart rate of 225 beats/min is assumed for Secretariat, his stroke volume would have been well in excess of 2000 mL/beat. Typically, stroke volume

increases sharply at exercise onset up to around 40% $\dot{V}O_{2max}$ consequent to increased blood volume, venous return, and filling pressures according to the Frank–Starling mechanism.[26,70] What is particularly remarkable is that ventricular filling (and thus stroke volume) does not appear to be compromised at maximal exercise despite heart rates of 4 beats/s.

Arterial O_2 content (CaO_2) and O_2 delivery ($\dot{Q} \times CaO_2 = \dot{Q}O_2$)

As described in the first section, arterial O_2 content, CaO_2, is determined principally by blood hemoglobin concentration (which sets the O_2 carrying capacity) and the % saturation of those hemoglobin binding sites with O_2. At rest, arterial hemoglobin concentration is 12–14 g/100 mL, whereas at maximal exercise the spleen has expelled sufficient red blood cells to increase this up to 21–24 g/100 mL. This corresponds to a packed cell volume increase from 35% at rest to 70% at maximal exercise. Thus, at maximal exercise if hemoglobin was 100% saturated with O_2, each 100 mL of blood would hold between 27 and 31 mL O_2. However, as discussed below arterial O_2 saturation falls from around 95% at rest to below 85% at maximal exercise,[10] and this will decrease CaO_2 to 23–26 mL/100 mL. Even considering this effect, with a $\dot{Q}$ of 400 L/min, the Thoroughbred can deliver a prodigious 100 L O_2/min to the body during maximal exercise.

Determinants of O_2 loading

Pulmonary circulation

The rapid increase in pulmonary blood flow at exercise onset in concert with the polycythemic hyperviscosity[37,71–73] elevates pulmonary vascular pressures (Fig. 32.27) and forces recruitment of non-flowing vessels and distension of flowing vessels (Fig. 32.21). This behavior elevates pulmonary vascular conductance several fold but does not prevent mean pulmonary arterial pressure from exceeding 120 mmHg in fit horses;[63,74–78] the consequences of this hypertension include exercise-induced pulmonary hemorrhage (EIPH) and are detailed below. Splenectomy (reduced blood viscosity),[37,73] diuretic therapy (furosemide),[78–82] and nitric oxide (vasodilator)[77] are all effective modalities for reducing maximal pulmonary arterial pressures during exercise. However, splenectomy reduces $\dot{Q}O_2$ and thus negatively impacts both $\dot{V}O_{2max}$ and performance.[37] As mentioned in the section, 'Anatomy of the cardiovascular system', in contrast to conventional wisdom, it has now been established that gravity is not the sole or even the primary regulator of the regional distribution of blood flow within the equine lung. Elegant fluorescent microsphere studies by Bernard, Hlastala, Erickson and colleagues have determined that pulmonary $\dot{Q}$ is preferentially distributed towards the dorsal aspect of the lung at rest and during exercise (Fig. 32.23)[51,83] likely due to a regional variation in sensitivity to endothelium-induced vasodilation.[52]

Exercise-induced arterial hypoxemia

As demonstrated in Fig. 32.28, blood leaving the horse's lung during maximal exercise is profoundly hypoxemic.[10,84] Several mechanisms impair O_2 loading in the pulmonary capillary. These are described below in order of importance.

Alveolar–capillary O_2 diffusion limitation (~ 70% of alveolar-to-capillary O_2 pressure gradient) During maximal exercise the horse develops a significant alveolar-to-capillary O_2 pressure (P) gradient.[84] Unlike in other species such as man, in whom alveolar hyperventilation drives arterial PCO_2 below resting and in which alveolar PO_2 becomes elevated during intense exercise, in the horse alveolar PO_2 may fall and consequently the increased alveolar-to-capillary O_2 pressure gradient results from the reduced arterial PO_2. The primary reason for the elevated alveolar-to-capillary O_2 pressure gradient and arterial hypoxemia relates to the prodigious values of $\dot{Q}$ achieved. The average transit time for a red blood cell (RBC) within the pulmonary capillary is determined by the ratio between pulmonary capillary blood volume and $\dot{Q}$. In the horse at rest, pulmonary capillary volume is some 1.8-fold that of an equivalently sized steer[50] and RBCs probably spend 0.75–1 s within the capillary, which is thought to be three to four times longer than necessary for equilibration with the alveolar O_2 (Fig. 32.28). However, as we have seen during maximal exercise, $\dot{Q}$ may increase from rest by up to 13-fold and although capillary volume does increase it can only do so by a small fraction of this. Consequently, red cell capillary transit time will decrease. Morphometric estimation of mean exercising red cell transit time places it at 0.3–0.5 s.[50,85] This is probably a gross overestimate of that present in very fit race horses that can achieve $\dot{Q}$ values around 400 L/min and it is pertinent that even if this were the mean transit time there would exist a substantial population of red cells with considerably shorter transit times. Because of the sigmoid shape of the O_2 dissociation curve, it is not possible for those cells with longer transit times to compensate for those that do not equilibrate with the alveolar gas. The consequence of this mixing of hypoxemic with normoxemic blood in the pulmonary veins will be arterial hypoxemia. In addition, the rightward shift of the O_2 dissociation curve consequent to elevated blood temperatures, arterial hypercapnia, and acidosis will reduce the hemoglobin–O_2 affinity and further exacerbate alveolar– capillary disequilibrium.

Alveolar hypoventilation As mentioned above, at maximal exercise the horse's arterial PCO_2 may exceed 65 mmHg.[10,72,74,86] As calculated from the alveolar gas equation, this will cause alveolar PO_2 to fall from approximately 100 mmHg at rest to approximately 90 mmHg at maximal exercise (Fig. 32.28).

Mild ventilation-to-perfusion ($\dot{V}/\dot{Q}$) mismatch During exercise, the horse develops a small but significant degree of $\dot{V}/\dot{Q}$ mismatch. However, this is not thought to contribute in a quantitatively important fashion to the exercise-induced arterial hypoxemia.[84,87] The percentage of $\dot{Q}$ that does not come into contact with alveolar gas (i.e. shunt) is trivially small (≤ 1%).

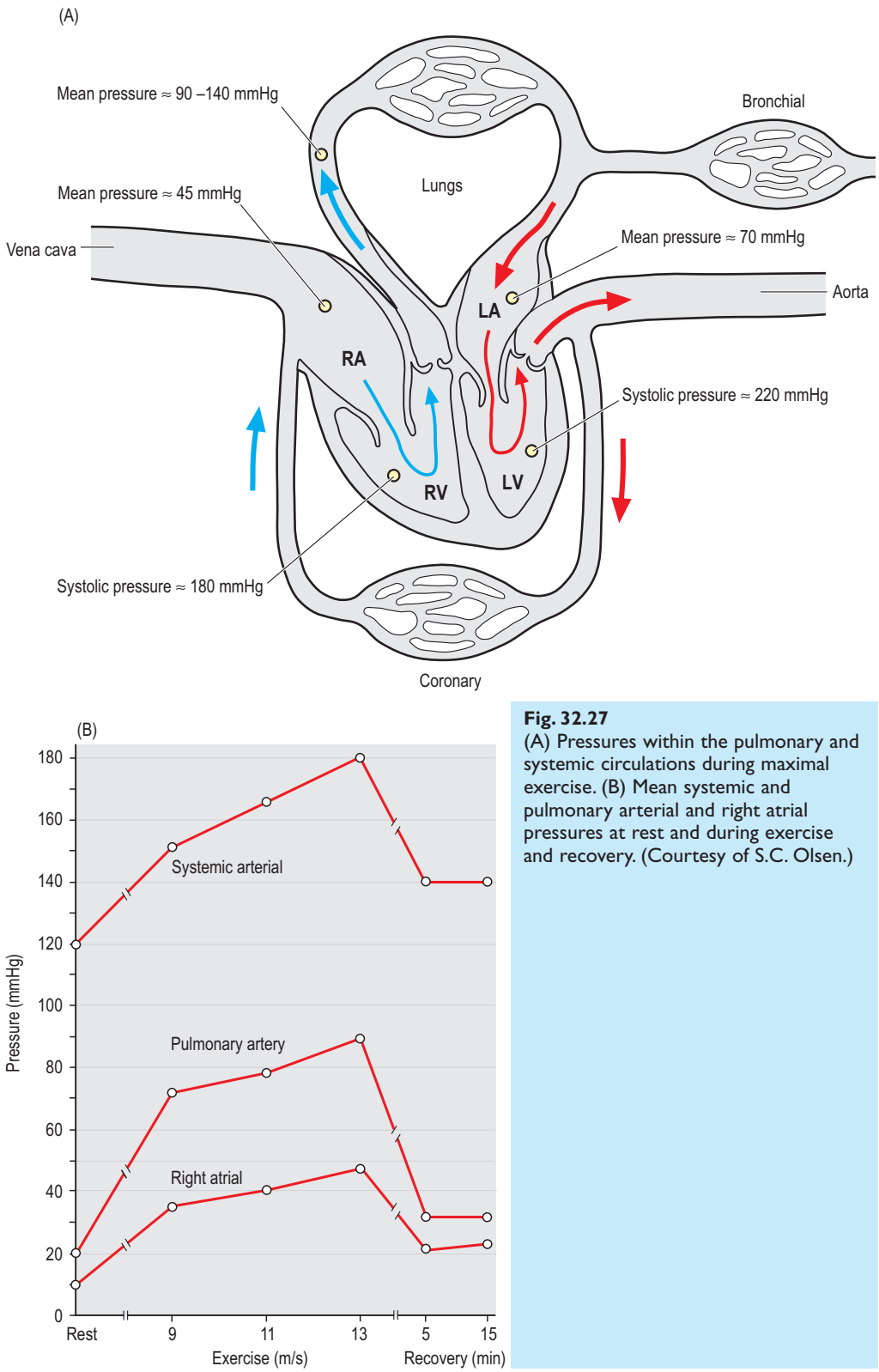


Fig. 32.27
(A) Pressures within the pulmonary and systemic circulations during maximal exercise. (B) Mean systemic and pulmonary arterial and right atrial pressures at rest and during exercise and recovery. (Courtesy of S.C. Olsen.)

Exercise-induced pulmonary hemorrhage

Exercise-induced pulmonary hemorrhage (EIPH) is characterized by rupture of the blood–gas barrier and the presence of blood in the alveolar space and airways. In extreme cases, frank epistaxis may occur. EIPH is prevalent in Thoroughbreds, Standardbreds, and also Quarter Horses during sprint racing, where repeated endoscopic examination indicates an incidence approaching 95%.[88–93] Microspheres (10–15 μm)

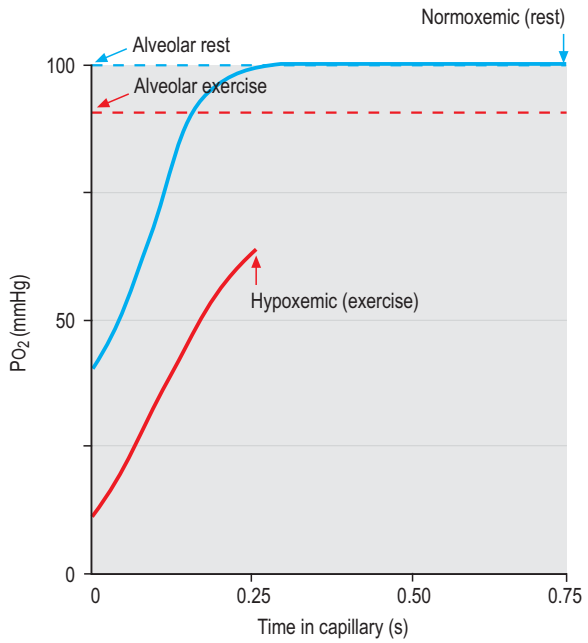


Fig. 32.28
Partial pressure of O_2 (P_{O_2}) in the red blood cell as a function of pulmonary capillary transit time at rest and during exercise. Note the reduction in alveolar P_{O_2} during exercise (alveolar hypoventilation) and the profound decrease in red cell P_{O_2} as it enters and leaves the capillary during maximal exercise.

injected into the jugular vein have identified the pulmonary rather than the bronchial (systemic) vasculature as the site of EIPH[75] and elegant electron microscopy studies have captured red cells actually erupting from breaks in the fragile blood–gas barrier (Fig. 32.29).[94,95]

EIPH must ultimately arise from high positive intraluminal pressures coupled with very negative alveolar pressures which summate across the blood–gas barrier causing failure (Fig. 32.29).[74,96,97] However, the etiology of EIPH is complex and numerous mechanisms have been implicated.[93] These include:

1. alveolar pressure fluctuations which may be exacerbated by upper airway obstruction (inspiratory nasal collapse;[98] laryngeal hemiplegia[99])
2. pulmonary hypertension consequent to high $\dot{Q}$ values (> 120 mmHg mean pulmonary artery pressure[74,75,80,97]), exercise-induced hyperviscosity,[71,100] and possibly arteriolar vasoconstriction[72,76,77]
3. redistribution of blood within the lung[83]
4. mechanical stresses of respiration and locomotion.[101]

Additional factors that may contribute to elevated pulmonary arterial pressures include flow limitation induced by the relatively small cross-sectional area of the atrioventricular (AV) valves,[93] possible regurgitation through the AV valves consequent to high ventricular pressures, and also a left ventricular relaxation rate that may be too slow to allow rapid filling at lower left atrial pressures.[93,102,103] With regard to valvular regurgitation, Young & Wood[104] performed cardiac auscultation on 111 Thoroughbreds aged 2–5 and reported that the incidence of mitral and tricuspid regurgitation was 7% and 13%, respectively. After training, this increased significantly to 22% (mitral) and 26% (tricuspid).

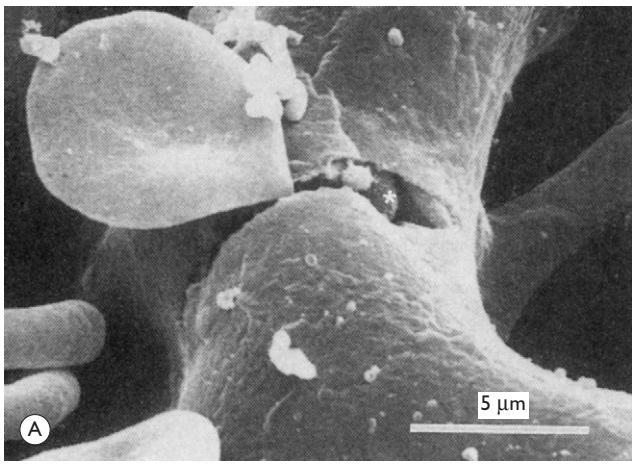
Following the observation that pulmonary artery pressures and capillary transmural pressures reach extraordinarily high levels in the exercising horse and that there are threshold pulmonary arterial and capillary pressures above which the integrity of the blood–gas barrier is disrupted,[97,105] EIPH research and therapeutic interventions have focused on reducing these pressures.[93] Diuretic treatment with furosemide which lowers pulmonary vascular pressures has the greatest proven efficacy in this regard.[78,80,106,107] Nasal passage support with the Flair nasal strip also reduces EIPH, presumably by reducing alveolar pressure swings and the transmural pressure gradient.[78,98,107,108] Other treatment strategies involving Chinese herbal remedies and IgG are currently being evaluated.[106] Experiments using furosemide,[78] nitric oxide inhalation,[77] and inhibition of nitric oxide synthase[72,76] have demonstrated that interventions which lower peak pulmonary artery pressure may not necessarily induce a corresponding reduction in EIPH.[93] Thus, regulation of the distribution of pulmonary $\dot{Q}$ and vascular conductance may be crucial for limiting EIPH and continues to be an active and important avenue of research.

Systemic circulation

Cardiovascular control must subserve two crucial and sometimes conflicting demands. Namely, muscle $\dot{Q}$ must achieve a level commensurate with O_2 and substrate requirements (up to 100-fold resting) whilst maintaining systemic mean arterial pressure (MAP) within acceptable limits. Excessive vasodilation lowers MAP and compromises blood flow to critical organs such as the brain. By contrast, excessive MAP impairs vascular integrity, elevates vascular fluid exudation, and causes tissue damage.

MAP is the product of $\dot{Q}$ and total peripheral resistance (TPR). TPR is determined principally by the aggregate cross-sectional area of all recruited arterioles and also blood viscosity. Figure 32.30 details many of the factors controlling vascular smooth muscle and thus vascular conductance within skeletal muscle. Even at maximal exercise, there is a profound sympathetic vasoconstrictor tone within skeletal muscle[110] and blood pressure regulation depends upon the interaction of central nervous system reflexes emanating from the brain (central command) and those within the working muscle.[111–115] MAP rises from 110 to 138 mmHg at rest to as high as 200 mmHg during maximal exercise (Table 32.6, Fig. 32.27).[53,55,72,76,116,117] In addition to MAP, systolic left ventricular and right atrial pressures increase substantially[53,56,66,75] and myocardial contractility (peak derivative of left ventricular pressure, LV$dp/dt$) rises progressively with running speed.[53]

From rest to exercise, skeletal muscle arterial and arteriolar vasodilation allows TPR to fall precipitously which facilitates enormous $\dot{Q}$ values with a relatively modest rise in



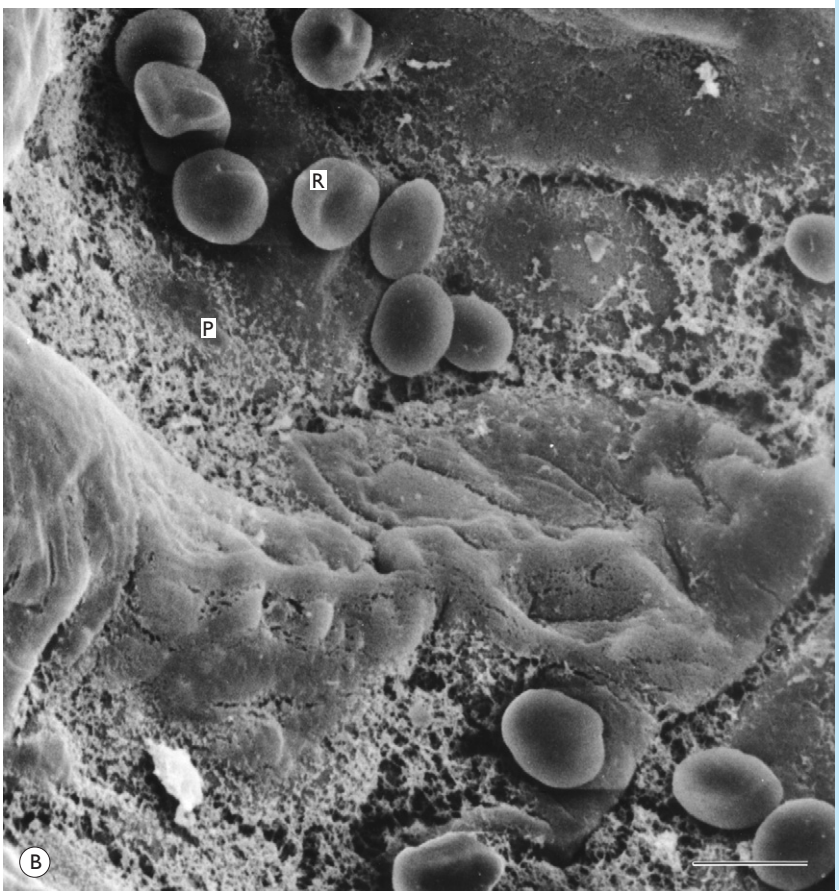


Fig. 32.29
Rupture of the pulmonary capillaries. (A) Red blood cell emerging from a split in the blood–gas barrier into the alveolar space. (Reproduced with kind permission from Fu et al.[94]) (B) Exercise-induced pulmonary hemorrhage in the alveolar space of a pony lung. (Reproduced with kind permission from Erickson et al.[95]) R, red blood cell; P, proteinaceous material. Scale bar = 5 μm.

MAP. Specifically, if $\dot{Q}$ increases from 30 (rest) to 450 (maximal exercise) L/min for a corresponding increase in MAP from 120 to 180 mmHg, TPR must fall by 90% (i.e., 4 to 0.4 mmHg/L/min). The control of skeletal muscle vasomotor tone involves a complex array of mechanical (muscle pump, shear stress, myogenic), humoral (vasoactive metabolites, catecholamines) and neural (sympathetic, anterograde and retrograde conducted vasodilation) mechanisms (Fig. 32.30). Recent findings from Kindig and colleagues[72,76,77] indicate a major role for NO in increasing systemic and vascular conductances during intense running (Fig. 32.31). There have been several excellent recent reviews on the regulation of muscle vascular conductance[113–115,118] and it is apparent that the precise mechanisms which mediate the rapid increase of muscle $\dot{Q}$ and $\dot{Q}o_2$ at exercise onset remain to be resolved.[119] The matching between $\dot{Q}o_2$ and $\dot{V}o_2$ during exercise is so precise that it has inspired the suggestion that the system behaves as though there is an O_2 sensor located within the muscle or its vascular bed.[115] However, if present such a sensor remains elusive.

During exercise, muscle $\dot{Q}$ is distributed heterogeneously between and within muscles depending on their recruitment,

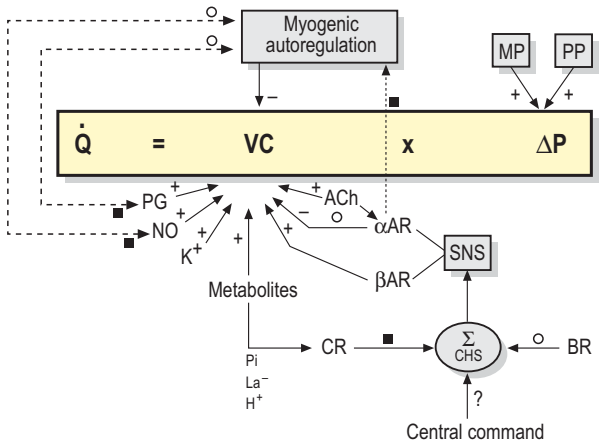


Fig. 32.30
Muscle blood flow (Qm) is regulated by the interaction of multiple mechanical (top row) and nonmechanical (bottom row) factors which act directly on vascular smooth muscle to either reduce (–) or increase (+) limb vascular conductance (VC). Qm will also increase if the pressure gradient (Δ*P*) across the capillary bed is enhanced by the muscle pump (MP) following muscle contraction or elevated perfusion pressure (PP). In addition, VC may be changed by the action of the sympathetic nervous system (SNS) after integration of opposing reflex inputs arising from the baroreflex (BR) and chemoreflex (CR) and also from higher centers within the brain. There are also other factors that may potentiate (solid squares) or constrain (hollow circles) the effect of other regulatory agents (dotted lines). The net blood flow response to exercise is the result of all of these factors. PG, prostaglandins; NO, nitric oxide; K^+, potassium ion; Pi, inorganic phosphate; La^-, lactate ion; βAR, beta-adrenergic receptor; αAR, alpha-adrenergic receptor; ACh, acetyl choline. (Redrawn from Shoemaker & Hughson.[109])

oxidative capacity, fiber type, and $\dot{V}O_2$ demands.[114] Thus, in the exercising horse, $\dot{Q}$ in heavily recruited, highly oxidative red muscles in the limbs and respiratory system may achieve peak values of 1–3 L/min/kg.[46,120–122] Specifically, Armstrong and colleagues[46] measured vastus intermedius $\dot{Q}$ at 1.5 L/min/kg in Standardbred horses running at $\dot{V}O_{2max}$ (134 mL/kg/min; $\dot{Q}$ 288 L/min). Within the thigh muscles sampled, the vastus intermedius had the highest citrate synthase activity (mitochondrial volume density, 9%) and myoglobin concentration and exhibited the greatest $\dot{Q}$. Indeed, across the several muscles/muscle portions sampled there was a strong correlation ($r = 0.947$) between citrate synthase activity and $\dot{Q}$ at $\dot{V}O_{2max}$.

The respiratory muscles, and in particular the diaphragm, are extremely oxidative and during near maximal exercise diaphragm $\dot{Q}$ may exceed 2.5 L/min/kg.[120,121] Vasodilation and inspiratory resistance studies have revealed that, even at $\dot{V}O_{2max}$, the diaphragm retains a considerable vasodilator reserve. Specifically, prodigious diaphragm $\dot{Q}$ values close to 4 L/kg/min are feasible.[120–123] It is quite possible that exceptional athletes or individuals with laryngeal hemiplegia exhibit substantially higher diaphragm blood flows than their less fit but healthy counterparts and that the respiratory muscles 'steal' $\dot{Q}$ from the exercising limb muscles,[124] thereby compromising running performance.

The heart, in keeping with its great energetic demands, rich vascularity, and mitochondrial content,[125] sustains an extraordinarily high blood flow during exercise. Specifically, in Standardbreds run at $\dot{V}O_{2max}$, left and right ventricular and septal blood flows increase from their pre-exercise value (0.4–0.6 L/kg/min) up to 2.6–2.9 L/kg/min[46,126] Atrial blood flows are somewhat lower at rest (0.3 L/kg/min) and at $\dot{V}O_{2max}$ (1.3–1.4 L/kg/min). One remarkable feature of the equine heart is that there is little or no gradation of blood flow across the myocardial wall. This is surprising given the high compressive forces to which the subendocardial vessels are subjected as systolic pressures greatly exceed 200 mmHg. There is also evidence that the myocardium retains a substantial vasodilator reserve during maximal exertion, at least in ponies.[127]

Muscle blood flow ($\dot{Q}m$) and O_2 delivery ($\dot{Q}O_2m$) across the rest–exercise transition

The close matching between $\dot{Q}O_2m$ and $\dot{V}O_2$ (Fig. 32.5) presents a strong case for $\dot{Q}O_2m$ being controlled ultimately by muscle metabolism.[16,113,115,128–131] However, $\dot{Q}O_2m$ increases within the first one or two contractions at exercise onset and this timecourse is generally accepted to be far faster than that of $\dot{V}O_2$[132] and is thus too rapid to be explained by metabolic feedback[131] and arteriolar vasodilation mediated by common vasodilators.[133] Consequently, it is thought that the muscle pump, which substantially reduces venular pressure, is key to increasing the pressure differential across the muscle vascular bed and augmenting flow almost instantaneously (Fig. 32.32).[132,134,135] It is also possible that conducted vasodilation, initiated within the capillaries adjacent to active muscle fibers, causes vasodilation upstream within the arteriolar bed.[118,136] Kindig and colleagues[63,64] have demonstrated recently that inhibition of nitric oxide formation using L-NAME actually speeds the rate of $\dot{V}O_2$ increase at exercise onset in Thoroughbreds (Fig. 32.33). Thus, despite any L-NAME induced $\dot{Q}O_2$ reduction,[72,137] relief of nitric oxide-mediated mitochondrial inhibition[138] allows a more rapid $\dot{V}O_2$ increase. This provides the most compelling evidence to date that muscle O_2 delivery does not limit the energetic ($\dot{V}O_2$) response to exercise.

Determinants of O_2 exchange within skeletal muscle: the microcirculation

In skeletal muscle, O_2 diffuses down its pressure gradient from the capillary towards the mitochondria at a rate ($\dot{V}O_2$) that is determined by the O_2 pressure (PO_2) difference between capillary and mitochondria and the tissue diffusing capacity for O_2 (D) according to Fick's law ($\dot{V}O_2 = D[PO_2cap - PO_2 mito]$). The enduring dogma that there is a large PO_2 gradient from the myocyte sarcolemma to the most distant

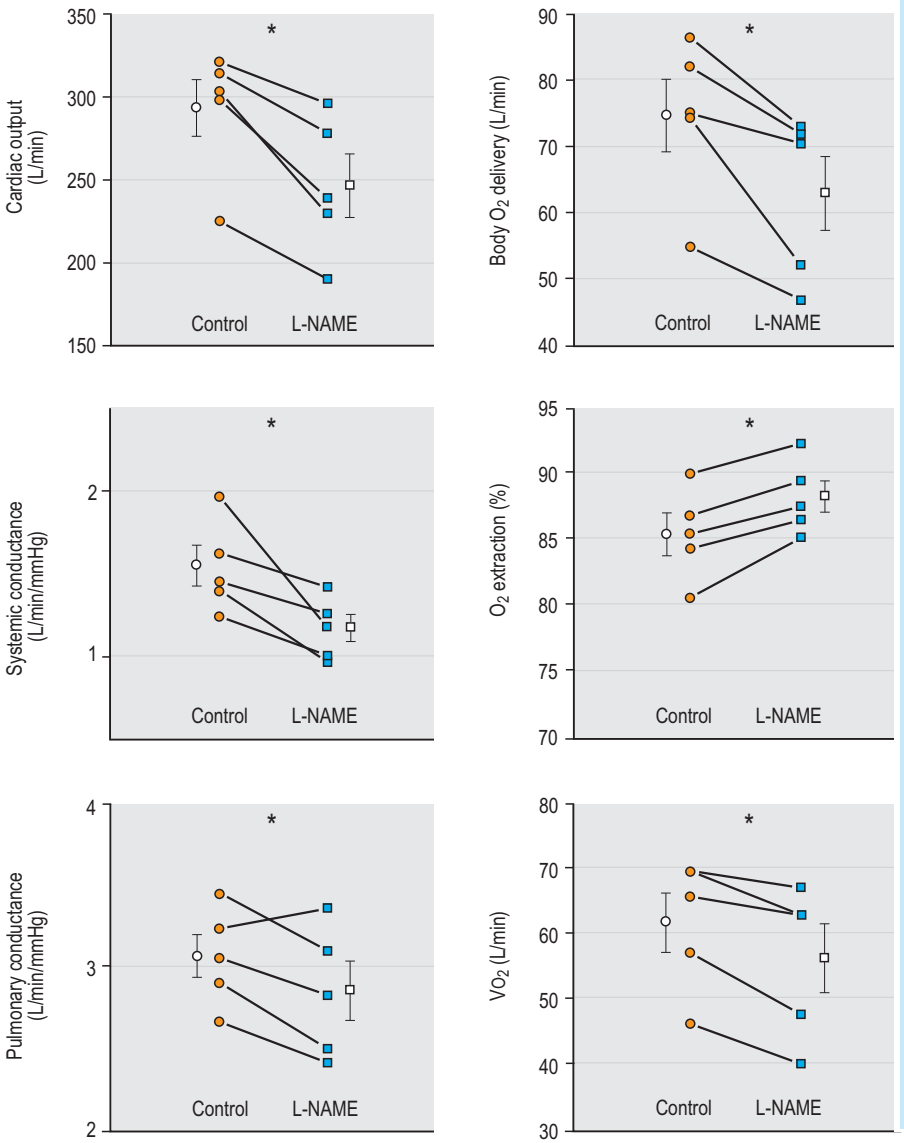


Fig. 32.31
Effect of inhibition of nitric oxide production by L-NAME (nitric oxide synthase inhibitor, N^G-L-nitro-arginine methyl ester) on cardiovascular responses, O_2 delivery ($\dot{Q}O_2$), O_2 extraction and O_2 uptake ($\dot{V}O_2$) at maximum exercise. Solid symbols denote individual horses, hollow symbols are mean ± standard error. The L-NAME condition significantly (* $P < 0.05$) reduced all variables in addition to the maximum speed attained. (Reproduced with kind permission from Kindig et al.[72])

mitochondrion is at odds with the more recent observation that intramyocyte Po_2 during exercise is low (1–3 mmHg) and without appreciable transverse or longitudinal variation (Fig. 32.34).[139] This is important because it means that the greatest fall in Po_2 occurs in very close proximity (1–2 μm) to the RBC even in the presence of potentially long diffusion distances (> 40 μm) to the mitochondrion. Intramyocyte O_2 transport is thought to be facilitated by myoglobin particularly within fibers in which oxidative enzyme activity is high. The mitochondrial system comprises a catenated network that may enhance O_2 and high-energy phosphate transport.[140,141]

From the above, the inescapable conclusion is that the size (surface area) and geometry (luminal diameter, tortuosity, branching) of the muscle capillary network combined with the flux and distribution of RBCs within that network are of paramount importance for gas exchange. Within skeletal muscle, capillary surface area is regulated as a function of fiber mitochondrial volume,[44] which itself is indicative of maximal O_2 demand (Fig. 32.35). Within the major limb muscles there are 700–800 km of capillary length per kg which supplies 40–50 mL of mitochondria.[42,46] The capillaries form a dense, interconnecting network of vessels that average 4–6 μm in diameter (RBCs are 5.5 μm in diameter) that becomes extremely tortuous at short muscle sarcomere lengths.[42] By contrast, at long sarcomere lengths (>2.8 μm), the capillaries become straight and highly aligned with the muscle fibers. As the capillaries stretch, their luminal diameter is reduced and this increases their resistance to RBC passage.[142,143]

Observation of capillary RBC flux and distribution during muscle contractions presents a formidable challenge to scientists. It is only very recently that events within muscle capillaries have been observed across the rest–contractions transition. At rest in rat spinotrapezius muscle, approximately 80% of capillaries support RBC flow[143] at a velocity of

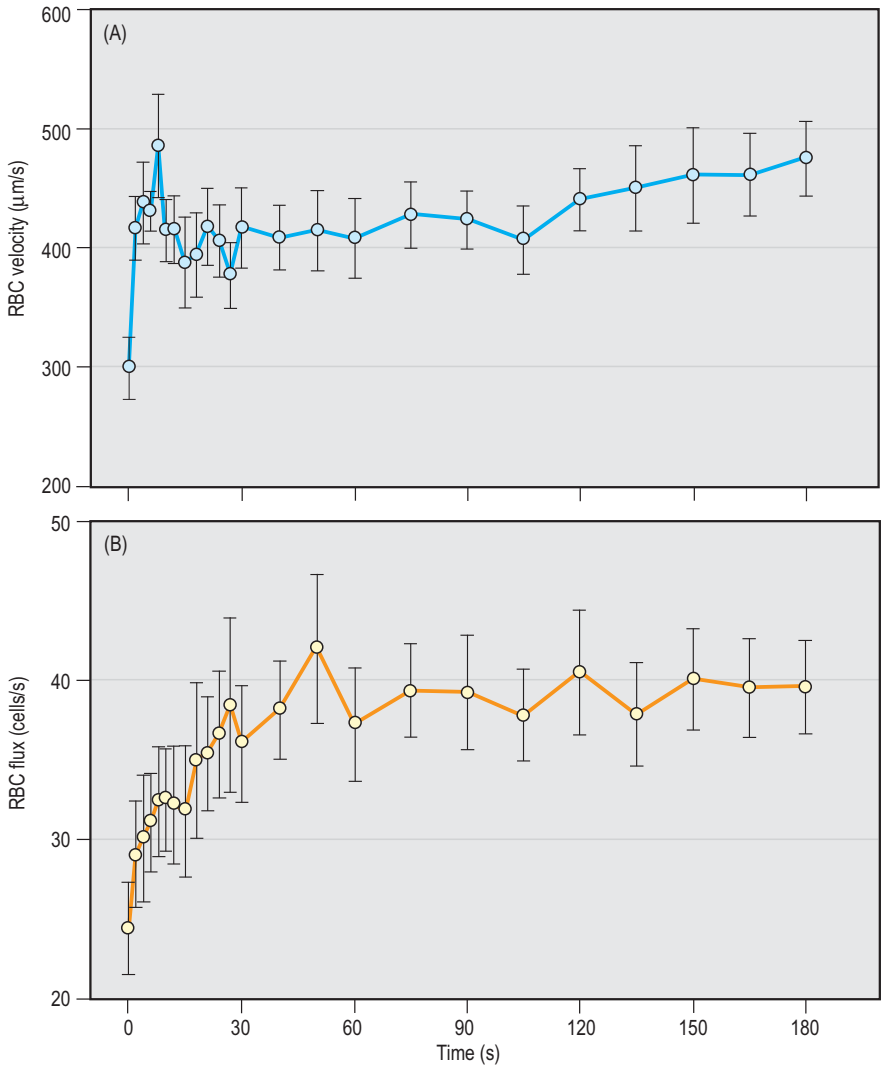


Fig. 32.32
Within the capillary bed of skeletal muscle, red blood cell (RBC) velocity (A) and flux (B) increase within the first few contractions at the start of exercise. (Reproduced with kind permission from Kindig et al.[134])

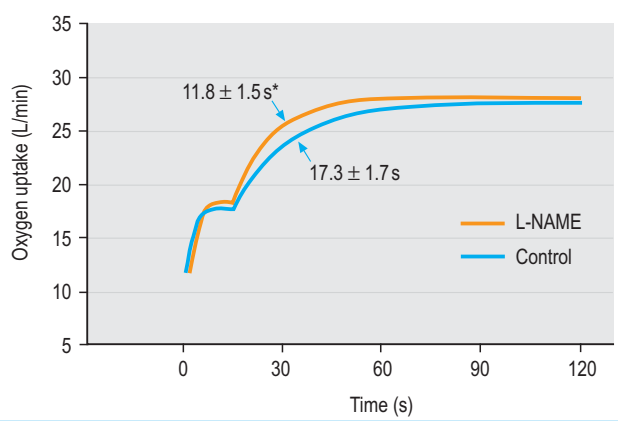


Fig. 32.33
Inhibition of nitric oxide production by L-NAME (nitric oxide synthase inhibitor, N^G-L-nitro-arginine methyl ester) significantly speeds the O_2 uptake ($\dot{V}O_2$) response at the onset of moderate speed running (7 m/s). (Reproduced with kind permission from Kindig et al.[64])

approximately 250 μm/s and a capillary tube hematocrit that averages only 25–50% of systemic values.[141] The instantaneous muscle O_2 diffusing capacity is thought to be determined by the number of RBCs in the capillary lying adjacent to the muscle fiber.[144] Consequently, the total length of capillaries adjacent to a muscle fiber in combination with their hematocrit (i.e. number of RBCs per unit length of capillary) will set the potential for O_2 flux. As muscle contracts and blood flow increases, capillary RBC velocity and flux are elevated rapidly (Fig. 32.32) and hematocrit increases towards systemic values.[134] If we extrapolate what is known from microscopic observations in contracting rodent muscle to the exercising horse using equine capillary morphometric[42] and blood flow[46] data, from rest to maximal exercise capillary hematocrit is predicted to increase from approximately 10% up to approximately 60% and mean RBC capillary transit time decreases to about 1–2 s (which is substantially longer than seen in the pulmonary capillaries). This presents a remarkable scenario. Specifically, during maximal exercise, if the systemic polycythemia is expressed at the microcirculatory level (as suggested from rodent studies), the sixfold increase in

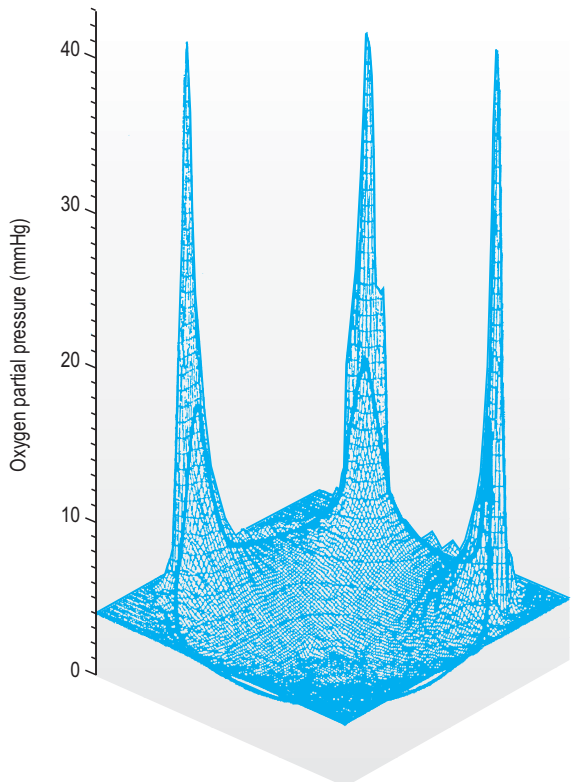


Fig. 32.34
Three-dimensional reconstruction of the O_2 partial pressure (P_{O_2}) profile within the muscle capillary and the contracting myocyte. Sarcolemma is indicated by thick line. Notice that the principal drop in P_{O_2} occurs in close proximity (within 1 μm) to the capillary spikes and that the intramyocyte P_{O_2} profile is remarkably flat without appreciable P_{O_2} gradients. This suggests that, at least in red muscle fibers containing myoglobin, even relatively large intracellular O_2 diffusion distances to the mitochondria are of little consequence. (Redrawn from Honig et al.[139])

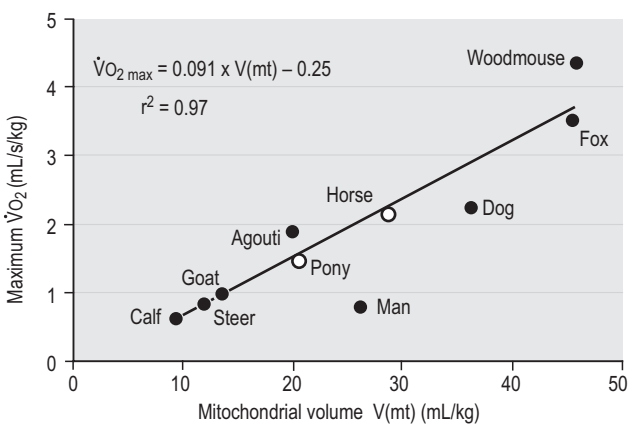


Fig. 32.35
There is a close relationship between whole body mitochondrial content and $\dot{V}O_{2max}$ across a wide range of mammalian species. This supports the notion that $\dot{V}O_{2max}$ increases in proportion to the structural capacity for muscle to utilize O_2. V(mt), mitochondrial volume. (Redrawn from Wagner et al.[18])

capillary hematocrit will facilitate rapid blood to muscle O_2 exchange. Moreover, as capillary RBC transit time is not thought to become limiting for O_2 offloading until values less than 0.3–0.5 s are reached, the mean transit time of 1–2 s in horse muscle is so long that there likely exists only a small proportion of capillaries where O_2 offloading is limited. These considerations help explain how the horse achieves such excellent O_2 extractions (up to 85–90%) at very high cardiac outputs.

Exercise training

Regular physical exercise or exercise training produces a coordinated pattern of structural and functional adaptations within the cardiovascular and muscular systems. The first three main sections of this chapter dealt with the anatomy and physiology of these systems and their responses to acute exercise (i.e. a single bout). This section details the remarkable plasticity of the cardiovascular and muscular systems in response to training and focuses primarily on those adaptations which elevate $\dot{V}O_{2max}$ and running performance. There exists a substantial literature on this topic in other species such as the human, dog, and rat,[45,113,131,145] and this section will avoid an exhaustive overview. Rather it will focus on understanding the mechanistic basis for the elevated training-induced $\dot{V}O_{2max}$ that occurs in both young and old horses.[59]

Historically, $\dot{Q}$ and $\dot{Q}O_2$ have been considered the principal, if not the sole, determinants of $\dot{V}O_{2max}$ and its increase with training. However, the insightful modeling and novel experiments of Professor Peter D. Wagner at the University of California at San Diego[18] and others[146–149] have established

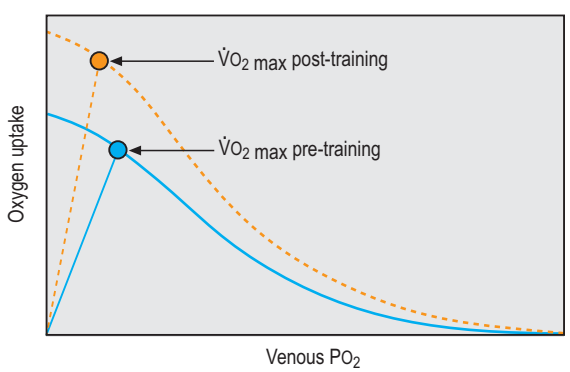


Fig. 32.36
The Wagner diagram demonstrates that exercise training increases $\dot{V}O_{2max}$ by elevating both conductive (curved line, due to increased stroke volume) and diffusive (straight line, due principally to increased muscle capillarity) O_2 transport. Note that even a modest reduction in venous P_{O_2} (5–10%)[150] after training requires a substantial increase (~ 30%) in muscle O_2 diffusing capacity. Moreover, if training solely increased convective O_2 delivery and there was no augmentation of muscle diffusing capacity, venous P_{O_2} would rise after training. This has not been observed. For additional information see legend to Fig. 32.7 and Table 32.7.

Table 32.7 Principal cardiovascular effects of exercise training in the horse at maximal exercise

Variable	% Increase	Reference(s)
$\dot{V}O_{2max}$	10–25	67,150,158–161
Mean arterial pressure (at max)	NC	
Total peripheral resistance	Decreased	
Conductive oxygen transport, max		
Heart weight	10+	22,25
Cardiac output, max	Increased	
Stroke volume, max	10+	56
Myocardial hypertrophy		
LV mass	33	25,152
LV internal diameter	7	152
Plasma volume	19–30	150,155,162
Central venous pressure	?	
Pericardial hypertrophy	Yes?	
Systemic [hemoglobin]/hematocrit	NC or decreased	150
Arterial O_2 content	NC or decreased	
Red cell mass	15	150
Heart rate, max	NC	59,158,163
Muscle diffusing capacity		
Arterial–venous O_2 extraction, max	5	150
Capillarity		
Capillary density	13–36	161,164,165
Capillary–fiber ratio	70	161,166
Myoglobin	?	
Oxidative enzymes	Up to 100	159,164,165,167–169,170
Mitochondrial volume	75–200	161,171
Capillary hematocrit	Increased?	
Capillary RBC transit time	?	
Velocity — submaximal heart rates/blood lactate concentrations		
V200	NC or increased	172
V140	Increased	173
V_{La4}	Up to 31	165,174
La_9	(–51)	174
Run time to fatigue (90–100% $\dot{V}O_{2max}$)		
Time	140	161

NC, no change; ?, unknown.
$\dot{V}O_{2max}$, maximal oxygen uptake; V200, V140, running velocity at a heart rate of 200 and 140 beats/min; respectively; V_{La4}, running velocity that induces a lactic acidosis of 4 mmol/L; La_9, blood lactate concentration at a running velocity of 9 m/s.

that $\dot{V}O_{2max}$ and training-induced increases thereof are the result of a coordinated sequence of adaptations that increases the capacity for conductive and diffusive movement of O_2 from the atmosphere to its site of utilization within muscle mitochondria. The 'Wagner' diagram combines these conductive and diffusive elements (as seen in Fig. 32.7), and it is instructive to use this diagram to understand how training increases $\dot{V}O_{2max}$ (Fig. 32.36). The relationship seen in Fig. 32.36 presents the increased $\dot{V}O_{2max}$ as an elevated cardiovascular O_2 delivery ($\dot{Q}O_2$) concomitant with an elevated fractional O_2 extraction (increased $Ca-CvO_2$) that reduces muscle effluent and mixed-venous PO_2. Typically, training-induced increases in fractional O_2 extraction and reduction of venous PO_2 are relatively modest, and this observation has led to the erroneous belief that adaptations to training within muscle that increase O_2 diffusing capacity (e.g. increased muscle capillarity) are of no, or at least, lesser importance than those cardiovascular changes that elevate $\dot{Q}O_2$. Nothing could be further from the truth. Notice from Fig. 32.36 that simply increasing $\dot{Q}O_2$ at the same diffusing capacity (i.e. slope of line from the origin to $\dot{V}O_{2max}$) will *decrease* O_2 extraction and *elevate* venous PO_2. That this response is not seen after training is the result of adaptations within the capillary bed (Table 32.7) that substantially increase muscle O_2 diffusing capacity.[44,131,151] Table 32.7 lists the primary adaptations to training that produce the response evident in Fig. 32.36.

Training usually increases $\dot{V}O_{2max}$ between 10 and 25% and as in other species[45,113,131,145] the % improvement is dependent upon initial fitness with fitter individuals having less room for improvement. In addition to an increased muscle O_2 diffusing capacity, the higher post-training $\dot{V}O_{2max}$ is driven by an elevated $\dot{Q}$ (and $\dot{Q}O_2$) consequent to increased SV. Maximal heart rate does not change. At maximal exercise,

the elevated $\dot{Q}$ occurs without any increase in MAP and so the elevated $\dot{Q}$ must be countered by a precisely matched fall in total peripheral resistance.[113]

Mechanistic bases for training-induced SV increase

After training, ventricular mass and volume is increased.[25,152] Training elevates blood/plasma volume and subsequently end-diastolic volume and this stretches the myocardial fibers and increases both the force and velocity of contraction. This adaptation occurs in the absence of any substantial changes in myocardial contractility per se[113,153,154] and as MAP is unchanged by training, it cannot be caused by modulation of cardiac afterload. Training expands plasma volume[150,155] and this may elevate ventricular preload by increasing central venous pressure. However, experiments in humans have not demonstrated that expanding plasma volume consistently increases central venous pressure and SV.[113] What is certain is that removal of the pericardium does increase SV and maximal $\dot{Q}$ in the absence of altered preload.[13,14] Indeed, removing the pericardial constraint to myocardial expansion produces an increased maximal $\dot{Q}$ similar to that found after weeks or months of training. There is evidence that volume overload chronically stretches the pericardial sac[156] and decreases its stiffness[157] such that after training a much smaller rise in cardiac filling pressure is needed to increase SV[113] and a greater SV can be achieved. To date, there is no available evidence that pericardectomies have been performed as an ergogenic aid in racing horses. It is pertinent that training-induced increases in heart size may promote valvular (mitral and tricuspid) insufficiencies and regurgitation which will act to limit the improvement in cardiac output.[104]

Mechanistic bases for increased muscle vascular conductance and O_2 diffusing capacity (and increased Ca_{O_2}–Cv_{O_2}) after training

Arterial O_2 content (Ca_{O_2}) is not elevated by training (although small increases in arterial P_{O_2} during submaximal exercise may be found),[173] hence any increased Ca_{O_2}–Cv_{O_2} must result from a decreased Cv_{O_2}. This decreased Cv_{O_2} does not arise from a greater vasoconstriction in other organs or inactive muscle vascular beds but rather from a preferential redistribution of the training-induced $\dot{Q}$ increase towards the active muscles[113,114,175] and a greater total and fractional extraction of O_2 within those muscles.

Exercise training induces a rapid and profound growth of arterioles and capillaries within skeletal muscle[45,176–179] and increases the sensitivity of cardiac[180] and skeletal muscle[181,182] arterioles to vasoactive mediators such as prostaglandins, catecholamines, and nitric oxide. Moreover, training increases the availability of nitric oxide in the myocardium by upregulating endothelial nitric oxide synthase, which is the enzyme responsible for much of the nitric oxide production within the arterial tree.[183] It is quite possible that this latter adaptation occurs also in skeletal muscle. Exercise training increases $\dot{Q}$ capacity in muscles composed of both slow- and fast-twitch fibers provided they are recruited during exercise.[184] The distribution of $\dot{Q}$ within and between muscles is altered after training which may be important for improving the matching of O_2 delivery ($\dot{Q}_{O_2}$) to O_2 utilization ($\dot{V}_{O_2}$).[114,141] After training, capillary length and surface area per fiber volume as well as capillary surface to fiber surface contact is increased in proportion to the elevated muscle oxidative enzyme capacity.[44,45,131,177] Such capillary proliferation increases the capillary surface area available for O_2 exchange and by increasing capillary volume may prevent or at least constrain any reduction in capillary RBC transit time that would otherwise result from the elevated muscle $\dot{Q}$. It is pertinent that the effect of training on capillary RBC transit time will depend on the precise proportionality between increased $\dot{Q}$ and elevated capillary volume. Moreover, the effect of training on capillary hematocrit (a key determinant of blood-muscle O_2 movement) is not at present known. What is certain is that muscle O_2 diffusing capacity increases dramatically with training to facilitate a substantially increased total O_2 extraction (Fig. 32.36).

Conclusions

Both the cardiovascular and muscular systems evidence great plasticity. During maximal exercise after training, improved cardiac function elevates total $\dot{Q}$ and muscle $\dot{Q}$ (and $\dot{Q}_{O_2}$) Synchronized muscle vascular and intramyocyte oxidative enzyme proliferation permits trained muscle to accept this increased $\dot{Q}$, elevate O_2 exchange, and facilitate a greater O_2 utilization at maximal exercise (increased $\dot{V}_{O_{2max}}$). At submaximal running speeds, exercise training speeds $\dot{V}_{O_2}$ kinetics,[131] tightens metabolic control which reduces glycolysis and glycogen utilization,[45,145] and elevates stroke volume thereby lowering heart rate. This in turn may actually reduce the $\dot{V}_{O_2}$ cost of running at submaximal speeds.[131] The training response may be augmented by hypoxia and is modulated by running speed, frequency, and duration.

References

1. Pratt GW. Clocking the fastest horses on earth. Quarter Racing J 1991; 4:36–40.
2. Jones JH, Lindstedt SL. Limits to maximal performance. Ann Rev Physiol 1993; 55:547–569.
3. Weibel ER. The pathway for oxygen: structure and function in the mammalian respiratory system. London: Harvard University Press; 1984; 399–404.
4. Lindstedt SL, Hokanson JF, Wells DJ, et al. Running energetics in the pronghorn antelope. Nature 1991; 353:748–750.
5. Young LE, Marlin DJ, Deaton C, et al. Heart size estimated by echocardiography correlates with maximal oxygen uptake. Equine Vet J Suppl 2002; 34:467–471.

6. Lyons AS, Petrucelli RJ. Medicine: an illustrated history. New York: Harry N Abrams; 1987; 603.
7. Derman KD, Noakes TD. Comparative aspects of exercise physiology. In: Hodgson DR, Rose RJ, eds. The athletic horse. Philadelphia: WB Saunders; 1994; 15.
8. Gunn HM. Muscle, bone and fat proportions and muscle distribution of Thoroughbreds and other horses. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis. CA: ICEEP; 1987; 253–264.
9. Kearns CF, McKeever KH, John-Adler H, et al. Relationship between body composition, blood volume and maximal oxygen uptake. Equine Vet J Suppl 2002; 34:485–490.
10. Wagner PD, Erickson BK, Seaman J, et al. Effects of altered FIo_2 on maximum Vo_2 in the horse. Respir Physiol 1996; 105:123–134.
11. Knight DR, Schaffartzik W, Poole DC, et al. Effects of hyperoxia on maximal leg O_2 supply and utilization in men. J Appl Physiol 1993; 75:2586–2594.
12. McDonough P, Kindig CA, Hildreth T, et al. Effect of body incline on cardiac performance. Equine Vet J Suppl 2002; 34:506–509.
13. Stray-Gundersen J, Musch TI, Haidet GC, et al. The effect of pericardiectomy on maximal oxygen consumption and maximal cardiac output in untrained dogs. Circ Res 1986; 58:523–530.
14. Hammond HK, White FC, Bhargava V, Shabetai R. Heart size and maximal cardiac output are limited by the pericardium. Am J Physiol 1992; 263:H1675–1681.
15. Andersen P, Saltin B. Maximal perfusion of skeletal muscle in man. J Physiol 1985; 366:233–249.
16. Richardson RS, Poole DC, Knight DR, et al. High muscle blood flow in man: is maximal O_2 extraction compromized? J Appl Physiol 1993; 75:1911–1916.
17. Gledhill N. Blood doping and related issues: a brief review. Med Sci Sports Exerc 1982; 14:183–189.
18. Wagner PD, Hoppeler H, Saltin B. Determinants of maximal oxygen uptake. In: Crystal RG, West JB, Barnes PJ et al, eds. The lung: scientific foundations, 2nd edn, New York: Lippincott-Raven; 1997; 2033–2041.
19. Hoppeler H, Weibel ER. Limits for oxygen and substrate transport in mammals. J Exp Biol 1998; 201:1051–1064.
20. Wasserman K, Hansen JE, Sue DY, et al. Principles of exercise testing and interpretation, 2nd edn. Philadelphia: Lea and Febiger; 1994.
21. Saltin B, Blomqvist G, Mitchell JH, et al. Response to exercise after bed rest and after training. Circulation 1968; 38(suppl VII):1–78.
22. Webb AI, Weaver BMQ. Body composition of the horse. Equine Vet J 1979; 11:39–47.
23. Rose RJ, Hendrikson DK, Knight PK. Clinical exercise testing in the normal thoroughbred race horse. Aust Vet J 1990; 67:345–348.
24. Snow DH, Valberg SJ. Muscle anatomy, physiology, and adaptations to exercise. In: Hodgson DR, Rose RJ, eds. The athletic horse. Philadelphia: WB Saunders; 1994; 145–179.
25. Kubo K, Senta T, Sugimoto O. Relationship between training and heart in the Thoroughbred race horse. Exp Rep Equine Health Lab 1974; 11:87–93.
26. Evans DL, Rose RJ. Cardiovascular and respiratory responses to exercise in thoroughbred horses. J Exp Biol 1988; 134:397–408.
27. Haun M. The X factor. What it is and how to find it. Neenah, WI: Russell Meerdink; 1997.
28. Kline H, Foreman JH. Heart and spleen weights as a function of breed and somatotype. Equine Exerc Physiol 1991; 3:17–21.
29. Gross DR, Muir WM, Pipers FS, Hamlin RL. Reevaluation of the equine heart score. South West Vet 1974; 27:231–233.
30. Leadon DP, Cunningham EP, Mahon GA, Todd AJ. Heart score and performance ability in the United Kingdom. Equine Vet J 1982; 14:89–90.
31. Leadon DP, McAllister H, Mullins E, Osborne M. Electrocardiographic and echocardiographic measurements and their relationships in Thoroughbred yearlings to subsequent performance. In: Persson SGB, Lindholm A, Jeffcot LB, eds. Equine exercise physiology 3. CA: ICEEP; 1991; 22–29.
32. Hanson CM, Kline KH, Foreman JH. Measurements of heart scores and heart weights in horses of two different morphic types. Comp Biochem Physiol 1993; 108A:175–178.
33. Sampson SN, Tucker RL, Bayly WM. Relationship between Vo_{2max}, heart score and echocardiographic measurements obtained at rest and immediately following maximal exercise in Thoroughbred horses. Equine Vet J Suppl 1999; 30:190–194.
34. Steel JD, Beilharz RG, Stewart GA, et al. The inheritance of heart score in race horses. Aust Vet J 1977; 53:306–309.
35. Persson SGB, Ekman L, Lydin G, et al. Circulatory effects of splenectomy in the horse. II. Effect on plasma volume and total and circulating red-cell volume. Zentralbl Veterinarmed A 1973; 20:456–468.
36. Moore J. Nature's supercharger. Equus 1994; 198:30–34.
37. Wagner PD, Erickson BK, Kubo K, et al. Maximum oxygen transport and utilisation before and after splenectomy. Equine Vet J Suppl 1995; 18:82–85.
38. Persson SGB, Bergsten G. Circulatory effects of splenectomy in the horse. IV. Effect on blood flow and blood lactate at rest and during exercise. Zentralbl Veterinarmed A 1975; 22:801–807.
39. Persson SGB. On blood volume and working capacity. Acta Vet Scand Suppl 1967; 19:1–189.
40. Altman PL, Dittmer DS. Biology data book, vol 2, 2nd edn. Bethesda, MD: FASEB;1974; 1847.
41. Erickson HH. Exercise physiology. In: Swenson MJ, Reece WO, eds. Dukes physiology of domestic animals, 11th edn. Ithaca: Cornell University Press; 1993; 305.
42. Mathieu-Costello O, Hoppeler H, Weibel ER. Capillary tortuosity in skeletal muscles of mammals depends on muscle contraction. J Appl Physiol 1989; 66:1436–1442.
43. Ishikawa H, Sawada H, Yamada E. Surface and internal morphology of skeletal muscle. In: Peachy LD, Adrian RH, Geiger SR, eds. Handbook of physiology. Section 10: skeletal muscle. Bethesda, MD: American Physiological Society; 1983; 1–22.
44. Poole DC, Mathieu-Costello O. Relationship between fiber capillarization and mitochondrial volume density in control and trained rat soleus and plantaris muscles. Microcirculation 1996; 3:175–186.
45. Saltin B, Gollnick PD. Skeletal muscle adaptability: significance for metabolism and performance. In: Handbook of physiology. Section 10: skeletal muscle. Bethesda, MD: American Physiological Society; 1983; 555–631.
46. Armstrong RB, Essen-Gustavsson B, Hoppeler H, et al. O_2 delivery at $\dot{V}o_{2max}$ and oxidative capacity in muscles of standardbred horses. J Appl Physiol 1992; 73:2274–2282.
47. Robinson NE. Respiratory function. In: Cunningham JG, ed. Textbook of veterinary physiology, 3rd edn. London: WB Saunders; 2002; 481.

48. West JB. Respiratory physiology, 4th edn. Baltimore: Williams and Wilkins; 1995; 36–37.
49. Birks EK, Mathieu-Costello O, Fu Z, et al. Comparative aspects of the strength of pulmonary capillaries in rabbit, dog, and horse. Respir Physiol 1994; 97:235–246.
50. Constantinopol M, Jones JH, Weibel ER, et al. Oxygen transport during exercise in large mammals. II. Oxygen uptake by the pulmonary gas exchanger. J Appl Physiol 1989; 67:871–878.
51. Hlastala MP, Bernard SL, Erickson HH, et al. Pulmonary blood flow distribution in standing horses is not dominated by gravity. J Appl Physiol 1996; 81:1051–1061.
52. Pelletier N, Robinson NE, Kaiser L, et al. Regional differences in endothelial function in horse lungs: possible role in blood flow distribution? J Appl Physiol 1998; 85:537–542.
53. Evans DL. The cardiovascular system: anatomy, physiology, and adaptations to exercise and training. In: Hodgson DR, Rose RJ, eds. The athletic horse. Philadelphia: WB Saunders; 1994; 129–144.
54. Bayly WM, Gabel AA, Barr SA. Cardiovascular effects of submaximal aerobic training on a treadmill in Standardbred horses using a standardized exercise test. Am J Vet Res 1983; 44:544–553.
55. Parks CM, Manohar M. Distribution of blood flow during moderate and strenuous exercise in ponies (*Equus caballus*). Am J Vet Res 1983; 44:1861–1866.
56. Thomas DP, Fregin GF, Gerber NH, Ailes NB. Effects of training on cardiorespiratory function in the horse. Am J Physiol 1983; 245:R160–165.
57. Evans DL, Rose RJ. Dynamics of cardiorespiratory function in standardbred horses during constant load exercise. J Comp Physiol [B] 1988; 157:791–799.
58. Hamlin RL, Klepinger WL, Gilpin KW, et al. Autonomic control of heart rate in the horse. Am J Physiol 1972; 222:976–978.
59. Betros CL, McKeever KH, Kearns CF, et al. Effects of aging and training on maximal heart rate and $\dot{V}O_{2max}$. Equine Vet J Suppl 2002; 34:100–105.
60. Astrand P-O, Rodahl K. Textbook of work physiology, 3rd edn. New York: McGraw-Hill; 1986.
61. Brooks GA, Fahey TD, White TP. Exercise physiology: human bioenergetics and its applications, 2nd edn. London: Mayfield Publishing; 1996.
62. Rose RJ, Evans DL. Cardiovascular and respiratory function in the athletic horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP; 1987; 1–24.
63. Kindig CA, McDonough P, Erickson HH, et al. Effect of L-NAME on oxygen uptake kinetics during heavy intensity exercise in the horse. J Appl Physiol 2001; 91:891–896.
64. Kindig CA, McDonough P, Erickson HH, et al. Nitric oxide synthase inhibition speeds oxygen uptake kinetics in horses during moderate domain running. Resp Physiol Neurobiol 2002; 132:169–178.
65. Lindholm A, Saltin B. The physiological and biochemical response of standardbred horses to exercise of varying speed and duration. Acta Vet Scand 1974; 15:310–324.
66. Thomas DP, Fregin GF. Cardiorespiratory and metabolic responses to treadmill exercise in the horse. J Appl Physiol 1981; 50:864–868.
67. Evans DL, Rose RJ. Maximal oxygen consumption in race horses: changes with training state and prediction from submaximal indices of cardiorespiratory function. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP; 1987; 52–67.
68. Thomas DP, Fregin GF. Cardiorespiratory drift during exercise in the horse. Equine Vet J Suppl 1990; 9:61–65.
69. Langsetmo I, Weigle GE, Fedde MR, et al. $\dot{V}o_2$ kinetics in the horse at moderate and heavy exercise. J Appl Physiol 1997; 83:1235–1241.
70. Stephenson RB. Cardiovascular physiology. In: Cunningham JG, ed. Textbook of veterinary physiology, 3rd edn. New York: WB Saunders; 2002; 109–219.
71. Fedde MR, Erickson HH. Increase in blood viscosity in the sprinting horse: can it account for the high pulmonary arterial pressure? Equine Vet J 1998; 30:329–334.
72. Kindig CA, Quackenbush D, Gallatin LL, et al. Cardiorespiratory impact of nitric oxide synthase inhibition in the exercising horse. Respir Physiol 2000; 120:151–166.
73. Davis JL, Manohar M. Effect of splenectomy on exercise-induced pulmonary and systemic hypertension in ponies. Am J Vet Res 1988; 49:1169–1172.
74. Erickson BK, Erickson HH, Coffman JR. Pulmonary artery, aortic and oesophageal pressure changes during high-intensity treadmill exercise in the horse: a possible relation to exercise induced pulmonary haemorrhage. Equine Vet J Suppl 1990; 9:47–52.
75. Jones JH, Smith BL, Tyler WS, et al. Why do horses bleed? Source and cause of exercise-induced pulmonary hemorrhage in horses. In: Clarke AF, ed. Proceedings of the International Exercise Induced Pulmonary Hemorrhage Conference. Guelph: Equine Research Center; 1993; 23–24.
76. Kindig CA, Erickson HH, Poole DC. Dissociation of exercise-induced pulmonary hemorrhage and pulmonary artery pressure via nitric oxide synthase inhibition. J Equine Vet Sci 2000; 20:715–721.
77. Kindig CA, McDonough P, Finley MR, et al. Nitric oxide inhalation reduces pulmonary hypertension but not hemorrhage in maximally exercising horses. J Appl Physiol 2001; 91:2674–2680.
78. Kindig CA, McDonough P, Fenton G, et al. Efficacy of nasal strip and furosemide in mitigating exercise-induced pulmonary hemorrhage in Thoroughbred horses. J Appl Physiol 2001; 91:1396–1400.
79. Hopper MK, Pieschl RL, Pelletier NG, et al. Cardiopulmonary effects of acute blood volume alteration prior to exercise. In: Persson SGB, Lindholm A, Jeffcot LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP; 1991; 3:9–16.
80. Olsen SC, Coyne CP, Lowe BS, et al. Influence of furosemide on hemodynamic responses during exercise in horses. Am J Vet Res 1992; 53:742–747.
81. Hinchcliff KW, McKeever KH. Frusemide. Equine Vet J Suppl 1995; 18:256–258.
82. Langsetmo I, Weigle GE, Erickson HH, et al. Influence of frusemide on dynamic cardiac variables during exercise. Equine Vet J Suppl 1999; 30:170–173.
83. Bernard SL, Glenny RW, Erickson HH, et al. Minimal redistribution of pulmonary blood flow with exercise in race horses. J Appl Physiol 1996; 81:1062–1070.
84. Wagner PD, Gillespie JR, Landgren GL, et al. Mechanism of exercise-induced hypoxemia in horses. J Appl Physiol 1989; 66:1227–1233.
85. Karas RH, Taylor CR, Jones JH, et al. Adaptive variation in the mammalian respiratory system in relation to energetic demand. VII. Flow of oxygen across the pulmonary gas exchanger. Respir Physiol 1987; 69:101–115.
86. McDonough P, Kindig CA, Erickson HH, et al. Mechanistic basis for the gas exchange threshold in the Thoroughbred horse. J Appl Physiol 2002; 92:1499–1505.
87. Seaman J, Erickson BK, Kubo K, et al. Exercise induced ventilation/perfusion inequality in the horse. Equine Vet J 1995; 27:104–109.

88. Burrell MH. Endoscopic and virologic observations on respiratory disease in a group of young Thoroughbred horses in training. Equine Vet J 1985; 17:99–103.
89. Hillidge CJ, Lane TJ, Johnson EL. Preliminary investigations of EIPH in racing Quarter Horses. J Equine Vet Sci 1984; 4:21–23.
90. Lapointe JM, Vrins A, McCarvill E. A survey of exercise-induced pulmonary haemorrhage in Quebec Standardbred race horses. Equine Vet J 1994; 26:482–485.
91. Mason DK, Collins EA, Watkins KL. Respiratory system. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 57–63.
92. Raphel CF, Soma LR. Exercise-induced pulmonary hemorrhage in Thoroughbreds after racing and breezing. Am J Vet Res 1982; 43:1123–1127.
93. Erickson HH, Poole DC. Exercise-induced pulmonary hemorrhage. In: Lekeux P, ed. Equine respiratory diseases. Ithaca: International Veterinary Information Services; 2002; B0320.0102.
94. Fu Z, Costello ML, Tsukimoto K, et al. High lung volume increases stress failure in pulmonary capillaries. J Appl Physiol 1992; 73:123–133.
95. Erickson HH, McAvoy JL, Westfall JA. Exercise-induced changes in the lung of Shetland ponies: ultrastructure and morphometry. J Submicrosc Cytol Pathol 1997; 29:65–72.
96. West JB, Mathieu-Costello O, Jones JH, et al. Stress failure of pulmonary capillaries in race horses with exercise-induced pulmonary hemorrhage. J Appl Physiol 1993; 75:1097–1109.
97. West JB, Mathieu-Costello O. Structure, strength, failure, and remodeling of the pulmonary blood–gas barrier. Annu Rev Physiol 1999; 61:543–572.
98. Poole DC, Kindig CA, Fenton G, et al. Effects of external nasal support on pulmonary gas exchange and EIPH in the horse. J Equine Vet Sci 2000; 20:579–585.
99. Cook WR, Williams RM, Kirker-Head CA, et al. Upper airway obstruction (partial asphyxia) as the possible cause of exercise-induced pulmonary hemorrhage in the horse: an hypothesis. Equine Vet Sci 1988; 8:11–26.
100. Fedde MR, Wood SC. Rheological characteristics of horse blood: significance during exercise. Respir Physiol 1993; 94:323–335.
101. Schroter RC, Marlin DJ, Denny E. Exercise-induced pulmonary haemorrhage (EIPH) in horses results from locomotory impact induced trauma – a novel, unifying concept. Equine Vet J 1998; 30:186–192.
102. Manohar M, Hutchens E, Coney E. Pulmonary hemodynamics in the exercising horse and their relationship to exercise-induced pulmonary hemorrhage. Br Vet J 1993; 149:419–428.
103. Erickson HH. A review of exercise-induced pulmonary hemorrhage and new concepts for prevention. Proc Am Assoc Equine Practs 2000; 46:193–196.
104. Young LE, Wood JLN. Effect of age and training on murmurs of atrioventricular valvular regurgitation in young Thoroughbreds. Equine Vet J 2000; 32:195–199.
105. Langsetmo I, Fedde MR, Meyer TS, et al. Relationship of pulmonary arterial pressure to pulmonary haemorrhage in exercising horses. Equine Vet J 2000; 32:379–384.
106. Erickson HH, Hildreth TS, Poole DC, et al. Management of exercise-induced pulmonary hemorrhage in non-racing performance horses. Comp Cont Educ Pract Vet 2001; 23:1090–1093.
107. Geor RJ, Ommundson L, Fenton G, et al. Effects of an external nasal strip and furosemide on pulmonary hemorrhage in Thoroughbreds following high-intensity exercise. Equine Vet J 2001; 33:577–584.
108. Holcombe SJ, Cornelisse CJ, Derksen FJ, et al. The effect of FLAIR nasal strips on upper airway mechanics in exercising horses. Am J Vet Res 2002; 63:1101–1105.
109. Shoemaker JK, Hughson RL. Adaptation of blood flow during the rest to work transition in humans. Med Sci Sports Exerc 1999; 31:1019–1026.
110. Rowell LB, Saltin B, Kiens B, et al. Is peak quadriceps blood flow in humans even higher during exercise with hypoxemia? Am J Physiol 1986; 251:H1038–H1044.
111. Mitchell JH, Kaufman MP, Iwamoto GA. The pressor reflex: its cardiovascular effects, afferent mechanisms, and central pathways. Annu Rev Physiol 1983; 45:229–242.
112. Rowell LB, O'Leary DS. Reflex control of the circulation during exercise: chemoreflexes and mechanoreflexes. J Appl Physiol 1990; 69:407–418.
113. Rowell LB. Human cardiovascular control. Oxford: Oxford University Press; 1993; 255–288.
114. Laughlin MH, McAllister RM, Delp MD. Heterogeneity of blood flow in skeletal muscle. In: Crystal RG, West JB, Weibel ER, et al, eds. The lung: scientific foundations. New York: Raven Press; 1997; 1945–1955.
115. Duling BR, Dora K. Control of striated muscle blood flow. In: Crystal RG, West JB, Weibel ER, et al, eds. The lung: scientific foundations. New York: Raven Press; 1997; 1935–1943.
116. Bergsten G. Blood pressure, cardiac output and blood gas tension in the horse at rest and during exercise. Acta Vet Scand Suppl 1974; 48:1–88.
117. Hornicke H, von Engelhardt W, Ehrlein HJ. Effect of exercise on systemic blood pressure and heart rate in horses. Pflugers Arch 1977; 372:95–99.
118. Segal SS. Integration of blood flow control to skeletal muscle: key role of feed arteries. Acta Physiol Scand 2000; 168:511–518.
119. Hughson RL, Tschakovsky ME, Houston ME. Regulation of oxygen consumption at the onset of exercise. Exer Sport Sci Rev 2001; 29:129–133
120. Manohar M. Vasodilator reserve in respiratory muscles during maximal exertion in ponies. J Appl Physiol 1986; 60:571–1577.
121. Manohar M. Costal vs. crural diaphragmatic blood flow during submaximal and near-maximal exercise in ponies. J Appl Physiol 1988; 65:1514–1519.
122. Manohar M. Inspiratory and expiratory muscle perfusion in maximally exercised ponies. J Appl Physiol 1990; 68: 544–548.
123. Manohar M. Blood flow in respiratory muscles during maximal exertion in ponies with laryngeal hemiplegia. J Appl Physiol 1987; 62:229–237.
124. Harms CA, Wetter TJ, McClaran SR, et al. Effects of respiratory muscle work on cardiac output and its distribution during maximal exercise. J Appl Physiol 1998; 85:609–618.
125. Poole DC, Mathieu-Costello O. Analysis of capillary geometry in rat sub-epicardium and sub-endocardium. Am J Physiol 1990; 259:H204–H210.
126. Manohar M, Goetz TE, Hutchens E, et al. Atrial and ventricular myocardial blood flows in horses at rest and during exercise. Am J Vet Res 1994; 55:1464–1469.
127. Manohar M. Transmural coronary vasodilator reserve and flow distribution during maximal exercise in normal and splenectomized ponies. J Physiol 1987; 387:425–440.
128. Knight DR, Poole DC, Schaffartzik W, et al. Relationship between body and leg $\dot{V}O_2$ during maximal cycle ergometry. J Appl Physiol 1992; 73:1114–1121.

129. Poole DC, Gaesser GA, Hogan MC, et al. Pulmonary and leg $\dot{V}O_2$ during submaximal exercise: implications for muscular efficiency. J Appl Physiol 1992; 72:805–810.
130. Laughlin MH, Korthuis RJ, Duncker DJ, et al. Control of blood flow to cardiac and skeletal muscle during exercise. In: Rowell LB, Shepherd JT, eds. Handbook of physiology. New York: Oxford University Press; 1996; 705–769.
131. Poole DC. Influence of exercise training on skeletal muscle oxygen delivery and utilization. In: Crystal RG, West JB, Weibel ER, et al, eds. The lung: scientific foundations. New York: Raven Press; 1997; 1957–1967.
132. Delp MD. Control of skeletal muscle perfusion at the onset of dynamic exercise. Med Sci Sports Exerc 1999; 31:1011–1018.
133. Wunsch SA, Muller-Delp J, Delp MD. Time course of vasodilatory responses in skeletal muscle arterioles: role in hyperemia at onset of exercise. Am J Physiol 2000; 279:H1715–H1723.
134. Kindig CA, Richardson TE, Poole DC. Skeletal muscle capillary hemodynamics from rest to contractions: implications for oxygen transfer. J Appl Physiol 2002; 92:2513–2520.
135. Sheriff DD, Hakeman AL. Role of speed vs. grade in relation to muscle pump function at locomotion onset. J Appl Physiol 2001; 91:269–276.
136. Berg BR, Cohen KD, Sarelius IH. Direct coupling between blood flow and metabolism at the capillary level in striated muscle. Am J Physiol 1997; 272:H2693–H2700.
137. Musch TI, McAllister RM, Symons JD, et al. Effects of nitric oxide synthase inhibition on vascular conductance during high speed treadmill exercise in rats. Exp Physiol 2001; 86:749–757.
138. Shen W, Xu X, Ochoa M, et al. Role of nitric oxide in the regulation of oxygen consumption in conscious dogs. Circ Res 1994; 75:1086–1095.
139. Honig CR, Gayeski TEJ, Groebe K. Myoglobin and oxygen gradients. In: Crystal RG, West JB, Weibel ER, et al, eds. The lung: scientific foundations. New York: Raven Press; 1997; 1925–1933.
140. Wagner PD. Determinants of maximal oxygen transport and utilization. Ann Rev Physiol 1996; 58:21–50.
141. Poole DC, Musch TI. Pulmonary and peripheral gas exchange during exercise. In: Roca J, Rodriguez-Roisin R, Wagner PD. eds. Pulmonary and peripheral gas exchange in health and disease. New York: Marcel Dekker; 2000; 469–523.
142. Poole DC, Mathieu-Costello O. Capillary and fiber geometry in rat diaphragm perfusion fixed in situ at different sarcomere lengths. J Appl Physiol 1992; 73:151–159.
143. Poole DC, Musch TI, Kindig CA. In vivo microvascular structural and functional consequences of muscle length changes. Am J Physiol 1997; 272:H2107–H2114.
144. Federspiel WJ, Popel AS. A theoretical analysis of the effect of the particulate nature of blood on oxygen release in capillaries. Microvasc Res 1986; 32:164–189.
145. Holloszy JO, Coyle EF. Adaptations of skeletal muscle to endurance exercise and their metabolic consequences. J Appl Physiol 1984; 56:831–838.
146. Weibel ER. Understanding the limitation of O_2 supply through comparative physiology. Respir Physiol 1999; 118:85–93.
147. Hogan MC, Bebout DE, Wagner PD, et al. Maximal O_2 uptake of in situ dog muscle during acute hypoxemia with constant perfusion. J Appl Physiol 1990; 69:570–576.
148. Roca J, Hogan MC, Story D, et al. Evidence for tissue diffusion limitation of $\dot{V}O_{2max}$ in normal humans. J Appl Physiol 1989; 67:291–299.
149. Bebout DE, Hogan MC, Hempleman SC, et al. Effects of training and immobilization on $\dot{V}O_2$ and DO_2 in dog gastrocnemius muscle in situ. J Appl Physiol 1993; 74:1697–1703.
150. Knight PK, Sinha AK, Rose RJ. Effects of training intensity on maximum oxygen uptake. In: Persson SGB, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP; 1991; 77–82.
151. Roca J, Agusti AG, Alonso A, et al. Effects of training on muscle O_2 transport at $\dot{V}O_{2max}$. J Appl Physiol 1992; 73:1067–1076.
152. Young LE. Cardiac responses to training in 2-year-old Thoroughbreds: an echocardiographic study. Equine Vet J Suppl 1999; 30:195–198.
153. Scheuer J, Tipton CM. Cardiovascular adaptations to physical training. Annu Rev Physiol 1977; 39:221–225.
154. Schiable TF, Scheuer J. Cardiac adaptations to chronic exercise. Prog Cardiovasc Dis 1985; 27:297–324.
155. McKeever KH, Schurg WA, Jarrett SH, et al. Exercise training induced hypervolemia in the horse. Med Sci Sports Exerc 1987; 19:21–27.
156. Freeman GL, LeWinter MM. Pericardial adaptations during chronic cardiac dilation in dogs. Circ Res 1984; 54:294–300.
157. Lee M-C, LeWinter MM, Freeman G, et al. Biaxial mechanical properties of the pericardium in normal and volume overload dogs. Am J Physiol 1985; 249:H222–H230.
158. Evans DL, Rose RJ. Cardiovascular and respiratory responses to submaximal exercise training in the thoroughbred horse. Pflugers Arch 1988; 411:316–321.
159. Eaton MD, Hodgson DR, Evans DL, et al. Effects of low- and moderate-intensity training on metabolic responses to exercise in Thoroughbreds. Equine Vet J Suppl 1999; 30:521–527.
160. Katz LM, Bayly WM, Roeder MJ, et al. Effects of training on oxygen consumption of ponies. Am J Vet Res 2000; 61:986–991.
161. Tyler CM, Golland LC, Evans DL, et al. Skeletal muscle adaptations to prolonged training, overtraining and detraining in horses. Pflugers Arch 1998; 436:391–397.
162. McKeever KH, Scali R, Geiser S, et al. Plasma aldosterone concentration and renal sodium excretion are altered during the first days of training. Equine Vet J Suppl 2002; 34: 524–531.
163. Foreman JH, Bayly WM, Grant BD, et al. Standardized exercise test and daily heart rate responses of thoroughbreds undergoing conventional race training and detraining. Am J Vet Res 1990; 51:914–920.
164. Essen-Gustavsson B, McMiken D, Karlstrom K, et al. Muscular adaptation of horses during intensive training and detraining. Equine Vet J 1989; 21:27–33.
165. Serrano AL, Quiroz-Rothe E, Rivero J-LL. Early and long-term changes of equine skeletal muscle in response to endurance training and detraining. Pflugers Arch 2000; 441:263–274.
166. Rivero JL, Ruz MC, Serrano AL, et al. Effects of a 3 month endurance training programme on skeletal muscle histochemistry in Andalusian, Arabian and Anglo-Arabian horses. Equine Vet J 1995; 27:51–59.
167. Essen-Gustavsson B, Lindholm A. Muscle fiber characteristics of active and inactive Standardbred horses. Equine Vet J 1985; 17:434–438.
168. Guy PS, Snow DH. The effect of training and detraining on muscle composition in the horse. J Physiol (Lond) 1977; 269:33–51.
169. Hodgson DR, Rose RJ, Dimauro J, et al. Effects of training on muscle composition in horses. Am J Vet Res 1986; 47:12–15.
170. Lovell DK, Rose RJ. Changes in skeletal muscle composition in response to interval and high intensity training. In: Persson SGB, Lindholm A, Jeffcot LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP; 1991; 215–222.

171. Straub R, Dettwiler M, Hoppeler H, et al. The use of morphometry and enzyme activity measurements in skeletal muscles for the assessment of the working capacity of horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granata; 1983; 193–199.
172. Courouce CA, Chretien M, Valette JP. Physiological variables measured under field conditions according to age and state of training in French trotters. Equine Vet J 2002; 34:91–97.
173. Sexton WL, Erickson HH, Coffman JR. Cardiopulmonary and metabolic responses to exercise in the Quarter Horse: effects of training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP; 1987; 77–91.
174. Evans DL, Rainger JR, Hodgson DR, et al. The effects of intensity and duration of training on blood lactate concentrations during and after exercise. Equine Vet J Suppl 1995; 18:422–425.
175. Saltin B, Rowell LB. Functional adaptations to physical activity and inactivity. Fed Proc 1980; 39:1506–1513.
176. Hudlicka O, Brown M, Egginton S. Angiogenesis in skeletal and cardiac muscle. Physiol Rev 1992; 72:369–417.
177. Poole DC, Mathieu-Costello O, West JB. Capillary tortuosity in rat soleus muscle is not affected by endurance training. Am J Physiol 1989; 256:H1110–H1116.
178. Hansen-Smith F, Egginton S, Hudlicka O. Growth of arterioles in chronically stimulated adult rat skeletal muscle. Microcirculation 1998; 5:49–59.
179. Suzuki J, Kobayashi T, Uruma T, et al. Time-course changes in arteriolar and venular portions of capillary in young treadmill-trained rats. Acta Physiol Scand 2001; 171:77–86.
180. Griffin KL, Woodman CR, Price EM, et al. Endothelium-mediated relaxation of porcine collateral-dependent arterioles is improved by exercise training. Circulation 2001; 104:1393–1398.
181. Lash JM. Exercise training enhances adrenergic constriction and dilation in the rat spinotrapezius muscle. J Appl Physiol 1998; 85:168–174.
182. Koller A, Huang A, Sun D, et al. Exercise training augments flow-dependent dilation in rat skeletal muscle arterioles. Role of endothelial nitric oxide and prostaglandins. Circ Res 1995; 76:544–550.
183. Laughlin MH, Pollock JS, Amann JF, et al. Training induces nonuniform increases in eNOS content along the coronary arterial tree. J Appl Physiol 2001; 90:501–510.
184. Laughlin MH, Ripperger J. Vascular transport capacity of hindlimb muscles of exercise-trained rats. J Appl Physiol 1987; 62:438–443.

CHAPTER 33

Diseases of the heart and vessels

Lesley Young

Cardiac murmurs and arrhythmias are detected commonly in performance horses, creating problems for veterinarians who must then determine their significance.[1–4] This chapter will address the diseases and abnormalities affecting the heart and vessels of the athletic horse:

- abnormalities of cardiac rhythm
- cardiac murmurs
- diseases of the myocardium and pericardium
- diseases of the vessels.

When performance horses are presented with a cardiac arrhythmia, or murmur, an accurate history and a thorough physical examination are often all that is required to determine the relevance of the abnormality. As determination of the significance of cardiac abnormalities detected by auscultation forms the largest part of performance horse cardiology, this chapter will first address the general approach to equine cardiology cases, including the technique of cardiac auscultation. During discussion of specific cardiovascular abnormalities, emphasis will be placed on diagnosis, the physical signs used to assess severity and prognosis, and the most useful ancillary aids for determining the significance of cardiovascular dysfunction in performance horses.

General approach to equine cardiology

Overall approach

The horse is equipped with enormous cardiac reserve (see Chapter 32) and as a result, evaluation of the equine cardiovascular system at rest provides limited information. Only when increased demand is placed on the heart during exercise will the effect of more subtle cardiac or vascular lesions become obvious. It is clearly important not to lose sight of the plethora of other reasons that cause horses to fail to perform to owners' expectations.[5] As has been emphasized elsewhere in this book, the probability of heart disease is low on the list of causes of poor performance, compared to orthopedic or respiratory disease. Clearly field, or treadmill, exercise tests provide the optimal environment to assess cardiac function in equine athletes, but it is often impractical or inappropriate to evaluate the heart at the limits of its reserve. As a result, the clinician must rely on clinical history to provide a subjective assessment of exercise tolerance and physical examination to assess the hemodynamic effect of any lesions present. In many cases, electrocardiography and echocardiography provide additional information useful in forming a diagnosis and prognosis.

Clinical history

The importance of obtaining a thorough case history cannot be overemphasized in considering the significance of cardiac murmurs or dysrhythmias in horses. It will usually be obvious if a horse is in overt heart failure, but this is not a frequent diagnosis in performance horses. It is much more common to discover a cardiac murmur or dysrhythmia in an apparently normal horse during a pre-purchase examination, when the horse is presented with a history of poor performance, or when a horse is examined because of illness.

As a result, the clinician must rely on clinical history to provide a subjective assessment of exercise tolerance and physical examination to assess the hemodynamic effect of any lesions present.

Cardiac auscultation

Despite advances in technology, cardiac auscultation remains the most important technique for the diagnosis of cardiac disease in horses. It is important to develop a systematic, logical approach to cardiac auscultation for it to yield maximum information. The recent suggestion that equine clinicians find interpretation of auscultation findings difficult only serves to emphasize the importance of developing the necessary skills to perform this very important technique with confidence.[6]

Findings from cardiac auscultation are always used in combination with performance history, patient details, and the remainder of the clinical examination to evaluate the significance of any suspected cardiovascular abnormalities.

Technique

Rules

- Always auscultate both sides of the chest.
- Always palpate for an apex beat on both sides of the chest (Fig. 33.1).
- Always maintain a standard systematic approach for listening to the whole cardiac cycle at each valve area.

Location of valve areas Classically landmarks for localization of cardiac valve areas have been described with reference to rib spaces and anatomic landmarks.[7] The mental effort of remembering the landmarks, coupled with marked breed variation in thoracic conformation, makes this approach difficult to put into practice. It also encourages the clinician to remove the stethoscope from the patient's chest, to examine each valve individually, potentially leaving wide areas of the cardiac auscultation area unexamined. An alternative approach is suggested.

Left hemithorax Palpation of the left apex beat (Fig. 33.1) provides an easy landmark for the mitral valve auscultation area. The apex beat should be palpated with the flat of the left hand. The stethoscope is then placed exactly over the apex beat. The point of maximal intensity (PMI) of sounds associated with the mitral valve is usually in this area. In this region the first heart sound, S_1, caused by various vibrations at the onset of ventricular systole, should be loud. The third sound, S_3, associated with the end of rapid early ventricular filling, may also be audible. It is important to appreciate that the normal diastolic sounds S_3 and S_4 are not always clearly audible in every horse. Once in position at the apex beat, the examiner should concentrate specifically on both diastole and systole for a number of complete heart cycles. The stethoscope is then moved slowly and deliberately in radiating directions around the mitral valve area while maintaining contact with the chest wall, until S_1 is no longer clearly audible.

The remaining valve areas on the left are then accessed by gradually moving the stethoscope in a cranial direction from the mitral valve area. Once more, the stethoscope remains in contact with the chest wall at all times. As the stethoscope is advanced slightly dorsal and cranial, the relative loudness of S_1 and S_2 is reversed, and S_2 is accentuated relative to S_1. As this occurs, the stethoscope is positioned at the point of maximal intensity of the semilunar valves. The first, more caudal and dorsal, valve encountered is the aortic valve. Once in the outflow valve area, the clinician performs the same radial scan of the area as for the mitral valve. S_2 will be loudest over the pulmonary valve, which is situated more cranial and slightly ventral to the area in which S_2 first becomes accentuated. Occasionally an audible splitting of S_2 may be heard in the area of the pulmonic valve. Usually the sound is split due to earlier closure of the aortic valve compared to the pulmonic valve, but the situation can also be reversed in horses.[8] The fourth heart sound, S_4, composed of vibrations arising from active atrial contraction is usually heard best in the area cranial and dorsal to the apex beat.

Right hemithorax It should also become standard to palpate for an apex beat on the right hemithorax. The vibrations are often palpable in narrow-chested athletic horses. If

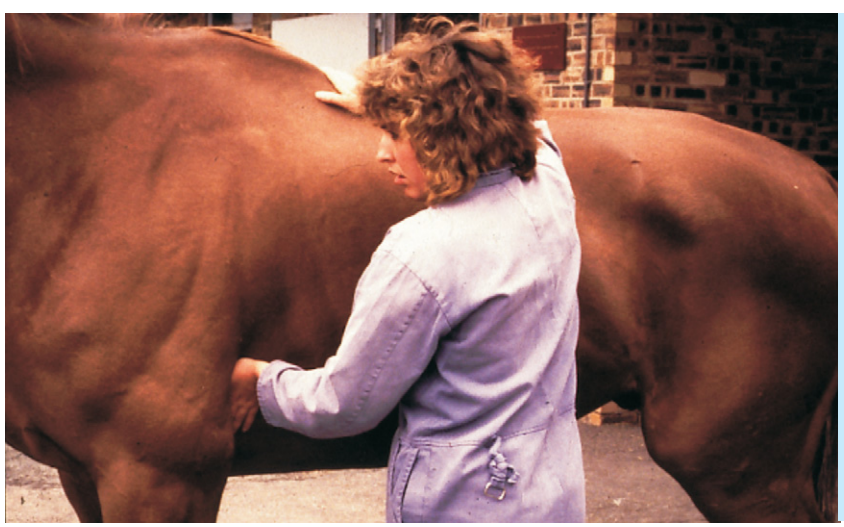


Fig. 33.1
Palpation of the cardiac apex beat. The apex beat provides an excellent starting point for auscultation on the left hemithorax. (Courtesy of Dr LE Young and Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

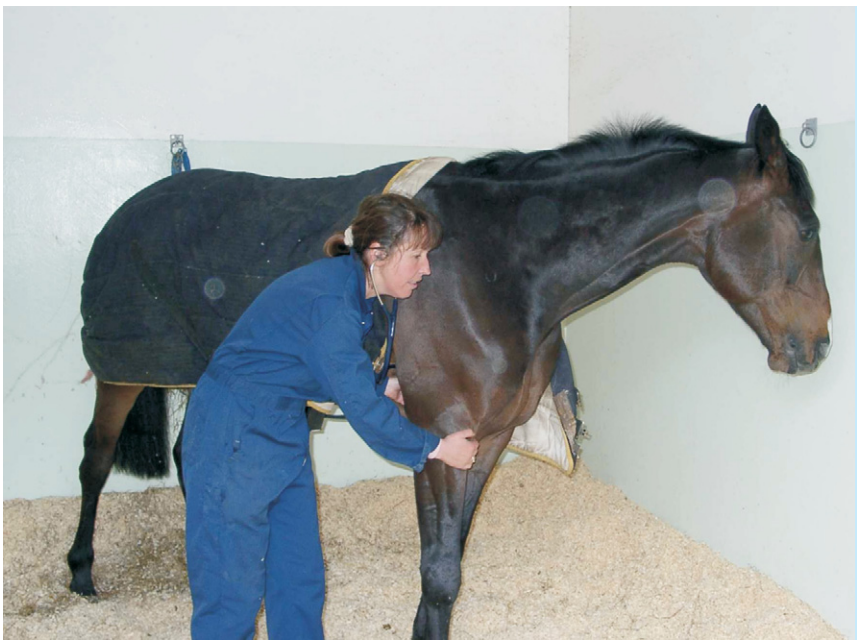


Fig. 33.2
Auscultation of the right hemithorax is best achieved when the right forelimb is pulled forward.

an apex beat is detected, it represents an excellent starting point for thoracic auscultation. The auscultation area is more cranial on the right, and forward placement of the forelimb is necessary in many horses (Fig. 33.2). The only valve sounds reliably heard in this area are associated with the tricuspid valve. A similar radiating survey, with the stethoscope in contact with the chest wall, should be performed around the point of maximal intensity of the heart sounds on this side. Many clinicians find auscultation of the right side unrewarding, because the heart sounds are usually quieter on the right and there is more variation between horses. When difficulties arise, it is usually because the stethoscope is not positioned sufficiently cranial.

Abnormalities of cardiac rhythm

General principles

- Arrhythmias occur commonly in athletic horses[9] and the majority, with the notable exception of atrial fibrillation (AF), usually do not affect performance.
- In horses, use of limb leads for recording ECG traces is not advised. Wires and crocodile clips attached to the limbs are poorly tolerated and subject to a large amount of movement artifact. In addition the pattern of depolarization of the equine ventricle precludes using multiple leads for assessment of cardiac size and mean electrical axis.[10–12]
- The base apex-lead system, or modifications to it, are used exclusively for rhythm diagnosis in equine medicine (Fig 33.3). This lead system produces large complexes, which are easy to identify.[13]
- Diagnosis of arrhythmias has been greatly enhanced by improvements in technology that allow ECG recordings to be taken readily in resting and exercising horses (Fig 33.4). The newer technology, based on palm-top computers and hand-held battery-operated devices, is becoming increasingly affordable for equine veterinarians (Fig 33.5). Increased availability and practicability of this equipment means that disorders of cardiac rhythm are diagnosed more frequently in horses at rest and during exercise and their significance must then be determined.

Cardiac disease is a rare primary cause of poor performance in the equine athlete, but on the rare occasion that performance is affected by cardiac disease, arrhythmia is the commonest underlying cause.[5] Paradoxically, alterations in cardiac rhythm are common in athletic horses because of their normal high parasympathetic drive,[14] so the equine clinician is faced with a wide variety of normal rhythms in resting horses. Bradyarrhythmias (slow rhythms) are normal findings in athletic horses, as are sinus and atrioventricular block.[9,15] Despite this, on rare occasions, all of these normal rhythms can also result from cardiac disease, when the arrhythmia causes serious decrements to performance and presents significant risks to the rider and horse.[16] Conversely, obvious arrhythmia such as atrial fibrillation, may have no obvious effect on the performance of horses engaged in activities that are not aerobically challenging (dressage or show jumping). By contrast, if all of the cardiac reserve must be used, the effect of the same arrhythmia on performance is devastating (racing, three-day eventing).[17–19] Finally, cardiac rhythm disturbances often occur as a result of disease in other body systems or metabolic disturbances.[20,21] In such cases, the arrhythmia rarely indicates primary heart disease.

The main hemodynamic effect of abnormalities of cardiac rhythm is to change cardiac output. These alterations can result from effects on heart rate or stroke volume. In some

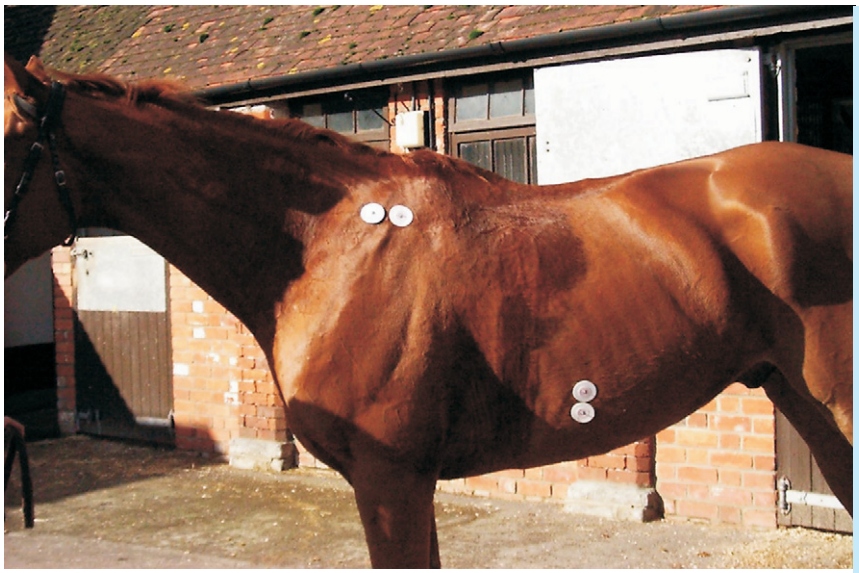


Fig. 33.3
Placement of four silver/silver chloride adhesive electrodes suitable for recording an ECG during ridden exercise. High-quality adhesive electrodes must always be used for exercising recordings and a spare electrode is always applied before exercise commences, in case one should become dislodged during fast work. This lead configuration is a modified base-apex system. The recording system used in this case was bipolar (positive and negative leads only) and did not require an earth. For recorders with an earth lead, a similar configuration can be used, with the extra earth electrode placed on the shoulder, or behind the withers near the negative lead.

To record a true base-apex lead the positive or left arm electrode is positioned at the left cardiac apex, and the right arm negative electrode is placed two-thirds of the way down the jugular groove on the right. The third (earth) electrode is placed in a remote position away from the heart. The ECG is recorded from lead 1 on a standard three-lead ECG machine. This configuration will give maximum deflections for both atrial and ventricular waveforms, but is completely unsuitable for prolonged monitoring, or exercising recordings. The vertical modification shown will still produce large QRS deflections, but the atrial deflection (P wave) will be slightly lower in amplitude than that of a true base-apex configuration.

cases, especially when the abnormal rhythm is fast, arrhythmia begets further arrhythmia as myocardial oxygen demand increases and coronary perfusion declines in the face of reduced diastolic blood pressure. It remains an important general rule that treatment of arrhythmia is only indicated when the abnormal rhythm has, or is likely to have, a significant effect on cardiac function, or when treatment is likely to resolve the arrhythmogenic mechanism (e.g. correction of acid–base and electrolyte imbalances).

Fig. 33.4
Placement of four silver/silver chloride adhesive electrodes suitable for recording an ECG during ridden exercise. Once in place as depicted in Fig. 33.3, the electrodes remain visible to the rider and/or examiner. As a result they can be reattached easily should they become dislodged, and are unlikely to be affected by the saddle or girth slipping backwards during fast exercise. The recording device is just visible attached to an elastic surcingle behind the rider's leg where it usually causes minimum disruption and discomfort. For harness racing the electrodes are positioned similarly, away from any moving harness straps. Radiotelelemetric recording systems can be used to obtain exercising traces. These units use a local transmitter carried by the horse that continuously transmits the signal to a local recorder. They are expensive and require that the recorder remain within at least 250 m of the exercising horse. This can create practical problems for many equine athletes, unless a horse regularly exercises with a scurry or there is good vehicular access to the exercise grounds.

Fig. 33.5
Portable devices have been developed that are competitively priced and able to record up to 60 minutes of ECG from exercising horses; these devices have promise for equine sports medicine. (Courtesy of Wheeler Monitoring (email: jcwheeler@iee.org).)

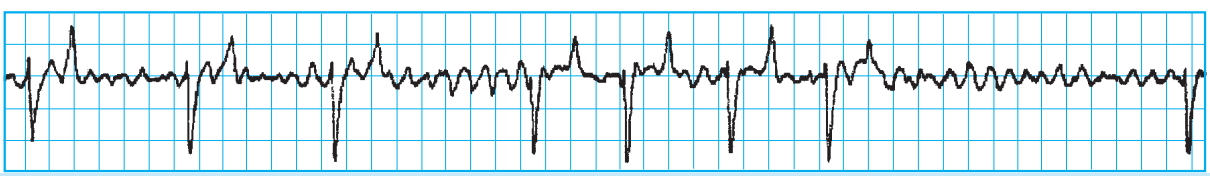


Fig. 33.6
Electrocardiogram (base-apex configuration) of a horse with atrial fibrillation. The typical characteristics include an irregularly irregular rhythm, coarse baseline perturbations called flutter (F) waves, and QRS complexes of normal width and morphology. (Courtesy of Dr Ken Hinchcliff, The Ohio State University.)

Atrial fibrillation

- A re-entrant rhythm disorder characterized by an irregularly irregular rhythm (Fig. 33.6).
- The abnormal rhythm may occasionally self-correct within hours to days of becoming established.
- Atrial fibrillation (AF) is the commonest cardiovascular cause of poor performance in racehorses.
- AF can be associated with severe cardiac disease, or occur in the absence of detectable cardiac lesions.
- Treatment depends on whether underlying cardiac disease is present and the effect of the abnormal rhythm on performance.
- The prognosis for successful treatment and return to previous athletic function in the absence of cardiac disease is fair to good.

Recognition

History

AF may occur in horses with no other evidence of cardiac disease, or it may be precipitated by atrial dilation secondary to underlying heart disease, most commonly longstanding mitral regurgitation[17] (Fig. 33.7). When AF occurs in isolation, it is often larger breed horses that are affected. Affected animals usually present with a history of poor performance at maximal exertion (during finishing or sprinting in racehorses, galloping or hill work in event horses and hunters). Although horses affected with AF can compensate for suboptimal cardiac filling by increasing heart rate at all levels of exercise to maintain forward cardiac output, they attain maximum heart rate at lower exercise intensity and therefore fatigue sooner.[22,23] Despite attaining peak heart rates exceeding 280 beats/min, affected horses fail to wholly compensate for their reduced diastolic function. In some horses, AF is associated with epistaxis.[18,24]

If AF develops suddenly, during fast work, there is an acute decrease in cardiac output, and affected horses may pull up suddenly, sometimes with ataxia and distress. Immediate thoracic auscultation reveals a rapid chaotic rhythm. Obvious performance decrements are not invariably the case, however, as affected horses may appear to work normally at submaximal intensity. The rhythm, once initiated can be sustained, but short-lived paroxysmal AF also occurs during exercise (Fig. 33.8).[25] Paroxysmal AF resolves in the minutes, hours, or days following exercise and may be difficult to

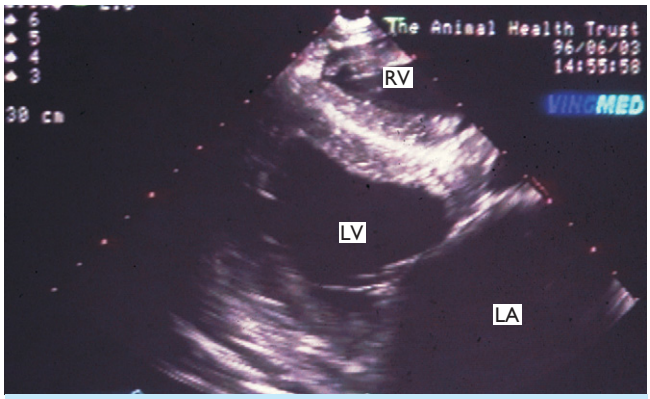


Fig. 33.7
Two-dimensional echocardiograph from a 3-year-old colt in training with a season-long history of poor performance, believed by the trainer to be due to chronic foot lameness. When the colt developed a cough, veterinary examination revealed a fast irregular heart rhythm and a grade 5/6 murmur suggestive of mitral valve regurgitation. The image is taken from the right hemithorax and shows massive left atrial enlargement from longstanding severe mitral regurgitation. Although the colt had no physical signs of heart failure, treatment was not attempted and the horse was euthanased. LA, left atrium; LV, left ventricle; RV, right ventricle.

detect. As a result, AF is a possible cause for fading during racing or competition when horses are subsequently presented in normal sinus rhythm.[26]

Physical examination

Auscultation findings in cases of AF will depend on the underlying cause. The irregularly irregular rhythm will be common to all cases of sustained AF, but in horses with AF secondary to atrial dilation from cardiac disease, there will be an elevated heart rate, characteristic cardiac murmurs, and physical signs of heart failure. Careful auscultation of these cases will reveal the underlying cause such as mitral regurgitation or ventricular septal defect. Horses with AF but no significant underlying heart disease usually have a normal resting heart rate. Vagal tone at the atrioventricular node will cause waxing and waning of the cardiac rhythm that can appear deceptively similar to second degree atrioventricular block.[27] This feature can be confusing, but the two rhythms can always be differentiated with patient auscultation because an unexpected early beat will be always be detected (Fig. 33.9A).

Other findings include a complete absence of the fourth heart sound (associated with atrial contraction), often with increased intensity of the third sound. The first and largest of the three jugular pulsations will also be absent. Other clinical signs will be evident if the abnormal rhythm is associated with heart failure.

Special examination

Electrocardiography will reveal an irregularly irregular rhythm with a complete absence of P waves. Cardiac rate will depend on the presence or absence of associated cardiac disease. Fibrillation or F waves may or may not be visible (Figs 33.6, 33.9B). Echocardiography can be a useful adjunctive aid to determine the presence or absence of cardiac lesions and assess chamber size, when physical examination and clinical history cannot rule out significant cardiac disease (Figs 33.7, 33.10B).

Laboratory tests

AF can be associated with alterations in electrolyte status. Plasma or serum concentrations of cardiac troponin I, isoenzymes of lactate dehydrogenase, and other biochemical markers of myocardial injury and inflammation are rarely elevated in cases of AF, unless the condition is associated with toxic damage to the heart, or end-stage valve disease.

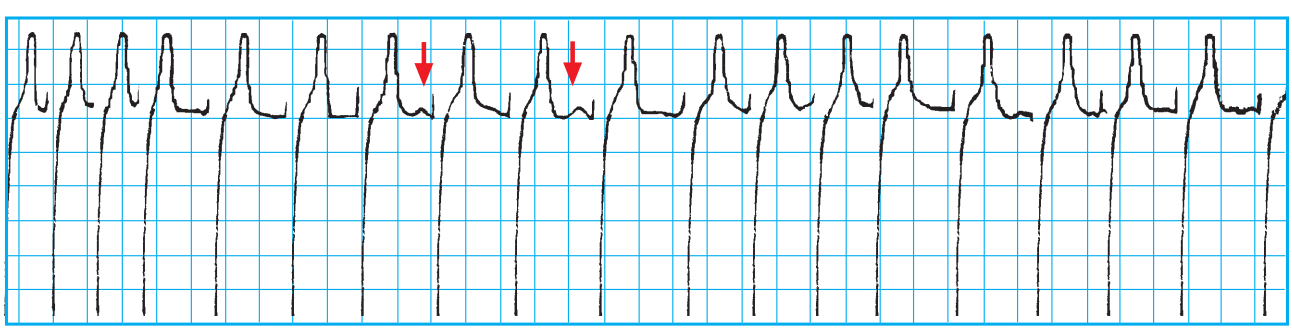


Fig. 33.8 Base apex ECG taken from a 7-year-old Thoroughbred mare, 20 minutes after dramatically fading during fast work. Heart rate is still elevated (average rate 140 beats/min) and the rhythm is irregularly irregular. The QRS complex width and morphology is normal and P waves are not visible. There are positive baseline undulations between the seventh and eighth and ninth and tenth beat that may be mistaken for P waves (downward pointing red arrows). Closer inspection reveals them to be too close to the QRS complex that follows and more characteristic F waves are visible in the long diastolic interval before the final QRS complex. This trace illustrates the high heart rate maintained by horses affected with paroxysmal atrial fibrillation. The horse spontaneously converted to normal sinus rhythm within 5 hours of the bout occurring.

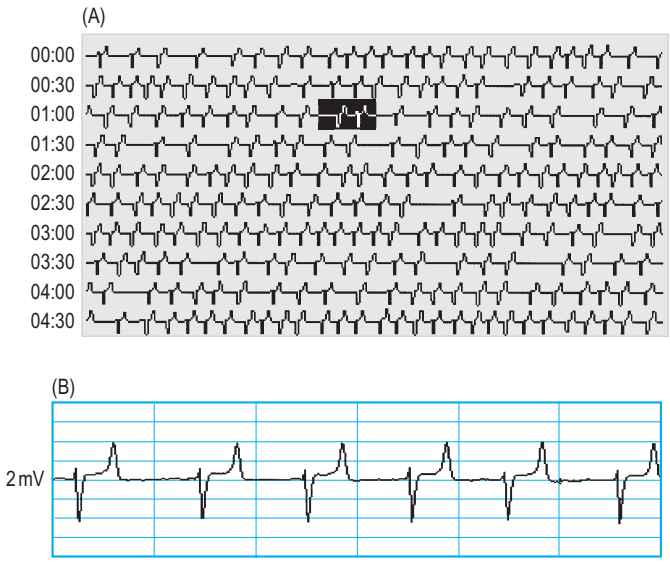


Fig. 33.9 (A) Summary of a continuous 5-minute ECG recording from a 5-year-old Thoroughbred race horse. The summary clearly demonstrates the irregular irregularity of atrial fibrillation that would become obvious with prolonged monitoring by auscultation. Notice that during periods of rapid conduction the rhythm can seem almost regular and that during periods of slow conduction it might be mistaken for sinus arrhythmia and second degree AV block. As a result, the rhythm is not infrequently missed when a cursory examination by auscultation is performed. (B) This expanded ECG trace of the horse in A shows fine atrial fibrillation. Even after increasing the sensitivity of the ECG recorder obvious coarse F waves were not visible. Only the absence of P waves and the fairly subtle irregularity of R–R intervals reveal the underlying rhythm disturbance. The horse converted to normal sinus rhythm after oral administration of a total of 24 g of quinidine sulfate.

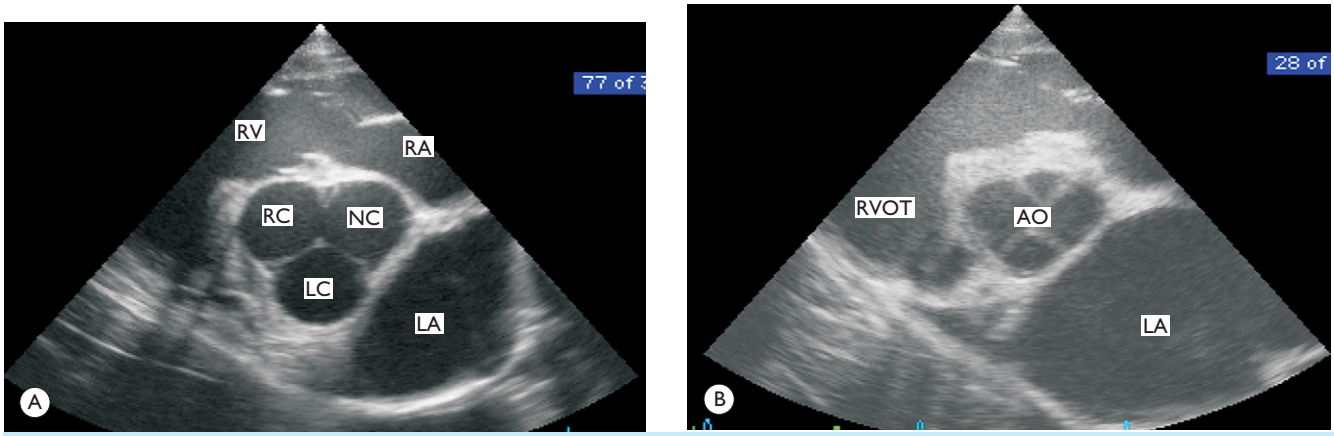


Fig. 33.10
(A) Two-dimensional echocardiograph from an 8-year-old Thoroughbred race horse with atrial fibrillation associated with a sudden decrease in race performance. The image is derived from the right hemithorax with the transducer positioned to obtain a short-axis view of the atrium and aorta. Comparison of the relative width of the left atrium with respect to the aortic root provides useful reference for determination of left atrial enlargement, regardless of horse size. Normal horses have a left atrial to aortic root ratio of less than 1.2:1. Although there was a grade 2/6 murmur of mitral regurgitation, the left atrial:aortic width ratio was within normal limits. The horse converted to normal sinus rhythm after administration of 45 g of quinidine sulfate p.o. LC, left coronary cusp of aortic valve; NC, non-coronary; RC, right coronary cusp; LA, left atrium; RV, right ventricle; RA, right atrium. (B) Two-year-old Thoroughbred flat racing filly with atrial fibrillation that presented with lethargy and poor exercise tolerance. The image is derived from the right hemithorax with the transducer positioned to obtain a short-axis view of the atrium and aorta. Visual inspection of the same image as in Fig. 33.10A shows the greatly increased left atrial:aortic width ratio (2.9:1). The difference is accentuated as low output cardiac failure has reduced left ventricular stroke volume and blood pressure and concurrently aortic diameter has also reduced. The filly was treated using digoxin to control cardiac rate, diuretics to reduce congestion, an angiotensin converting enzyme inhibitor (enalapril) to reduce cardiac afterload, and a calcium-sensitizing agent and phosphodiesterase inhibitor (pimobendan) to enhance myocardial contractility and further reduce afterload. Quinidine treatment is not appropriate when atrial fibrillation occurs secondary to left atrial enlargement. AO, aorta; RVOT, right ventricular outflow tract; LA, left atrium.

Treatment

Therapeutic aims

The therapeutic aims vary depending on the circumstances and cause of AF. When AF affects athletic performance and there is no evidence of underlying heart disease, therapy aims to convert AF to normal sinus rhythm and to prevent its recurrence. However, if AF is not associated with performance decrements, treatment may not be required, provided underlying heart disease can be ruled out. When AF coexists with heart failure, the abnormal rhythm should not be

specifically treated. Treatment goals in this instance include control of ventricular response rate, reduction of volume overload by diuretics, and cardiac afterload reduction by vasodilation.[28,29]

Therapy

Before drug therapy is contemplated, any underlying fluid, electrolyte or acid–base abnormalities should be corrected. When horses become dehydrated, or develop abnormalities of acid–base and electrolyte abnormalities, as might occur during three-day events or endurance competitions, restoration of fluid and electrolyte balance alone may be sufficient for normal sinus rhythm to restore itself.

Quinidine sulfate, a Class 1A antiarrhythmic, is traditionally administered to affected horses via a stomach tube to convert AF to normal sinus rhythm.[30,31] Intravenous administration of quinidine gluconate has been described,[32] but this preparation, though more convenient, is less effective when the arrhythmia is longstanding.[31,33] The intravenous preparation of quinidine gluconate is not available in the UK and production of quinidine sulfate has recently been discontinued. As a result quinidine must now be imported and as difficulty in obtaining quinidine sulfate increases in Europe, there has been a drive to investigate alternative treatments of equine AF. The Class 1C antiarrhythmic, flecainide, is more efficacious than quinidine in returning human patients to sinus rhythm after sustained[34] and paroxysmal AF,[35] and its use has been investigated in horses.[36] Flecainide was effective in returning horses to normal sinus rhythm after AF was induced by rapid atrial pacing,[37] but there are currently no data available on the efficacy of flecainide in naturally occurring disease. Class 3 agents, amioderone, sotalol, dofetilide, and ibutilide, also lengthen action potential duration and are being increasingly used alone and in combination for acute and chronic treatment of paroxysmal[35] and sustained AF in humans.[38] These agents have not been fully investigated in horses and their cost is likely to be prohibitive. Direct current cardioversion is also used in human medicine to convert AF to normal sinus rhythm and a similar technique has been used successfully to treat refractory atrial flutter in a horse.[39]

Treatment of atrial fibrillation with quinidine sulfate

Horses should not be treated for the first 72–96 hours following the development of AF, as some will spontaneously revert to normal sinus rhythm. Treatment should be contemplated only if there is no evidence of cardiac failure and if there is compromise of athletic ability.

Regime Traditionally the administration of a test dose of quinidine sulfate (10 mg/kg p.o.) was given to check for idiosyncratic reactions before commencing treatment. However this is not necessary and treatment is begun with 20 mg/kg quinidine sulfate administered via nasogastric tube (10 g per 500 kg horse). This dosage is repeated every 2 hours until sinus rhythm is restored, signs of toxicity develop, or a maximum total dose of 60–80 g (120 mg/kg) is achieved.

Signs of toxicity include urticaria, diarrhea, anorexia, weakness, ataxia, and tachycardia.[18,31] Nasal edema with stertorous breathing, and depression are commonly observed after only a few doses. Horses receiving quinidine should not be moved, as quinidine causes hypotension through α-receptor blockade.[40] A relationship has been demonstrated between high plasma quinidine concentrations ataxia and respiratory tract stridor, but not between plasma quinidine concentrations and tachycardia, diarrhea, or colic.[31] These authors also noted that conversion to normal sinus rhythm was less likely when signs of quinidine intoxication were present.[31] Laminitis has also been reported after quinidine treatment, but this side effect appears to be rare. Sudden death can also occur, usually without premonitory signs. In common with all Class 1A antiarrhythmic drugs, quinidine also has pro-arrhythmic properties.[41] By lengthening the myocardial cell refractory period through an effect on the repolarizing potassium channels, quinidine increases the risk of severe ventricular rhythm disturbances.[40] Because the drug increases atrioventricular (AV) nodal conduction, it has the potential to produce rapid supraventricular, as well as ventricular, tachycardia.[40] ECG recordings should be made before each treatment, and the QRS and QT interval measured. A 25% increase in the width of the QRS interval is associated with quinidine intoxication.[31]

Heart rate and rhythm must be monitored throughout treatment. The most common arrhythmia is supraventricular tachycardia (SVT) and it can be treated by the intravenous administration of 0.002 mg/kg digoxin.[31] However, digoxin has a slow onset of action and a long half-life and although the drug decreases AV nodal conduction and reduces heart rate, it also tends to stabilize AF by increasing the number of wavelets circulating in the atria and decreasing their wavelength.[42] This electrophysiological property makes digoxin of questionable benefit in the conversion of AF and it may be best withheld unless the supraventricular rhythm is life threatening. Usually, provided no further quinidine is given, tachycardia gradually subsides as plasma quinidine concentrations fall.

Horses that fail to revert to sinus rhythm after administration of 120 mg/kg quinidine, or that develop unacceptable side effects during cumulative dosing, sometimes respond to a second series of 20 mg/kg treatments after 24 hours without drug administration. Indeed some horses convert to normal sinus rhythm up to 24 hours after the final dose of quinidine has been administered without any additional drug administration or treatment. Recognition that horses are less likely to convert to normal sinus rhythm during quinidine intoxication,[31] probably explains this phenomenon, as the plasma concentration of the drug will return to the therapeutic range with time. The potential severity of quinidine's side effects has led to modifications of the traditional cumulative 2-hourly regime and an alternative regime has been suggested.[31] If a horse fails to respond to the initial 2-hourly treatments, when signs of toxicity develop, or when the maximum dose of quinidine has been reached, quinidine administration is continued at 6-hourly

intervals. These workers also recommend that digoxin (0.01 mg/kg) be given orally every 12 hours until sinus rhythm is restored. It has been suggested that this treatment regime reduces side effects, and decreases the total dosage of quinidine needed for successful conversion. It is worthy of note, however, that there is a possibility that the horse might convert to normal sinus rhythm once quinidine treatment has been discontinued without additional treatment, making the actual benefit of this regime difficult to assess. As a result, a pragmatic approach to patients failing to respond on day 1 of treatment is to wait for 24 hours without further drug administration and then commence 6-hourly quinidine administration, only if the 2-hourly regime fails for a second time. This modified regime avoids the practical difficulties of treatments during night hours. The use of digoxin in cases with pre-existing myocardial dysfunction has also been suggested, or after initial treatment fails,[31] but as discussed previously, concurrent use of digoxin also carries the risk that the abnormal rhythm may be stabilized, rather than abolished.

Aftercare Following successful conversion to normal sinus rhythm and return to a normal resting heart rate, it has been suggested that the horse should be checked for the presence of atrial premature systoles using 24-hour Holter monitoring.[43] The presence of frequent premature atrial systoles and atrial arrhythmias is suggested to indicate an increased risk of recurrence of AF. These authors suggest specific antiarrhythmic therapy (quinidine or digoxin) or anti-inflammatory therapy (see later) and prolonged rest (3–4 months) for such cases to reduce the likelihood of recurrence.[40] Unfortunately, there is no data available to assess critically the benefit of these various strategies for horses following successful conversion to normal sinus rhythm. As a result, in commercial practice when there are considerable financial pressures for horses to perform, coupled with a short competitive season, only after a patient reverts repeatedly to AF would such measures be contemplated.

A more pragmatic approach, even when AF may have been longstanding, is to rest the horse completely for 5–7 days, to allow the residual affects of quinidine to subside. The horse is then gradually returned to fast training over 3–4 weeks. Owners/trainers are advised to monitor cardiac rhythm regularly by palpation of the apex beat (Fig. 33.1), especially after fast work, throughout this period. While longer periods of rest may be optimal to allow the atria the best chance to remodel both mechanically and electrophysiologically, the cost–benefit of prolonged rest is currently unknown and commercial pressures usually preclude this.

Prognosis

Horses with longstanding AF (> 4 months) are less likely to convert to normal sinus rhythm and are more likely to revert to fibrillation after treatment than horses with more recent onset of the arrhythmia.[17,31] The success rate for conversion from AF to normal sinus rhythm using quinidine varies between 82 and 87%.[18,31] As a result, failure to achieve normal sinus rhythm occurs not uncommonly and owners should always be forewarned that success is not inevitable. When treatment of AF is successful, horses should return to their previous exercise tolerance. However, if the dysrhythmia is not affecting performance, in most cases, treatment should not be attempted. In some horses, recurrence of paroxysmal or sustained AF is a problem, although some owners and trainers become aware of the trigger factors and learn to manage them accordingly. In other cases when frequent recurrence or poor tolerance of treatment occurs, an alternative career can often be found for the horse. In such cases, and before treatment is attempted, it is important to establish that the rhythm is present in isolation and has not occurred secondary to atrial enlargement and heart failure (Figs 33.7, 33.10B). It is also advisable to monitor the heart rate and rhythm regularly at the intensity of exercise at which the horse is expected to perform. When AF exists with signs of heart failure, prognosis for return to athletic activity is hopeless.

Etiology and pathophysiology

AF is a re-entrant rhythm disturbance. The mechanism that was widely held to underlie the arrhythmia was that of multiple wavelets, a model that hypothesized that large numbers of wavelets moved randomly through the atria.[44] This theory has recently been superseded by evidence from complex electrophysiologic mapping studies that have suggested the wavefronts actually originate from the uninterrupted periodic activity of a small number of discrete re-entrant sites in the left atrium (rotors) possibly in the region of the pulmonary veins.[45] It seems likely that the rhythm is maintained because of differences in electrophysiologic characteristics between anatomic sites in the atria and between the left and right atria themselves. Regardless of the mechanism, the rhythm is maintained by a large atrial mass and inherent differences in the length of the refractory periods of atrial cells. The cells with long refractory periods produce physiologic blocks, and the large mass of tissue allows cells to repolarize before the initial wavefront has died out. As a result, waves of excitation continuously circle around the atria. Both atrial flutter and true AF occur in the horse. The difference probably reflects the number of wavelets in circulation. (Figs 33.6, 33.9B).

The risk of re-entry becoming established is increased with changes in autonomic tone.[46] Both parasympathetic and sympathetic stimulation increase the inhomogeneity of refractoriness within the atria, by changing the refractory period of the myocytes.[47] Most commonly in horses these changes occur during fast exercise or recovery, but they can also be invoked by use of vagotonic drugs such the α-adrenoreceptor agonists (xylazine, romifidine, and deto-

midine) and the opiates (butorphanol). Paroxysmal and sustained AF can also follow sedation, anesthesia,[48] and occasionally occurs after disease in other body systems.[49,50]

AF results in a decreased stroke volume due to the loss of the atrial contribution to filling. The atria contribute up to 15–20% to ventricular filling, but in most horses at rest the loss of the atrial contraction has little effect on cardiac output.[49] However during exercise when the heart rate is high and the time available for ventricular filling is reduced, the atrial contribution to filling becomes important. Therefore horses with AF have reduced performance only during maximal exertion, unless there is some other underlying cardiac disease that has precipitated the dysrhythmia. When present, AF always affects performance in racehorses.

Longstanding AF results in extensive electromechanical remodeling of the atrial muscle cells, including changes in the expression of membrane-bound ion channels.[45] This effect probably explains why sinus rhythm is difficult to recapture and subsequently maintain in some of these horses. In the series of cases examined by Else & Holmes,[51] 36/45 affected horses had gross lesions affecting the atria, including dilation, thinning, and fibrosis. The left atrium was more commonly affected than the right. Eighty percent of affected horses had lesions affecting the cardiac valves, most commonly the mitral valve, confirming clinical evidence that left atrial enlargement and mitral valve disease are important in the pathogenesis of sustained AF in horses.

Epidemiology

This arrhythmia is the commonest cardiovascular cause of poor performance in horses. Based on this author's epidemiologic studies on UK training yards, the approximate incidence of the sustained form of the arrhythmia is 1% in National Hunt Thoroughbreds. When large numbers of horses from a mixed population were examined, the prevalence of AF varied between 2.5 and 2.4%[51] and increased with age, an observation that probably explains the difference between the two groups of horses. Else & Holmes also observed that draught and heavy horses were overrepresented in their affected horses. The prevalence of the sustained form of AF is lower in smaller Thoroughbreds, but it appears to have a similar prevalence in Standardbred horses.[17] It is likely that paroxysmal AF occurs more commonly than is recognized in horses of all types, since unless performance is obviously affected, the rhythm goes unnoticed,[25] a situation that is similar in people.[52] Standardbreds, young horses, and males predominated in a group of 67 horses studied by Reef and colleagues (1988), but it is likely that these data reflect the bias of sex, breed and age in athletic horses, rather than relate to prevalence of AF in the horse population per se.[17] In the same study the majority of horses affected with AF had no clinical evidence of other cardiac disease (56.7%),

Supraventricular premature systoles

- Supraventricular premature beats arise from tissue above the level of the atrioventricular node. They usually originate in the atria and occur not infrequently in athletic horses.
- Their significance and underlying etiology is not well understood, although increased excitability of atrial tissue is associated with atrial stretch in severe cardiac disease (Figs 33.7, 33.10B).
- They can also be associated with primary myocardial damage (myocarditis), systemic disease, and electrolyte and acid–base derangement.
- Electrocardiographic examination is required for a definitive diagnosis.
- Electrocardiographic monitoring during appropriate exercise will be required to assess the effects of changes in autonomic tone and to determine the effect, if any, of the arrhythmia on performance.

Recognition

History

Supraventricular premature beats are usually detected incidentally during cardiac auscultation or palpation of arterial pulses in otherwise normal horses. They may be detected in association with myocardial inflammation or, more commonly, severe cardiac disease that has resulted in atrial dilation e.g. atrioventricular valve disease, large ventricular septal defect, or dilated cardiomyopathy. Supraventricular arrhythmia may also accompany systemic disease or any condition that modifies autonomic tone and alters electrolyte and acid–base status.

Physical examination

Isolated cardiac contractions are noted to follow too early in an otherwise normal rhythm during cardiac auscultation or pulse palpation. During supraventricular tachycardia, a fast regular rhythm will be noted by auscultation.

Special examination

A definitive diagnosis and the origin of all ectopic complexes must be determined by electrocardiography (Figs 33.11, 33.12A). When the complexes are atrial in origin, one or more premature complexes with normal QRS morphology will break the regular cardiac rhythm. The morphology of the preceding P wave may be different to the sinus beats (Fig. 33.12A), but the QRS complex will follow after the normal P–R interval. Occasionally the premature P wave will be buried in the preceding T wave and may be difficult to locate (Fig. 33.11).

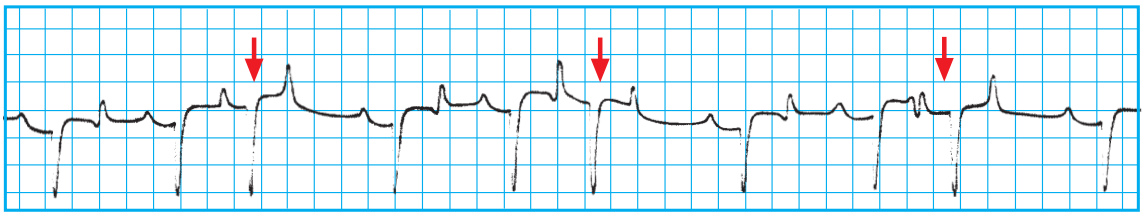


Fig. 33.11
Atrial premature beats in a 4-year-old National Hunt horse. The cardiac rhythm is broken by premature QRS waves indicated by red arrows. The premature complexes have a normal morphology and width. Their origin is not immediately obvious, as discrete associated ectopic P′ waves are difficult to discern because of their close proximity to the preceding T wave. Only in the third complex is a P′ wave obvious as it interrupts the preceding T wave. Note the normal P′–R interval that precedes the ectopic beat. Closer inspection of the T wave of the first two ectopic beats reveals them to be subtly different from the sinus T waves, suggesting that they also contain a P′ wave.

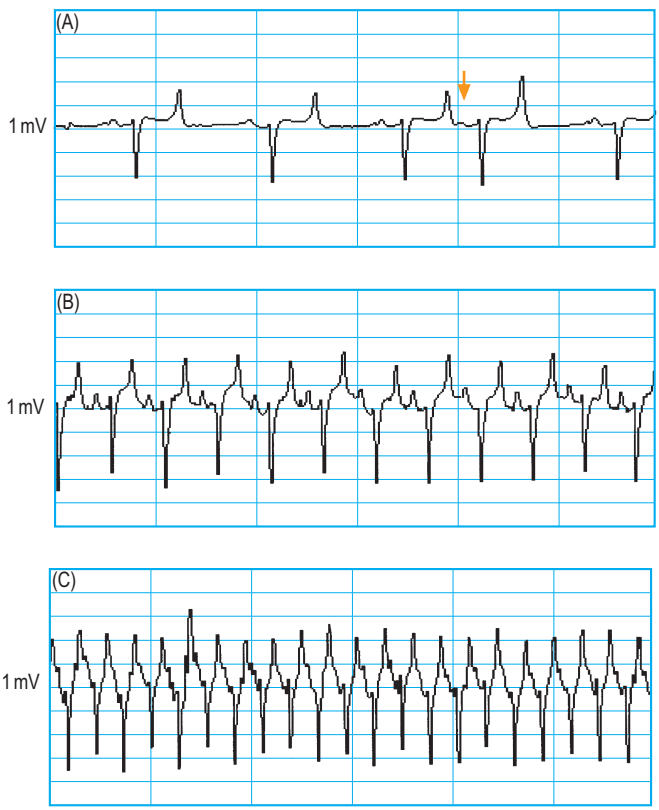


Fig. 33.12
(A) Atrial ectopy in an 8-year-old National Hunt gelding first diagnosed with the condition as a 2-year-old colt. Note the single atrial ectopic beat (arrow) followed by a normal P′–P interval. The ectopic P′ wave has a slightly different shape; unlike the sinus beats it is not bifid. (B) Same horse as in A. On exercise the ectopic focus was overridden, as shown in this trace from the horse taken during trotting (heart rate = 110). The R–R interval is constant and P waves are still visible, distinct from the preceding T waves. (C) Same horse as in A and B. At very fast heart rates (heart rate = 232) the P wave becomes increasingly difficult to discern, as it is now buried in the preceding T wave, but the R–R interval is absolutely regular. There is thus no evidence that the atrial arrhythmia present should be affecting performance in this individual. The condition was never treated and the horse was a successful flat and jumps racehorse, until lameness terminated his career at 8 years old.

In horses with isolated atrial premature beats without underlying disease, an ECG during appropriate ridden exercise will be required to assess the effect of exertion upon the arrhythmia and to evaluate its effect on athletic performance (Fig. 33.12).

Other tests In all cases of persistent supraventricular ectopic activity in horses, thorough evaluation of electrolyte status and assessment of other body systems should precede expensive specialized cardiac examinations.

Laboratory analysis of blood samples for concentrations of cardiac troponin I and isoenzymes of lactate dehydrogenase may also be useful to assess active myocardial necrosis and inflammation.

Echocardiography is also used to rule out cardiac chamber enlargement and abnormal wall motion suggestive of previous myocardial damage. In the majority of cases the results of all these examinations are unremarkable, or equivocal.

Treatment

Therapeutic aim

It is a general rule that arrhythmia should always be considered in the context of the patient's concurrent disease. Treatment of an atrial rhythm disturbance is only warranted when there is obvious decrement to cardiac function as a result of the abnormal rhythm, or if the rhythm is likely to degenerate into a more sinister life-threatening arrhythmia, a situation that is unlikely for most atrial arrhythmias.

As isolated atrial premature beats are not infrequently encountered in performance horses, they present a dilemma to the veterinarian. Usually specific antiarrhythmic treatment is not indicated, as the premature beats are too infrequent to significantly affect cardiac output at rest. Clearly in these animals it is important to establish what happens to heart rhythm during exercise. In many cases when sinus rate exceeds the firing rate of the single ectopic focus, there is overdrive suppression of the ectopic focus and cardiac rhythm is normal (Fig. 33.12).

Therapy

Atrial arrhythmias due to confirmed or suspected non-infectious myocardial disease may respond to treatment with

anti-inflammatory agents (dexamethasone 0.02–0.2 mg/kg) and rest. However the efficacy of treatment is not proven and a period of rest alone (2–3 months) can also result in resolution of the arrhythmia. We have also used oral prednisolone therapy in some cases. This treatment's efficacy is not proven either, but seems to be well tolerated. Our usual regime for a 500 kg horse is 400 mg prednisolone, orally, once daily for 4–7 days, 200 mg prednisolone daily for 4–7 days, and then 100 mg prednisolone daily for 4–7 days.

Prognosis

The prognosis for horses with atrial prematurity in the absence of cardiac disease is good. In these horses, the arrhythmia is rarely associated with poor performance and although there is a theoretical increased risk of AF developing in affected horses, this complication seems to occur rarely. Usually these horses remain in full work and competition, the arrhythmia may resolve, or be evident at each subsequent examination. When the arrhythmia is associated with laboratory or echocardiographic evidence of myocarditis, the prognosis is more guarded, although a percentage of affected animals will return to athletic performance following rest, steroid therapy, or the combination. When supraventricular arrhythmia is associated with severe cardiac disease, the prognosis is poor.

Etiology and pathophysiology

Specific information regarding the etiology of supraventricular ectopic beats in horses is lacking, but based on data from other species, the condition is associated with cardiac disease resulting in atrial dilation, stretch, and hypoxia. In the absence of specific cardiac pathology, electrolyte abnormalities alter atrial myocyte automaticity and, coupled with alterations in autonomic balance, promote ectopic activity and arrhythmias in other species. In horses, it has been suggested that the ectopic foci come from areas of local ischemia in the atria that provide the physiologic substrate for increased automaticity as the myocytes become hypoxic and die. Indeed areas of diffuse and focal fibrosis are common in the equine myocardium at post-mortem examination.[53–55] The precise etiology of the lesions is unknown, but the hypothesis that they are important in the pathogenesis of atrial arrhythmia is supported by a case report by Button and colleagues.[56] These authors identified areas of myocytolysis and replacement with fibrous tissue in the atrial myocardium of a Quarter Horse with multiple atrial arrhythmias.

Ventricular premature systoles

- Ventricular premature beats arise from tissue at or below the level of the atrioventricular junction (Figs 33.13, 33.14).
- Five or more consecutive ventricular premature beats constitute ventricular tachycardia, a rapid and potentially life-threatening rhythm that can lead to ventricular fibrillation and death.
- The significance and underlying etiology of ventricular premature beats in horses is not well understood, although in common with other species, increased excitability of equine ventricular myocardium is associated with ventricular dilation and myocardial hypoxia, inflammation, or necrosis.
- In horses ventricular premature beats are most often associated with disease of other body systems, electrolyte and acid–base derangement.[20]
- Ventricular premature beats occur commonly in the early cardiac slowing period after fast exercise in athletic horses when their presence rarely indicates cardiac pathology (Fig. 33.15).
- Because of the possibility of life-threatening ventricular tachycardia developing during exercise, horses with ventricular premature beats at rest should be retired from ridden work until thorough systemic and cardiovascular examinations can be performed.

Recognition

History

Ventricular premature beats are usually detected incidentally during cardiac auscultation or palpation of arterial pulses in otherwise normal horses. They may be detected in association with severe cardiac disease that has resulted in ventricular dilation (e.g. aortic valve disease or dilated cardiomyopathy), myocardial inflammation (e.g. myocarditis), or during disruption of the normal intracardiac conduction system (e.g. intra-interventricular septal rupture of an aortic root aneurysm).[57] Ventricular arrhythmia may also accompany systemic disease[21] or extreme exertion,[58] and any other conditions that modify autonomic tone, induce hypoxia, and alter electrolyte and acid–base status.[20]

Isolated and multiple ventricular ectopic beats are commonly detected in horses during the immediate early slowing period after maximal exercise. They rarely seem to be associated with primary cardiac disease and probably should not be overinterpreted when they appear only at this time. If they occur during work, the situation is quite different and an underlying cause should be sought and treated if possible. In the meantime the horse must be retired from ridden work because the risk of ventricular fibrillation is a significant danger to both horse and rider.

In general when considering ventricular ectopic beats in horses 'judge them according to the company they keep'.

Physical examination

Ventricular premature beats are usually detected incidentally during cardiac auscultation or palpation of arterial pulses, when they can be difficult to distinguish from

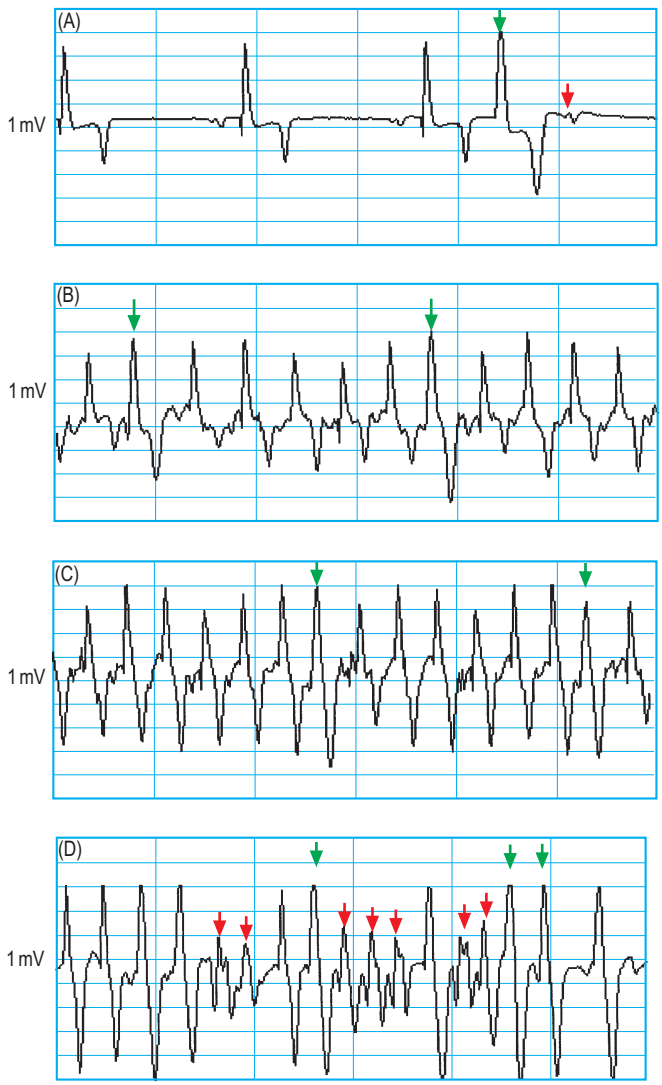


Fig. 33.13
(A) Inverted base apex ECG obtained from a 9-year-old Thoroughbred race horse with an arrhythmia at rest. A wide bizarre complex occurs after the third sinus beat. The bizarre shape of the premature QRS complex (green arrow) suggests ventricular origin and this is confirmed by the presence of the dissociated sinus P wave (red arrow) that follows at the normal sinus rate. Atrioventricular (AV) dissociation is another hallmark of ventricular prematurity. The sinus P wave follows as normal, but is not conducted to the ventricles, as they remain refractory due to the premature beat. In cases like this it is important to determine the effect of exercise on the ectopic focus and cardiac rhythm. In this case treadmill exercise was used. (B) Inverted base apex ECG from the same horse during trot. Note the increased sinus rate (heart rate = 120). Beats 2 and 8 are premature (green arrows) and have a slightly different conformation and are slightly wider suggesting a ventricular origin. There is still AV dissociation, but as sinus rate has increased the inverted P wave is just visible at the start of the inverted QRS complex of the premature beat. (C) As in A and B, the ventricular prematurity continues (green arrows, beats 8 and 15) during hack canter at 10 m/s.
(D) Inverted base-apex ECG from the horse in A–C 30 seconds after exercise to fatigue. Although ectopic beats are common in the early recovery period after exercise in athletic horses, (see Fig. 32.15), this horse suffered multiple sustained runs of ventricular prematurity. Beats 5, 6, 9, 10, 11, 13, and 14 are ventricular fusion beats (red arrows). These complexes occur when an ectopic ventricular beat is superimposed on a normal sinus beat. Beats 8, 12, 15, and 16 are premature ventricular beats (green arrows). This horse was rested for 3 months and repeat exercise testing showed the ectopic focus to have resolved. He returned to full competition.

supraventricular premature beats. Depending on their proximity to the previous conducted beat, they may be associated with a palpable pulse deficit. Isolated cardiac contractions are noted to follow too early in an otherwise normal rhythm and are usually followed by an obvious pause that might help to distinguish them from atrial premature contractions. During ventricular tachycardia, a fast regular rhythm will be noted by auscultation.

Special examination

A definitive diagnosis and the origin of the ectopic complexes can be determined by electrocardiography. When the complexes are ventricular in origin, one or more premature complexes with normal or abnormal QRS morphology will break the regular cardiac rhythm. Although QRS morphology may vary, these complexes are always dissociated from normal sinus activity. The sinus node continues to fire at its normal rate, since the atria are electrically isolated from the ventricles and the site of ectopic activity (Fig. 33.13A, 33.14). If the premature beat originates in the ventricular myocardium it will have a wide and bizarre configuration, since it will not be conducted using the normal His–Purkinje system (Fig. 33.13A). By contrast, if it arises from the atrioventricular junctional tissue, or from high up in the His–Purkinje system, the QRS complex may be similar in configuration to the normal sinus beats (Fig. 33.14). In this case, the premature impulse is still conducted through the ventricle using normal conduction pathways and therefore is neither altered in shape, nor abnormally prolonged.

Other tests In all cases of persistent ventricular ectopic activity in horses, thorough evaluation of electrolyte status and assessment of other body systems should precede expensive specialized cardiac examinations.

Laboratory determination of plasma or serum concentrations of cardiac troponin I and the isoenzymes of lactate dehydrogenase may be useful to assess active myocardial necrosis and inflammation.

Echocardiography is also used to rule out cardiac chamber enlargement and abnormal wall motion suggestive of previous myocardial damage. The results of all these examinations may be unremarkable or equivocal.

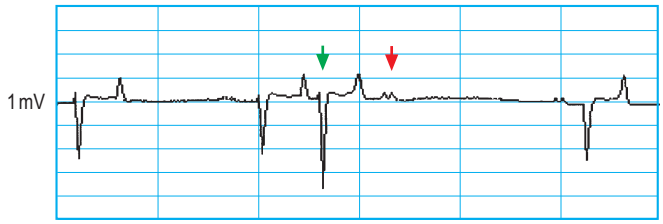


Fig. 33.14
Junctional ventricular ectopic beats in a horse presented with poor performance. The normal sinus rhythm is broken by a premature QRS complex with similar morphology to the normal sinus beats. The premature beat (green arrow) is followed immediately by a P wave (red arrow). As the ventricle is still refractory, the P wave does not result in a QRS complex, but normal sinus rhythm is not interrupted. This AV dissociation is a hallmark of ventricular prematurity. Although the premature complex is not noticeably wider than the sinus beats, it is still ventricular in origin. Its configuration suggests that it originates from the AV junctional, or His–Purkinje system, and has been conducted using the normal conduction pathways. Note that the T wave preceding the ectopic beat is exactly the same as the other sinus T waves, so that an ectopic P′ wave could not have been hidden within it (compare with Fig. 33.11). (ECG courtesy of Mr Charlie Smith MRCVS, Greenwood Ellis & Ptners, Newmarket, UK.)

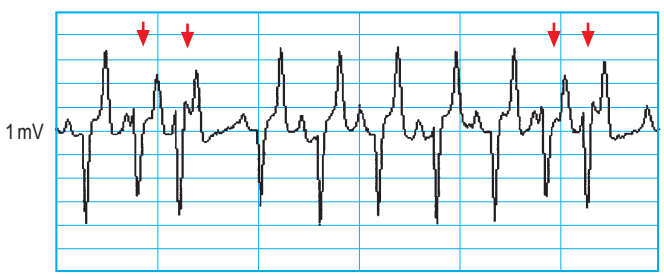


Fig. 33.15
The difficulty of interpretation of postexercise ventricular ectopy is illustrated by the trace recorded from a Thoroughbred race horse during recovery from work at home. The horse worked only at three-quarters pace. This rhythm shows ventricular ectopic beats occurring in pairs or couplets (red arrows). Couplets occur after the first and the eighth beats and were frequent for 2 minutes after exercise. In this case the abnormal complexes are not unduly wider than the normal sinus beats, indicating a junctional origin. This finding is not uncommon in horses. A definite diagnosis of a ventricular origin is possible however, because there is clear evidence of AV dissociation. Note that the first abnormal complex appears too close to its preceding P wave, that in turn has followed the P wave of the normal beat after an appropriate time. The third normal sinus P wave in each case is buried in the ST segment between the coupled ectopic beats. This recording was taken from an 8-year-old National Hunt horse rated in the top 10% of National Hunt racehorses in the UK. The trace was recorded 2 weeks after the horse had won a £13 000 race and 1 week before finishing second in a £17 000 race. The ECG was taken during normal work at home on a 'slow' day. There was no history of poor performance. The horse lost his place in the second race after jumping badly. There was no evidence of cardiorespiratory, systemic disease nor poor athletic performance in this individual.

Treatment

Therapeutic aim

The therapeutic aims are to treat the underlying disease process, restore normal electrolyte and acid–base status, return the heart to normal sinus rhythm if the ventricular rhythm disturbance is life threatening, and abolish abnormal ventricular automaticity.

Therapy

It is a general rule that arrhythmia should always be considered in the context of the patient's concurrent disease. Premature systoles are usually associated with hypoxia, myocardial disease, electrolyte and metabolic disturbances, elevated sympathetic tone, fever, and toxemia. Therefore the first therapeutic aim is to treat any of the predisposing disorders rather than the arrhythmia per se.

Treatment of a ventricular rhythm disturbance with antiarrhythmic agents is only warranted when there is obvious decrement to cardiac function as a result of the abnormal rhythm, or if the rhythm is likely to degenerate into a more sinister life-threatening arrhythmia (ventricular fibrillation). This scenario is most likely to occur during general anesthesia, the postoperative period, or during generalized sickness. The Class 1B, fast sodium channel blocker lidocaine is generally accepted to be the drug of choice for the treatment and management of ventricular arrhythmia in this context.[59]

Specific antiarrhythmic treatment for ventricular ectopic beats in performance horses is usually not indicated, as they are too infrequent to significantly affect cardiac output at rest. However ventricular ectopic beats may be the only abnormal finding in horses presented for poor or loss of performance when their significance is much more perplexing. In most cases the ectopic beats do not occur with sufficient frequency during exercise to significantly compromise cardiac output (Fig. 33.13), yet despite extensive investigations, no other cause of poor performance can be established. It seems possible that increased ventricular automaticity reflects myocardial cellular damage or is a marker of subtle damage to other elements of the oxygen transfer chain that in themselves are responsible for reduced aerobic capacity and performance limitation. The precise nature of the insult, or its etiology, is unknown and further studies of affected horses are clearly required. However, clinical experience and anecdotal evidence suggest that a clinical syndrome of poor performance associated with ventricular ectopy and reduced heart rate recovery following fast exercise exists in Thoroughbred race horses in the UK. Usually biochemical markers of myocardial damage (isoenzymes of lactate dehydrogenase or cardiac troponin I) are not significantly elevated at the time horses are presented. There is usually no specific indication to treat the arrhythmia, so treatment is usually empiric including rest with, or without, steroid therapy section (see 'Therapy' in 'Supraventricular premature systoles').

Prognosis

The prognosis for ventricular prematurity and ventricular arrhythmia is dependent upon the severity of the underlying disease. When the arrhythmia is associated with laboratory or echocardiographic evidence of myocarditis, the prognosis is guarded/poor, although a percentage of affected animals will return to their previous athletic performance following rest and/or steroid therapy.

Ventricular ectopic beats that occur only in recovery from fast exercise are usually of no significance (Fig. 33.15).

Etiology and pathophysiology

Specific information regarding the etiology of ventricular ectopic beats in horses is lacking, but based on data from other species, increased automaticity of ventricular myocytes is associated with cardiac disease resulting in ventricular dilation, stretch, and hypoxia. In the absence of primary cardiac pathology, electrolyte abnormalities, hypoxia, toxins and alterations in acid–base status can provide the physiologic substrates for increased myocyte and pacemaker irritability and invoke re-entry.[60]

It has been suggested that isolated ventricular ectopic beats emanate from ischemic foci that provide the physiologic substrates for increased ventricular automaticity during myocyte death. There is circumstantial evidence to support this hypothesis, as areas of focal fibrosis are common in the equine myocardium at post-mortem examination.[53–55] The precise etiology of these lesions is unknown, although small coronary artery occlusion by arterial atherosclerosis has been proposed as a possible underlying cause.[55,61] Canley & McCullogh[55] demonstrated a significant association between the occurrence of proximal aortic *Strongylus vulgaris* lesions and the presence of focal ischemic lesions in the myocardium. They hypothesized that this association was not the result of direct larval damage to the heart but was caused by microembolization from the parasitic lesions in the proximal aorta that caused myocardial obstructive arteriosclerosis. The role of myocardial cell death and ischemia in the etiology of ventricular rhythm disturbances in horses is supported by case reports by Traub-Dargatz and colleagues in 1994 and Machida and colleagues (in 1992). These workers identified areas of myocytolyis and replacement fibrosis in the ventricular myocardium of horses after fatal ventricular dysrhythmias.[62,63]

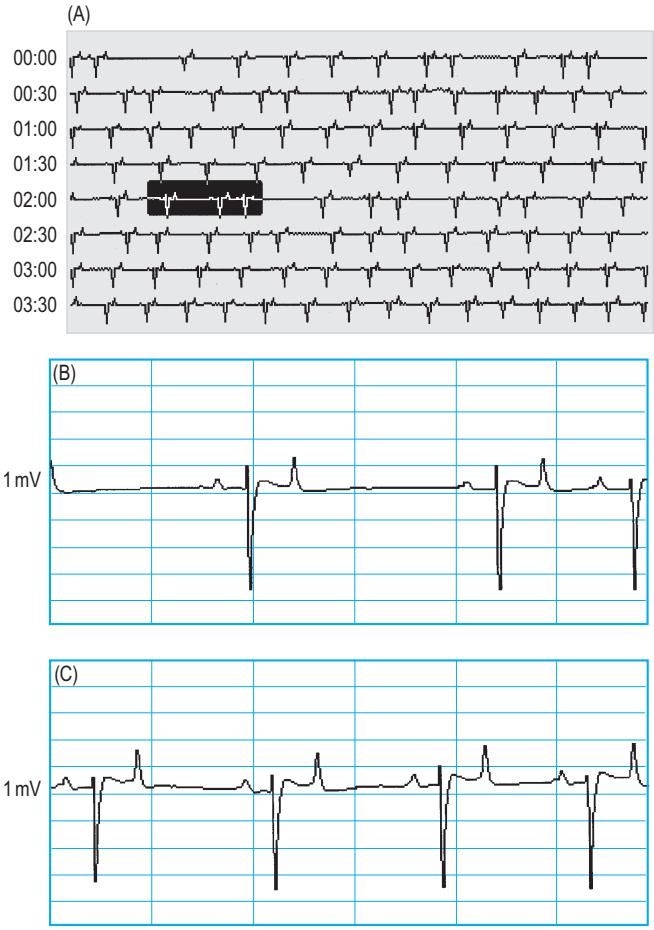


Fig. 33.16
(A) Sustained base apex ECG recording at rest in a 2-year-old colt presented for poor performance. Atrial fibrillation was suspected during cardiac auscultation. The summary trace shows that the arrhythmia is caused by apparent variations in sinus firing rate (sinus arrhythmia) and sinus block when there is complete absence of sinus activity for at least one R–R interval. (B) Expansion of the ECG trace confirms the presence of atrial activity P waves preceding each QRS complex. (C) Same horse as in B. Excitement or exercise rapidly restored the rhythm to normal. Heart rate and rhythm during fast exercise were also normal. Treadmill exercise testing revealed the colt to have dynamic airflow obstruction caused by dorsal displacement of the soft palate.

Bradydysrhythmias

- These include sinus bradycardia and arrest (Fig. 33.16), second (Fig. 33.17) and third degree atrioventricular (AV) block (Fig. 33.18).
- All these rhythms, except third degree atrioventricular block, are also normal findings in athletic horses, reflecting high resting parasympathetic tone.
- When pathologic, they are characterized by an inappropriately low heart rate and blunted chronotropic responses to exercise, or sympathomimetic agents (atropine).
- Third degree AV block is rarely diagnosed in athletic horses, but when present it always affects performance and carries a guarded prognosis.

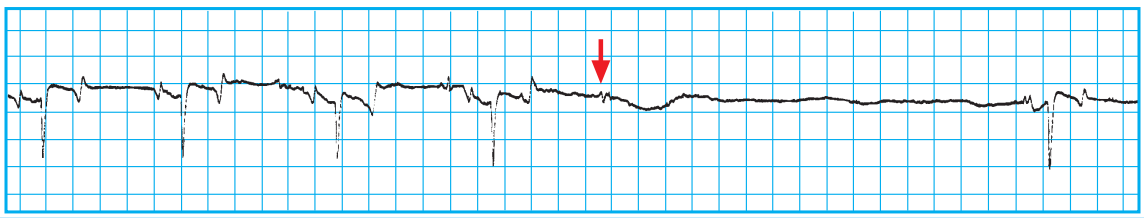


Fig. 33.17
Sinus arrest and second degree block in a 14-year-old endurance horse. One nonconducted P wave (red arrow) is visible during the long pause and is followed by complete sinus arrest. There is a total absence of ventricular escape activity. The clinical history that follows is fairly typical. The pony initially presented with traumatic uveitis. Two weeks later she was found with a severely swollen carpus and damage to buckets in the loose box. One week later the pony was observed to collapse by her owner. Holter for 24 hours monitoring showed maximum pauses of 10 seconds, but as is frustratingly common in these cases, no collapse occurred during the monitoring period. The pony responded to oral clenbuterol therapy and after a period of 6 months rest, returned to ridden work. The response to treatment in older animals may be less impressive, possibly because the underlying pathology is advanced disease of the conduction tissues.

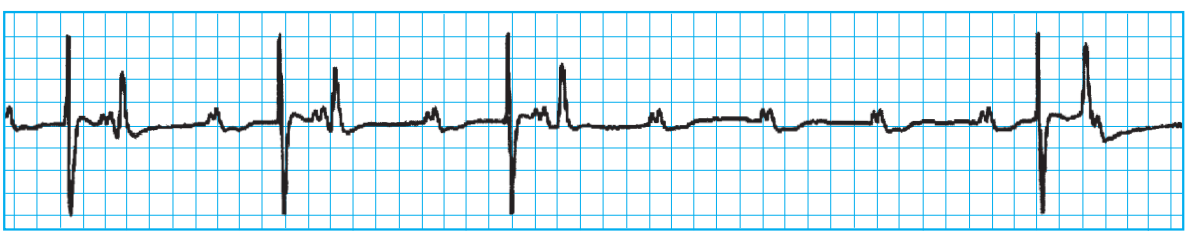


Fig. 33.18
Third degree atrioventricular block in a 12-year-old Thoroughbred. There is complete AV dissociation or third degree AV block. Bifid P waves occur at a rapid rate and can be visualized within the ST segment of the QRS complexes. In this case the QRS complexes are not regular, but their rate is slow. They are junctional ventricular escape complexes. The mare had a variety of atrial arrhythmias over a 24-hour period including third degree AV block. She presented acutely after multiple episodes of collapse in a single day. The referring veterinary surgeon administered antibiotics and corticosteroids. Without further treatment the mare reverted to normal sinus rhythm within 72 hours. ECG courtesy of Miss Constance Fintl MRCVS (Dick Vet, Edinburgh).

Recognition

History

The usual presenting signs for horses with significant bradydysrrhythmias include syncope, ataxia, exercise intolerance, and collapse.

Significant cardiac disease can usually be ruled out in a horse with a very low resting heart rate or marked arrhythmia at rest, if excitement or exercise restore rate and rhythm to normal.

It is common for a marked arrhythmia to be noticed within a minute of cardiac slowing after fast exercise in athletic horses. This arrhythmia is a normal manifestation of increasing parasympathetic influence and usually occurs when heart rate falls to 130–150 beats/min. When electrocardiographic examination is performed, the arrhythmia is usually a marked sinus arrhythmia and is thus described as 'transient post-exercise sinus arrhythmia' (Fig. 33.19). The arrhythmia is usually short-lived, but can cause alarm for an inexperienced examiner. Postexercise sinus arrhythmia is another normal arrhythmia, found commonly in athletic horses, that does not indicate cardiac pathology.

Physical examination

In horses affected with significant bradydysrhythmia, auscultation usually reveals an inappropriately slow resting heart rate that may be regular. Resting heart rate may be less than 20 beats/min.

Occasionally horses present with evidence of unexplained trauma when collapse occurs at night, or is not observed.

During severe second degree AV block, one or more isolated fourth (atrial) heart sounds, S_4, will be audible during the long diastolic pauses. In sinus block, S_4 will be absent and the diastolic pauses silent. In third degree AV block, S_4 may be audible in a regular fast rhythm underlying the predominant slow ventricular rhythm. In third degree AV block pronounced waves, 'cannon a waves', that travel rapidly all the way up the jugular vein are also obvious.

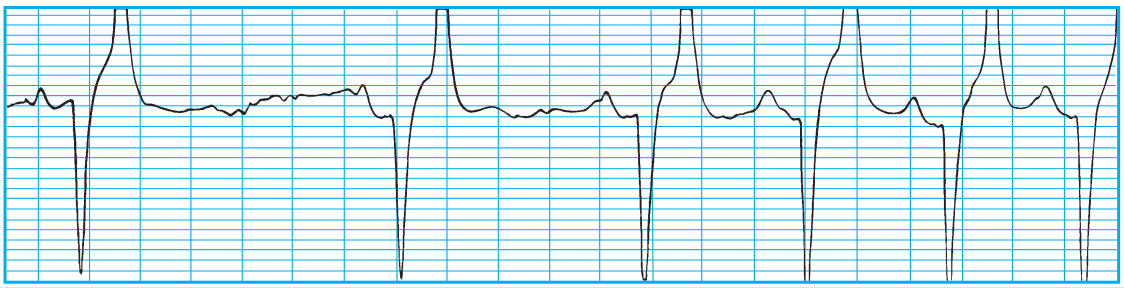


Fig. 33.19
Electrocardiographic recording taken from a Thoroughbred race horse, 20 seconds after completion of exercise to fatigue. The trace illustrates transient postexercise sinus arrhythmia. There is some baseline interference as the horse is walking and blowing heavily, but positive P waves are visible before each QRS complex. The rhythm is noticeably irregular representing sinus arrhythmia. This is a common finding in athletic horses following exercise.

Increased atrial pressure causes the augmented waves as the right atrium contracts against the closed tricuspid valve.

Special tests

Electrocardiography will provide a definitive diagnosis (Figs 33.16–33.19). Ideally 24-hour ambulatory ECG monitoring (Holter) should be employed for a definitive diagnosis in cases of collapse. Affected cases often have blunted chronotropic responses to both exercise and parasympatholytic agents, but these tests are frequently difficult to interpret.

Treatment

Therapeutic aims

To restore normal sinus rhythm, normal heart rate at rest, and to normalize heart rate response to exercise.

Therapy

Pathologic sinus bradycardia is found most commonly in elderly performance horses. Occasionally horses affected with profound second degree AV block and sinus bradycardia respond favorably to daily oral administration of β_2-adrenoreceptor agonist drugs, e.g. clenbuterol.

Third degree AV block is very rare in horses, and is rarely amenable to medical treatment when it occurs in older animals. In most species third degree AV block is permanent and transvenous pacing is required for permanent relief of clinical signs. Dual chamber pacing has been described in horses.[64,65] The technique has also been used successfully to treat third degree AV block in a horse that subsequently returned to competition.[16]

In contrast to other species, in younger and middle-aged horses, third degree AV block can be transient and normal sinus activity can resume after variable periods of time elapse. It seems likely that in these cases, a reversible inflammatory process causes transient complete block at the AV junction. Based on this unproven hypothesis, the use of corticosteroid drugs is sometimes recommended for these individuals.[33]

Prognosis

In all cases of symptomatic bradyarrhythmia, the prognosis is guarded to poor. In younger horses with acute onset of clinical signs the condition is sometimes reversible and affected animals can return to previous levels of activity. Transvenous pacing carries a fair prognosis for return to athletic performance, but as in all species, the technique can be associated with complications.[66]

Etiology and pathophysiology

In the resting horse most bradydysrhythmias are of no clinical significance, as within limits cardiac output can be maintained by an increase in stroke volume. The trained horse has an increased resting stroke volume and therefore the resting heart rate is usually low. During exercise, however, there is an increased requirement for muscle perfusion, systemic vascular resistance falls and cardiac output must therefore increase in order to maintain arterial blood pressure. As increasing heart rate is the major cause of the increased cardiac output, if low heart rate is maintained during exercise, cardiac output will be inadequate and performance will be limited.

Although second degree AV block is the commonest manifestation of high vagal tone in horses, other bizarre sinus arrhythmias, including sinus block, can occasionally be encountered in normal individuals (Fig. 33.16). Normal heart rate responses to exercise and excitement rule out significant pathology in these individuals.

Pathologic sinus, second and third degree AV block indicates total or partial block in conduction in the sinus, atria, or AV node. This clearly results from cardiac lesions, thought to be associated with transient or permanent inflammation or degeneration and fibrosis of the intracardiac conduction system.

Epidemiology

Profound sinus bradycardia, pathologic second degree and third degree AV block occur only rarely in athletic horses, being much more common in aged animals. Sporadically the condition can be seen in younger horses and is usually associated with inflammation of the conduction system and/ or myocardium.

Cardiac murmurs

General principles

This section will cover the basic approach to heart murmurs in athletic horses, their diagnosis, prognosis, and assessment of their significance.

A number of murmurs occur in normal horses that are not associated with underlying cardiac disease. These murmurs have been variously called, **functional**, **physiologic**, **innocent** or **flow** murmurs. These murmurs are common in athletic horses of all breeds (Table 33.1).

Murmurs associated with mitral and tricuspid valve regurgitation are also commonly detected in performance horses (Table 33.1, 33.2), yet any influence on their athletic performance remains controversial. Although there is no doubt that severe regurgitation and resultant cardiac failure cause obvious performance decrements,[67,68] the effect of mild and moderate regurgitant murmurs is less certain.[1]

Recent data[3] have shown that AV valve regurgitation increases after 6 months race training in Thoroughbreds (Table 33.3). It seems likely that the eccentric cardiac hypertrophy and increased blood volume that accompany athletic training[69] result in secondary stretch of the valve annulus and increased regurgitation.

Endocarditis is a rare condition causing valvular regurgitation and cardiac murmurs. Blood-borne bacteria colonize the valves (usually mitral and aortic) and the resulting inflammation and deformation leads to chronic regurgitation. *Pasteurella*, *Actinobacillus* and *Streptococcus* species are most likely to be causative in horses,[70] although other agents have also been reported.[71–73] Prognosis is poor, even if the horse survives the early acute phase and bacterial cure is achieved; there may be sufficient damage to the cardiac valves to preclude return to previous performance, or cause death from heart failure.[74]

Table 33.1 Prevalence of cardiac murmurs by auscultation in 2-year-old Thoroughbreds in training

Murmur	% of population affected		
	Young & Wood[3]	Kriz et al.[1]	Patteson & Cripps[2]
Mitral regurgitation	21	3.8	1.2
Tricuspid regurgitation	25.5	27.4	4.7
Aortic regurgitation	2	0.5	0
Diastolic flow	65	33	44
Systolic ejection	34	57.4	55
No murmurs	11	18.9	24.7

Note: Patteson & Cripps defined mitral and tricuspid valve regurgitation as pansystolic murmurs only. As it is now generally accepted that murmurs of mitral and tricuspid valve prolapse may not extend throughout systole, this may explain the difference in prevalences of atrioventricular valve regurgitation. Patteson & Cripps also noted a much higher prevalence of systolic murmurs on the left and right hemithorax, suggesting that some early systolic murmurs of mitral and tricuspid valve prolapse were classified as systolic ejection murmurs

Table 33.2 Prevalence of cardiac murmurs by auscultation and color flow Doppler echocardiography in older race-fit National Hunt steeplechase horses

Regurgitaton	% Prevalence by auscultation		% Prevalence by Doppler
	Patteson & Cripps[2]	Young & Wood[4]	Young & Wood[4]
Mitral	5.6	22	58
Tricuspid	16.4	47	88
Aortic	2.2	4	62

Physiological murmurs

Systolic ejection murmurs

Systolic ejection murmurs are commonly heard over the pulmonary and aortic valves in normal horses. Usually the

Table 33.3 Prevalence of murmurs and regurgitation by color flow Doppler echocardiography at the aortic mitral and tricuspid valves in fifty 2-year-old Thoroughbreds before and after 6 months' race training.[3]

Regurgitation	% Prevalence before training		% Prevalence after training	
	Auscultation	Doppler	Auscultation	Doppler
Mitral	7.3	25	21	35
Tricuspid	12.7	57	25.5	66
Aortic	0	18	2	44

murmur is early–mid systolic, crescendo–decrescendo in character and variable in intensity. Usually these murmurs are heard best over the left hemithorax, cranial over the heart base when S_2 becomes accentuated. Submaximal exercise often increases the intensity of these murmurs. In some horses, it can be difficult to separate a functional ejection murmur from a murmur of mitral regurgitation, but an ejection murmur, unlike the murmur of mitral regurgitation, should end before S_2. Ejection murmurs will disappear at maximal heart rates, but the amount of exercise needed to achieve this varies according to the fitness of the horse. Ejection murmurs are equally prevalent in other conditions that provoke high sympathetic tone, e.g. colic, anemia, sepsis, pain, or fever. A major feature of all physiologic murmurs is their variability with changes in heart rate and or excitement.

Functional diastolic murmurs: diastolic filling murmurs

Most physiologic filling murmurs occur either in early diastole (before S_3) or are presystolic (after S_4 but before S_1). The **presystolic** murmurs are associated with vibrations in the atria, and are usually low pitched and rumbling. The murmur can be heard on either side of the chest. The **early diastolic murmurs**, closely following S_2 are soft and blowing and are believed to be associated with rapid ventricular filling. They usually end at S_3 and are heard from the left and right hemithorax. An early diastolic musical murmur is not infrequently heard in conditioned horses. This murmur is very variable, and is usually heard best from the mitral or tricuspid valve area. The murmur follows S_2 by a short interval and ends abruptly at S_3. It is commonly known as a '2-year-old squeak,' although it is present in athletic horses of all ages. Diastolic murmurs are also very variable depending on heart rate and excitement.

Murmurs associated with cardiac dysfunction

Tricuspid regurgitation

Recognition

History

These murmurs are usually detected incidentally during cardiac auscultation. Tricuspid regurgitation is unlikely to be a primary cause of poor performance or heart failure.

A murmur of tricuspid regurgitation is often detected in horses presenting with heart failure due to mitral valve insufficiency. Severe pulmonary hypertension results in secondary dilation of the right ventricle and tricuspid annulus and causes tricuspid valve regurgitation.

Physical examination

The murmur of tricuspid regurgitation (TR) is a systolic murmur heard over the right side of the thorax. It is usually soft and band shaped and extends throughout systole and may incorporate S_1 and S_2. Occasionally tricuspid regurgitation is crescendo in character and may not occupy all of systole, in this case it is usually described as 'tricuspid valve prolapse.'

Special examination

Color flow Doppler echocardiography (Fig. 33.20) will confirm the presence of tricuspid regurgitation. The use of pulsed or continuous wave Doppler techniques allows an estimate of pulmonary artery pressure to be obtained from the modified Bernoulli equation.[75] Two-dimensional and M-mode echocardiography allow cardiac chamber size to be visually assessed. The nonsymmetric shape of the right ventricle and atrium mean that it is very difficult to obtain repeatable and meaningful measurements of chamber size[76] and it is probably advisable to visually appraise the two chambers relative to the left ventricle. The tricuspid valve of affected horses invariably appears morphologically normal, but may prolapse into the right atrium during systole (Fig. 33.21).

Treatment

There is no specific treatment available.

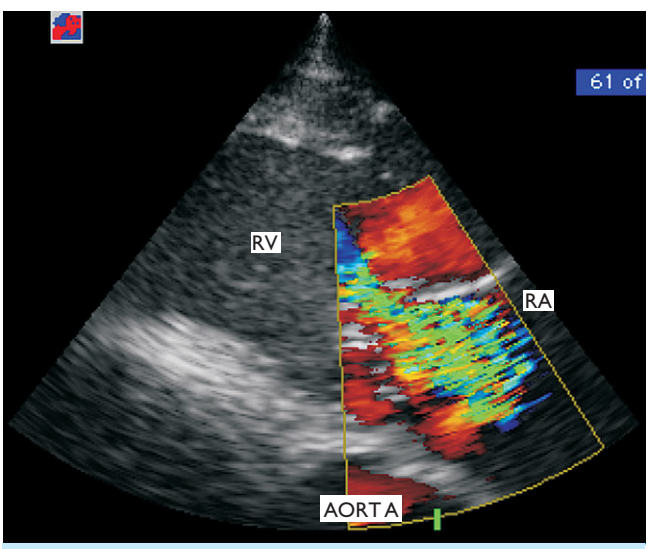


Fig. 33.20
Color flow Doppler study of tricuspid valve regurgitation in an 8-year-old race horse. A grade 4/6 systolic murmur on the right hemithorax was detected incidentally at a veterinary examination. The horse was a successful handicap steeplechaser with no history of poor race performance. A green jet of blood can be seen entering the right atrium through the closed tricuspid valve. RA, right atrium; RV, right ventricle.

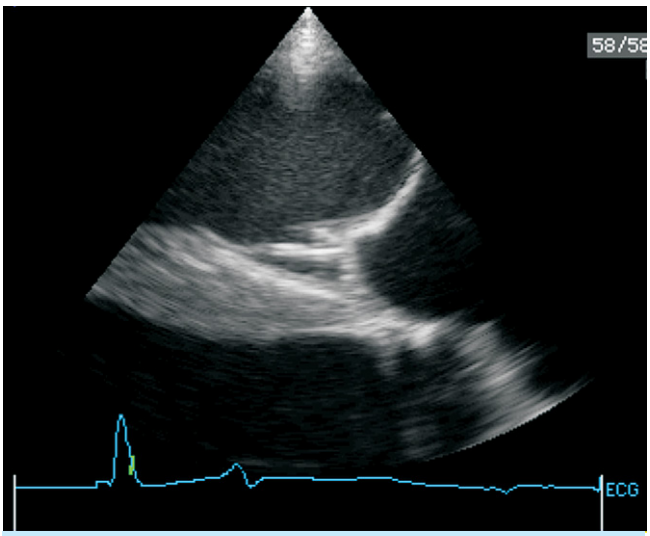


Fig. 33.21
Two-dimensional image of the tricuspid valve of the horse shown in Fig. 33.20. Abnormal systolic valve motion was visible in real time. The anterior valve leaflet buckled backwards into the right atrium during systole. However, there is no structural valve abnormality. Abnormal systolic movement is the most frequently encountered echocardiographic feature of tricuspid valve dysfunction in performance horses. Unfortunately due to their geometry, right atrial and ventricular echocardiographic measurements are not very repeatable in horses, making assessment of volume overload of the right heart very difficult. It is rare to see convincing evidence of right heart enlargement due to primary tricuspid valve dysfunction in performance horses.

Prognosis

Echocardiographic follow-up of an increasing number of horses affected with tricuspid valve regurgitation indicates that the valve dysfunction rarely progresses to cause clinical signs of heart disease. The condition does not seem to predispose to rupture of chordae tendinae, nor readily result in congestive heart failure. Equally it is unlikely that low or moderate grade tricuspid regurgitation as an isolated finding will cause performance-related problems in the vast majority of horses.

While tricuspid regurgitation is likely not normal, it is certainly very common, and in horses without evidence of valve lesions the condition does not render the horse unfit to ride and carries an excellent prognosis. Although theoretically right atrial enlargement as a result of severe tricuspid regurgitation should increase the risk of development of AF, in the author's experience primary tricuspid valve disease is a rare underlying cause of AF and congestive heart failure. It is important to note that AF is common in large athletic horses, a group in which the prevalence of audible tricuspid regurgitation is high (Table 33.2). This obvious association does not necessarily mean that the two conditions are necessarily related, indeed it seems unlikely from clinical experience, but a causative influence of tricuspid regurgitation on AF cannot be ruled out based on currently available data.

Etiology and pathophysiology

Tricuspid valve regurgitation is the commonest valve insufficiency in athletic horses.[1–4] Tricuspid regurgitation is also increased after athletic training,[3] suggesting that training-induced eccentric hypertrophy is important in the pathogenesis of the condition. These data are supported by that of Pollak and colleagues,[77] who found that tricuspid regurgitation was more common in elite female athletes than in sedentary women. Else & Holmes[53,54] found evidence of fibrous thickening and distortion of tricuspid valve leaflets and similar changes in the chordae tendinae. These authors also noted a smaller prevalence of hemorrhagic lesions on the right ventricular first order chordae and suggested that they might be precursors to chordae rupture, although their precise etiology was not established. Interestingly, the prevalence of tricuspid valve lesions in the large post-mortem survey of Else & Holmes was much lower than the prevalence of murmurs of tricuspid valve regurgitation and regurgitation detected by Doppler techniques in athletic horses.[1–4] These data support the growing suspicion that in many athletic horses, tricuspid regurgitation is physiologic, rather than caused directly by valve disease.

Secondary dilation of the tricuspid valve annulus resulting in tricuspid regurgitation also occurs during severe pulmonary hypertension.[51] Increased pressure in the pulmonary circulation increases afterload on the right heart and stimulates eccentric and concentric right ventricular hypertrophy. Deformation of the tricuspid valve apparatus then results in tricuspid valve regurgitation. Pulmonary hypertension is associated most commonly with left-sided cardiac failure and more rarely with pulmonary thromboembolic and hypoxic pulmonary diseases.

Epidemiology

Our recent work[4] shows that isolated TR is the most commonly encountered murmur in National Hunt type horses, occurring in almost 50% of mature horses at full race fitness (Table 33.2). The prevalence is less in flat racing Thoroughbreds based on our data[3] and that of others.[1,2] Young & Wood noted a relationship between body weight and the presence of tricuspid regurgitation in flat racing Thoroughbreds.[3]

Mitral regurgitation (Figs 33.22, 33.23)

Recognition

History

The condition is usually detected incidentally during cardiac auscultation.

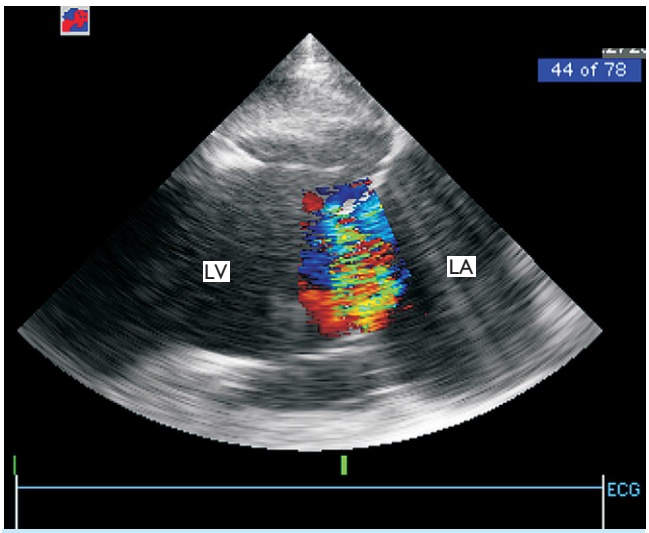


Fig. 33.22
Color flow Doppler image showing moderate to severe mitral valve regurgitation in a 6-year-old Thoroughbred race horse. The horse had a grade 5/6 murmur over the apex beat area of the left hemithorax. A grade 3/6 murmur of tricuspid regurgitation was also audible at the right hemithorax. The murmurs were detected incidentally during epidemiologic studies on the horse's training yard. Despite the moderate to severe regurgitation present over 2 years of the study, the horse had won races and been moderately successful as a handicap steeplechaser. He had however never really lived up to the owner and trainer's initial expectations and had the reputation of being 'ungenuine'. In the UK, it is not uncommon for this description to be applied to racing Thoroughbreds, later found to be affected with moderate to severe AV valve regurgitation. LA, left atrium; LV, left ventricle.

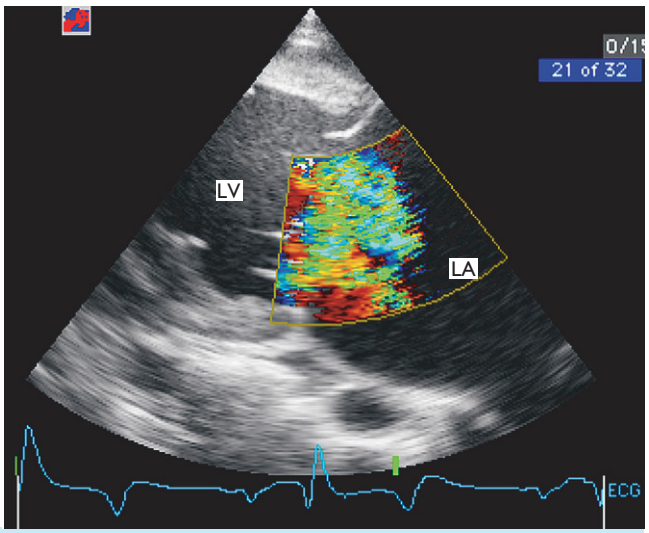


Fig. 33.23
Color flow Doppler study showing severe mitral regurgitation in a 2-year-old filly in training. There is a large green/blue regurgitant jet entering a grossly dilated left atrium. The filly presented with recurrent pyrexia due to repeated bouts of respiratory infection. A grade 5/6 left-sided cardiac murmur and elevated heart rate (58 beats/min) were noted on auscultation. Despite being in cardiac failure, poor performance was not noted by the trainer, as the filly had only just begun canter work. As in this case, coughing usually arises due to secondary bacterial infection, rather than primarily from the interstitial and alveolar edema present concurrently. LA, left atrium; LV, left ventricle.

The murmur of mitral regurgitation is often detected in horses that present in heart failure, as severe mitral valve insufficiency is the commonest cause of the heart failure syndrome in horses.[78]

Physical examination

The murmur of mitral regurgitation is loudest on the left hemithorax, in the area of the apex beat. It can radiate forwards towards the heart base, which may cause confusion, if there is a coexistent functional ejection murmur. In common with tricuspid regurgitation, the murmur is usually band shaped and pansystolic. It should not vary with exercise. If mitral regurgitation is severe, resulting in the retrograde flow of large quantities of blood into the left atrium, S_3 may be more pronounced.

Occasionally mitral regurgitation is crescendo in character and may be musical or vibrant. In this case the murmur may not occupy all of systole. The presence and intensity of the murmur may also be variable. When the murmur has these characteristics it is usually classified as 'mitral valve prolapse.'

Rupture of a mitral chord (Fig. 33.23) or severe longstanding mitral regurgitation usually results in acute left-sided heart failure and a plethora of associated signs:

- pulmonary edema and increased respiratory rate (Fig. 33.24)
- increased heart rate
- rapid acute onset cardiac cachexia (Fig. 33.25)
- poor peripheral pulses (Fig. 33.26) and cold extremities
- the murmur associated with such catastrophic valve dysfunction might be expected to be very loud, but this is not invariably the case; the murmur is usually associated with a precordial thrill, and will invariably radiate over very large areas of the chest wall
- severe left atrial enlargement (Figs 33.7, 33.10B), which not uncommonly results in the development of AF (Fig. 33.6).

Although heart failure almost always results from primary mitral valve dysfunction, horses not infrequently present with biventricular failure, the signs of which include:

- peripheral edema (Figs 33.27, 33.28)
- jugular engorgement
- development of a loud right-sided murmur of tricuspid regurgitation (Fig. 33.20).

Special examination

Color flow Doppler echocardiography will confirm the presence of mitral regurgitation (Figs 33.22, 33.23, 33.29). The

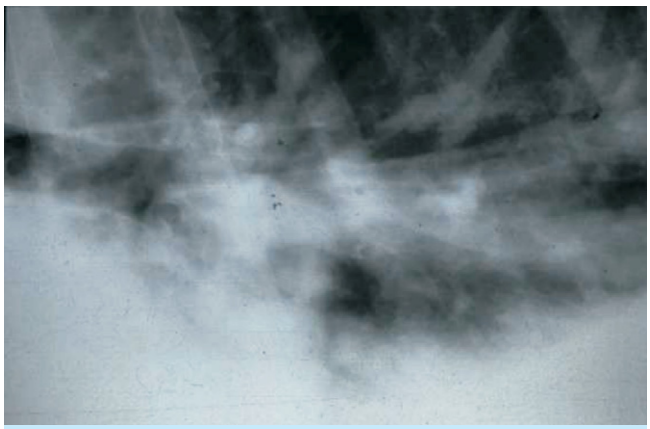


Fig. 33.24
Thoracic radiograph from a horse with acute rupture of a major mitral chordae tendinae. There is an alveolar and interstitial pattern most marked in the cardiophrenic angle in this lateral radiograph. Coughing is not a feature usually noted with pulmonary edema in horses, unless there is secondary bacterial infection, which occurs not infrequently. Alveolar and interstitial edema occurs as a consequence of marked elevations in left atrial pressure, from left-sided heart failure. Thoracic auscultation is frequently disappointing in these patients even though pulmonary edema is known to be present. The increased respiratory rate that always accompanies severe alveolar edema is the most reliable method for detecting pulmonary congestion in horses. Occasionally white (occasionally blood-tinged) frothy edema fluid may appear at the nostrils.

use of pulsed or continuous wave Doppler techniques allows an estimate of transmitral pressure gradient to be obtained and thence assessment of left ventricular systolic function. Two-dimensional and M-mode echocardiography are used to evaluate cardiac chamber size and left ventricular wall motion. In severe mitral regurgitation, there is dilation and septal hypermotility as the volume overloaded left ventricle ejects into the low pressure left atrium. The left atrium will be dilated as evidenced by an increase in the ratio of the aortic diameter to that of the left atrium (Fig. 33.10). There may be evidence of pulmonary hypertension and dilation of the main and right pulmonary artery, best assessed by comparison with the diameter of the aorta.

In mild disease, cardiac dimensions will remain within normal range and often the valve appears morphologically normal. Valve thickening or noticeably abnormal valve motion may be observed in more severe cases. Occasionally a flail valve leaflet may be visible after mitral chordae rupture has occurred.

In horses with mild–moderate mitral regurgitation and without evidence of heart failure, ECG examination during appropriate exercise is recommended to assess heart rate response to exercise. This is especially important when the cardiac murmur is implicated in poor performance or is detected at a pre-purchase examination.

When there is overt heart failure, thoracic radiography is useful to confirm the presence of the alveolar-interstitial infiltrate characteristic of pulmonary edema.

Treatment

There is no specific treatment for valve regurgitation and in horses with compensated valve dysfunction, no treatment is indicated. When signs of heart failure become evident (Fig. 33.10B) therapy focuses upon control of heart rate (digoxin), reduction of volume overload (diuretics), and reduction of cardiac afterload (angiotensin converting enzyme inhibitors). Once signs of heart failure are present, the horse must be immediately retired from ridden exercise. Aggressive treatment is expensive and palliative only, it will not return the horse to its previous athletic performance. In

Fig. 33.25
Yearling Thoroughbred colt with severe mitral valve regurgitation and atrial fibrillation. Cardiac cachexia or loss of lean body mass is an inevitable consequence of heart failure and occurs in the absence of obvious inappatence. It is often dramatic in onset, occurring within a very short time of cardiac decompensation. It is usually most obvious in the highly muscled areas, e.g. the hindquarters in mature conditioned horses or, as in this case, in the neck and shoulders of young stock.

Fig. 33.26
Palpation of a peripheral pulse provides a 'window' to the heart's function as a pump. It may also provide a clue to the severity of valve lesions that are picked up on auscultation. The facial artery provides a convenient site for examination. If a patient is in heart failure, heart rate will be elevated above the normal expected value for the animal's type and fitness. These patients usually sustain their heart rates between 55 and 80 beats/min dependent on type and severity of disease. Pulse quality reflects the difference between the systolic and diastolic blood pressure. The difference between the two, rather than the magnitude of either, is detected when the pulse is palpated. To obtain an estimate of mean arterial pressure, the amount of digital pressure needed to occlude the pulse can be assessed. Pulse quality can also reflect the severity or type of underlying cardiac disease. A characteristically bounding pulse (i.e. a wide difference between systolic and diastolic pressure) can be indicative of marked aortic insufficiency in older horses, or extracardiac left to right shunts in foals. (Courtesy of Dr LE Young and Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

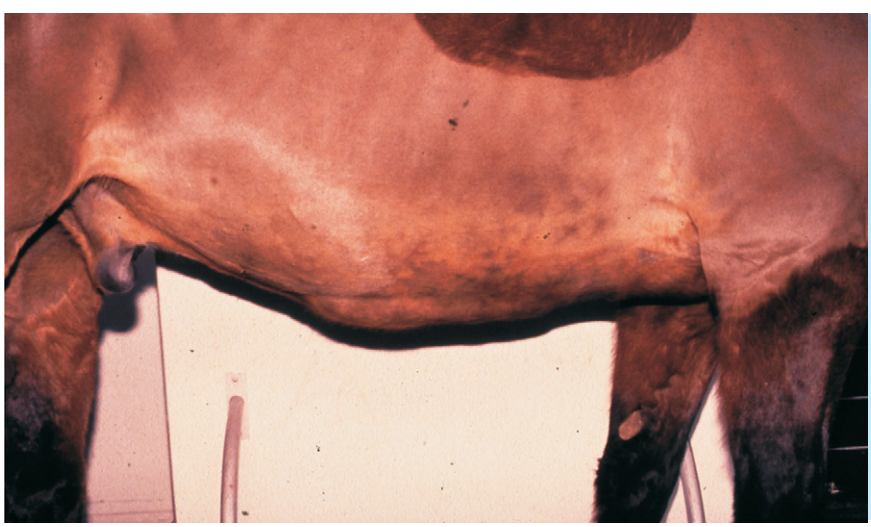


Fig. 33.27
Dependent edema in a 9-year-old hunt horse, 2 weeks after rupture of a mitral chordae tendinae. A plaque of pitting edema is visible in the most dependent area of the ventral abdomen. Occasionally the sheath and brisket are also involved. Although the underlying cause of heart failure in this case was left sided, as is typical, after a variable time, increased pulmonary vascular pressures cause secondary failure of the right ventricle, resulting in systemic congestion. (Courtesy of Dr LE Young and Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

view of the hopeless prognosis, many owners request immediate euthanasia for their horses and as a result treatment is rarely performed.

Prognosis

Mitral valve disease of sufficient severity to cause cardiac failure will have a devastating effect on athletic performance and a very poor prognosis for life. The prognosis for isolated compensated mitral regurgitation remains much less certain. This is because overall the condition is less common than tricuspid valve regurgitation, and although there has been some long-term follow-up of horses with mild to moderately loud mitral valve murmurs, mitral valve disease remains the commonest cause of congestive heart failure in horses. Despite this, the general consensus amongst cardiologists is that, like tricuspid valve dysfunction, provided valve lesions do not accompany the regurgitation, prognosis is usually good.

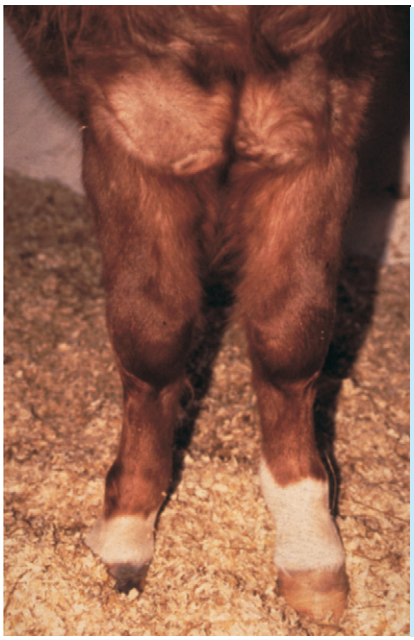


Fig. 33.28
Edema of the lower limbs occurs commonly in horses, but is rarely associated with cardiac disease. This 6-year-old riding pony has end-stage heart failure from a large ventricular septal defect. He has edema of his brisket and the antebrachium, but minimal swelling of his lower limbs. (Courtesy of Dr LE Young and Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

Most investigators agree that isolated low-grade mitral valve regurgitation (Fig. 33.29) should not significantly affect athletic performance in horses engaged in less strenuous disciplines. There is strong suspicion that AV valve dysfunction might reduce maximum aerobic capacity and prevent an individual from realizing their genetically conferred maximal athletic potential, but for most horses, even moderate decreases are unlikely to be noticed by the owner or rider.

Of all murmurs detected, isolated mitral valve regurgitation is most problematic when detected during pre-purchase examinations. Because of the current paucity of follow-up information, there is no definitive solution and ultimately the prospective rider/owner/trainer must make up his or her own mind regarding the suitability of the horse. Most investigators are confident that a horse with low-grade mitral valve regurgitation and a normal resting heart rate is safe to ride, and that its performance is unlikely to be noticeably affected by a small amount of valve dysfunction. Auscultation is useful to monitor the progression of regurgitation over long periods, but in a one-off physical examination, the veterinary surgeon knows nothing about the appearance of the valves, the extent of left atrial or ventricular enlargement, or the previous or subsequent rate of development of the valve dysfunction. Invariably when a moderately loud murmur is detected at a pre-purchase or insurance examination, it is usually advisable to refer the horse for specialist echocardiographic and ECG examinations. In the majority of performance horses, it is unlikely that the murmur has arisen as a result of serious progressive valve lesions, but this can never be guaranteed in the absence of more detailed examinations. In some cases, commercial pressures may dictate that the veterinarian informs the prospective client of the existence of the murmur and is then forced to make an educated guess about its likely impact. In these cases, when heart rate and work history are normal and the murmur is equal to or less than grade 3/6 in intensity, it is unlikely that the murmur will be associated with reduced performance, or be rapidly progressive. Referral to a specialist center for cardiac ultrasound examination is the best approach whenever any doubt exists regarding the origin or significance of a murmur detected during pre-purchase or insurance examination. It is important to note that murmurs of mitral valve regurgitation are rare in yearling Thoroughbreds, though the prevalence of murmurs increases in older horses (Table 33.2). As a result, young animals destined for racing with a confirmed mitral valve murmur should be viewed with great suspicion.

The variable systolic murmurs of mitral valve prolapse are generally considered to carry a good prognosis. In other species, notably dogs and humans, mitral valve prolapse is a precursor of progressive mucinous valvular degeneration

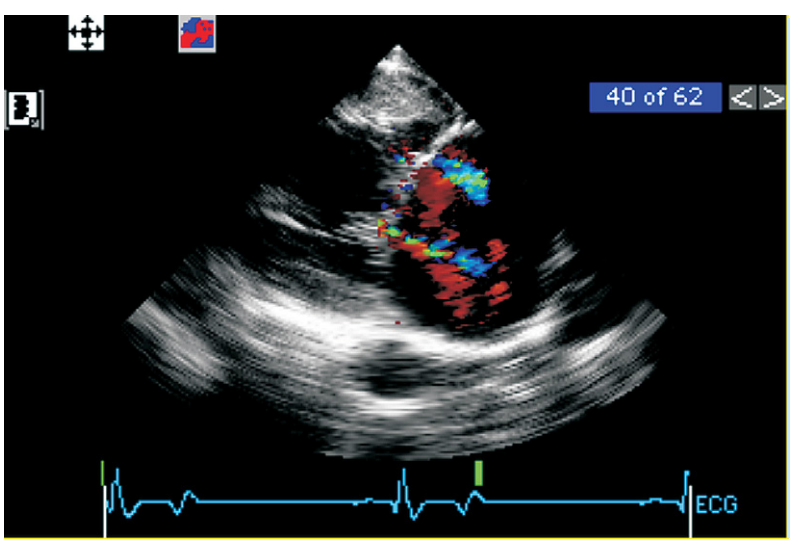


Fig. 33.29
Color flow Doppler echocardiograph obtained from the left hemithorax of a 9-year-old Thoroughbred race horse. The image shows two discrete regurgitant jets entering the left atrium through the closed mitral valve in systole. The horse had a grade 2–3/6 murmur of mitral valve regurgitation. It is not uncommon to visualize more than one regurgitant jet in horses with mitral valve dysfunction. In this case, the jets were small, traveled at high velocity, and occupied only a small area of the left atrium. Left atrial and ventricular size was normal.

and severe mitral valve regurgitation. Similar data is not available for horses, but current opinion suggests that isolated mitral prolapse rarely progresses to cause significant cardiac disease during the career of most performance horses.

Etiology and pathophysiology

During mitral insufficiency, blood is ejected retrograde into the left atrium. For the most part the regurgitant fraction is small and the condition remains well compensated. Only when the regurgitant fraction is large, or increases through progressive valve dysfunction, will forward cardiac output be compromised and volume and pressure overload of the left atrium begin. As a progressively greater proportion of the left ventricular output is ejected into the low-pressure left atrium, progressive dilation of both chambers occurs and stretching of the fibrous annulus further exacerbates mitral valve incompetence. Reduction in arterial blood pressure as forward cardiac output decreases causes activation of neurohumeral reflexes that further accelerate the vicious cycle of the heart failure syndrome; a syndrome that is always terminal. Congestive signs develop when horses with severe mitral valve disease survive low-output left-sided failure for even a short period of time. Increased left atrial pressure causes pulmonary venous congestion and increased afterload to the right ventricle. There is subsequent pressure overload of the right ventricle and dilation of the tricuspid valve annulus so that progressive tricuspid regurgitation develops. Meanwhile low output failure of the left ventricle and pulmonary edema compromise coronary perfusion and oxygenation and worsen the mechanical function of both ventricles.

The recently observed variability of mild mitral valve murmurs with changes in sympathetic tone and exercise can be explained because the mitral valve is an apparatus composed of leaflets, chordae, and papillary muscles, and not simply an inert fibrous structure. Changes in the loading conditions of the heart and papillary muscles and alterations in myocardial function with changing neurohumoral drive probably change leaflet coaptation, thus preventing, reducing or increasing the regurgitation present at the valve.

The mitral valve was the valve most likely to be affected by gross post-mortem changes in the post mortem study of Else & Holmes.[53,54] Microscopic changes included variable fibrosis and infiltration of the superficial valve layers (atrialis and spongiosa) with histiocytes, lymphocytes, and fibrobalsts.[53,54] Occasionally the deeper (fibrosa and ventricularis) layers of the valve were involved and their involvement usually resulted in deformation of the valve cusps. The precise etiology of valvular damage was not established, but the absence of polymorphonucleated cells, except in two animals, led these authors to speculate that an infectious cause was unlikely in the majority of cases. Their speculation is supported by clinical evidence suggesting that bacterial endocarditis occurs only rarely in horses.[70] Rupture of a first order mitral chordae has been repeatedly reported in association with severe mitral regurgitation and heart failure in horses,[79–81] but the precise etiology of the damage to the chordae is yet to be fully explored or explained.

Epidemiology

Recent data show that the prevalence of mitral valve regurgitation in racing Thoroughbreds varies between 3.8 and 21% (Tables 33.1, 33.2). As there is convincing evidence that athletic training increases the prevalence of AV valve regurgitation (mitral and tricuspid) in Thoroughbreds, this relationship might in part explain the difference in prevalence of AV valve regurgitation found by different investigators (Table 33.3). The effect of age on prevalence of AV valve regurgitation has yet to be established, although from our own ongoing epidemiologic studies the prevalence of AV valve murmurs assessed by color flow Doppler and auscultation is much lower in Thoroughbred yearlings than in all other groups. The prevalence of gross mitral valve lesions also increased with age in a large post-mortem study.[53,54]

Ventricular septal defect (Fig. 33.30)

- The ventricular septal defect is the most commonly occurring congenital heart defect in horses. Experience suggests that although the defect can be found in all breeds, it seems especially common in Arabians, Standardbreds and small pony breeds (Welsh Section A and Shetland ponies).
- The condition is not restricted to foals. Because of the huge cardiac reserve of the horse, large lesions are often detected before athletic training commences at insurance or pre-purchase examinations. Indeed this is probably the most frequently encountered clinical scenario.
- The defect can also be associated with other more complex congenital abnormalities (Fig. 33.31), but these cases are rare amongst athletic horses.
- Ventricular septal defects can cause secondary aortic valve insufficiency.

Recognition

History

Loud cardiac murmurs are usually detected during a pre-purchase or insurance examination of a horse without clinical signs. However, when the ventricular septal defect is large, the horse/pony might present in biventricular heart failure or with signs of poor performance. These scenarios are unusual. Occasionally affected horses present with unexpectedly early-onset diastolic murmur of aortic valve insufficiency (see below).

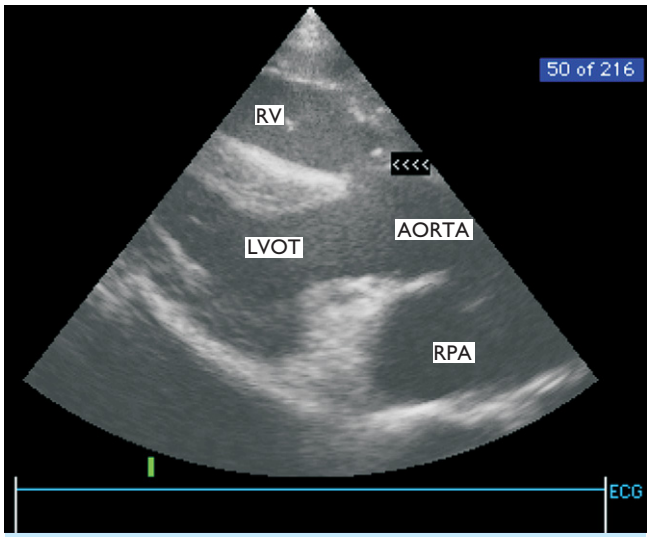


Fig. 33.30
Two-dimensional echocardiograph from the right hemithorax of a yearling Thoroughbred with a grade 5/6 pansystolic murmur with point of maximal intensity on the right side. There is a moderately large ventricular septal defect (labeled <<<<) at the top of the interventricular septum. This image has been optimized to visualize the septal defect so that the right pulmonary artery (RPA) is transected obliquely, rather than in true short axis. Failure to attain standard images of intra- and extracardiac structures can lead to errors in measurements of chamber and vessel size and great caution must be applied when interpreting nonstandard views. Despite this, the RPA does appear to be dilated when compared to the aorta, seen here in oblique long axis. This observation was repeatable in other 2D images that were optimized for the vessels. This observation suggests that there is significant pulmonary overperfusion, a finding supported by an increased right ventricular stroke volume as estimated by pulsed Doppler echocardiography. Although the filly is currently compensating for the defect, the defect size and the resultant large left to right shunt fraction suggests that she has no future as a racehorse. Smaller restrictive defects, despite being associated with a loud murmur, are sometimes compatible with an athletic career, especially in less strenuous disciplines. RV, right ventricle; LVOT, left ventricular outflow tract; RPA, right pulmonary artery.

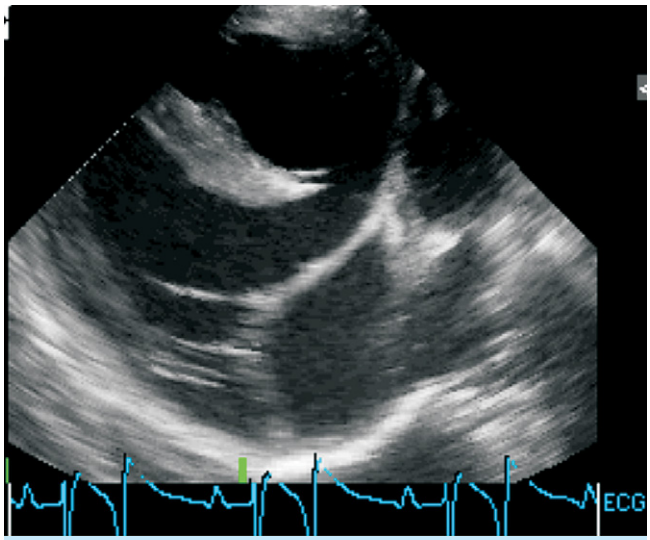


Fig. 33.31
Large ventricular septal defect in an 18-month-old Thoroughbred colt, examined after failing a veterinary examination for insurance because of a loud heart murmur. The large septal defect was found in association with other complex congenital abnormalities including dextroposition of the aorta, right ventricular hypertrophy, and subvalvular pulmonic stenosis,. These abnormalities are collectively known as tetralogy of Fallot. Despite such severe congenital abnormalities, the colt had no history suggestive of cardiac disease.

Presenting signs. The murmur of ventricular septal defect is loudest cranial on the right side of the chest. It is usually band shaped and is often associated with a precordial thrill. This murmur is caused by blood shunting across the defect, from the left ventricle to the right. Most ventricular septal defects occur in the membranous septum, close to the aortic valve (Fig. 33.30). The resultant high-velocity jet of blood then impinges on the right ventricular free wall and swirls ventrally towards the pulmonary artery (Fig. 33.32). The vibrations caused by this flow pattern result in the characteristic cranial and ventral radiation of the right-sided murmur. The murmur may be audible as far ventral as the sternum.

Though much less common, defects can also occur in the muscular part of the interventricular septum (Fig. 33.33) or in the area of the pulmonary outflow. The former still result in a right-sided cardiac murmur, but the pattern of radiation of the murmur differs. By contrast, defects that open into the pulmonary outflow tract result in a murmur whose point of maximal intensity is cranial and ventral on the left hemithorax at the level of the pulmonary valve.

Another discrete murmur is often also heard in association with large septal defects in horses. It is best heard over the heart base on the left hemithorax. Contrary to popular opinion this is not referred from the right side. This is an ejection murmur, with PMI over the pulmonary valve area. It is known as a murmur of **relative pulmonary stenosis**. It arises as a result of augmented flow of blood through a normal pulmonary valve.

A further secondary finding, associated with a large defect and shunt fraction, is an increased intensity of S_3 that results from augmented filling of the left ventricle in diastole. When the defect is large, the resultant left atrial and ventricular enlargement eventually result in left heart failure and the plethora of associated clinical signs.

Special tests

Two-dimensional and M-mode echocardiography are necessary to evaluate the size of the defect. The loudness of the primary murmur may not be helpful in this condition, since loud murmurs are often associated with restrictive

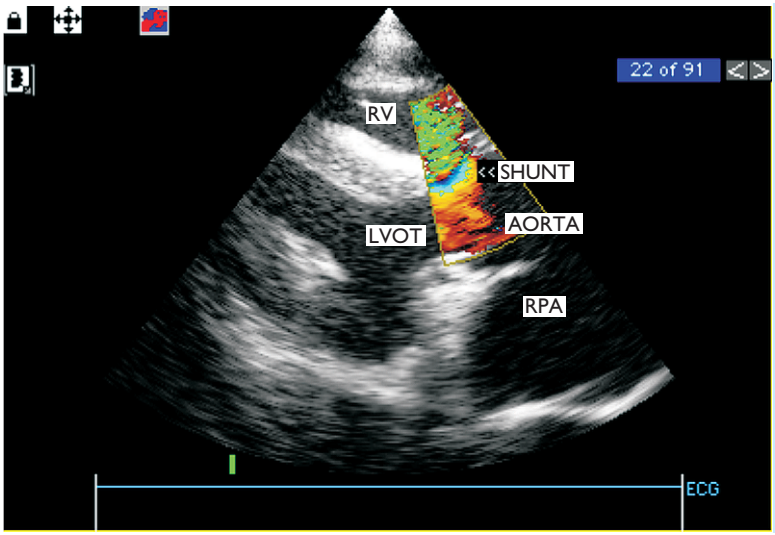


Fig. 33.32
Color flow Doppler study obtained from the filly in Fig. 33.30. The color flow study demonstrates left to right flow of blood through the defect during systole. The shunted blood travels through the defect and swirls ventrally and cranially towards the pulmonary valve, giving rise to the characteristic ventral and cranial radiation of the murmurs associated with membranous septal defects. LVOT, left ventricular outflow tract; RPA, right pulmonary artery; RV, right ventricle.

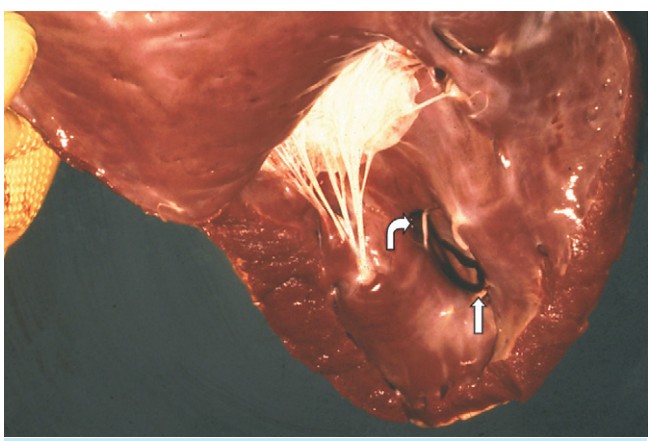


Fig. 33.33
Post-mortem specimen showing a large muscular ventricular septal defect in a 2-year-old Arabian filly. A widely radiating grade 5/6 murmur was detected from the right hemithorax at a pre-purchase examination. There was no medical history consistent with cardiac disease and the filly appeared to have normal exercise tolerance relative to her peer group. As her prognosis for useful athletic performance was hopeless and a congenital cardiac defect rendered her unsuitable for breeding, her owners elected her for euthanasia. (Courtesy of Dr LE Young and Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

(nonsignificant) defects. It has been suggested that defects less than 2.5 cm in diameter in an adult horse are compatible with normal athletic performance and are unlikely to result in heart failure.[82] Since ponies are often affected, a more universally applicable method is to use Doppler echocardiography to measure peak flow across the defect, or to compare stroke volume from the right and left ventricle. Reef and colleagues[82] suggested that velocity across the defect that exceeded 4 m/s was likely to be associated with a restrictive defect. When using these methods, it is crucial to ensure that the continuous wave ultrasound beam or pulsed Doppler sample volume are aligned parallel to the shunt or ventricular outflow. If adequate alignment is not achieved, blood flow velocity will be significantly underestimated and the defect's significance overestimated. Left atrial size and pulmonary artery dilation can also be assessed using two-dimensional (2D) methods, and these measurements are also helpful in determining a prognosis for life and performance.

While auscultation findings and clinical signs are helpful in assessing size of a defect and its clinical impact, only 2D and Doppler echocardiography are ultimately able to provide information about the severity of volume overload and a quantitative assessment of defect size.

Treatment

No surgical or medical treatment for ventricular septal defects is currently available for horses. Only if heart failure develops is treatment warranted and should include drugs to control heart rate (digoxin), diuretics to reduce volume overload, and angiotensin converting enzyme inhibitors for reduction of cardiac afterload.

Prognosis

The prognosis for small restrictive defects found incidentally in performance horses is generally good. Certainly absence of a separate murmur of relative pulmonary stenosis and loud S_3 sounds indicate that the volume of abnormal blood flow through the defect is small and that the defect is likely to be restrictive. Such defects rarely progress to cause clinical problems. Progression of disease, even with moderately large defects, can be slow, affected horses often compensating well into adulthood. As with all cases of heart disease, echocardiographic examination of an affected horse allows the size of lesion and its hemodynamic impact to be determined. Whether an animal is suit-

able for athletic duties will depend upon the size of the defect and the degree of volume overload, and the type of work to be performed.

When detected at pre-purchase examination all septal defects undoubtedly constitute unsoundness, but the horse may still be able to perform a useful job in all but the most athletic of disciplines, especially when the defects are small and restrictive. Although small membranous defects may have minimal impact on blood flow, their position can cause disruption and instability of the aortic valve leaflets that results in rapidly progressive aortic valve regurgitation and secondary left ventricular volume overload (see below).

Etiology and pathophysiology

The condition occurs as a result of anomalous development of any of the components of the interventricular septum, most commonly the dorsal membranous portion that forms part of the fibrous skeleton of the heart. Although the precise genetics and mechanisms of inheritance of the condition in horses are unknown, affected animals should not be used for breeding.

Restrictive defects that result in a small shunt are usually well tolerated and have minimal hemodynamic impact. When defects are large, left-sided heart failure develops due to volume overload of the left atrium. The right ventricle tends to be relatively spared, as the pulmonary valve is open when the bulk of the volume is shunted across the defect and it passes directly into the pulmonary artery. Pulmonary overcirculation occurs and marked dilation of the pulmonary artery can result in pulmonary artery rupture. As a result horses with evidence of pulmonary overcirculation should be retired from ridden work.

Epidemiology

In the series of 27 cases described by Reef,[82] Standardbreds and Arabians were overrepresented compared to the hospital population and Thoroughbreds were underrepresented. European experience suggests that Welsh section A and Shetland ponies also have a high prevalence of the condition.

Aortic insufficiency

Recognition

History

Diastolic cardiac murmur is usually detected incidentally. Occasionally horses may have a history of ataxia during exercise or die suddenly, usually during exercise. Aortic regurgitation may be found in association with congestive heart failure, AF, and mitral valve regurgitation.

Presenting signs Aortic insufficiency occurs commonly in older horses. The murmur is diastolic, usually decrescendo, and has a PMI at the aortic valve, although it will often radiate widely towards the apex. Because the aorta is a midline structure, as the disease progresses, the murmur often becomes audible over the right hemithorax. It is thus the only murmur that can be routinely auscultated from both sides of the thorax. The murmur often has a musical quality and may appear to 'buzz' or 'whoo'. The musical quality is believed to arise as the regurgitant jet hits the anterior leaflet of the mitral valve (Fig. 33.34), or is due to resonance and vibration of the aortic root.

When severe, the condition can result in noticeably bounding arterial pulses (Fig. 33.26). This occurs because there is a rapid run off of aortic pressure in diastole, as blood leaks backwards into the low-pressure chamber of the relaxed left ventricle.

When the regurgitant fraction is large, there is volume overload of the left ventricle (Fig. 33.35). There is also dilation of the mitral valve annulus and, in consequence, secondary mitral regurgitation may occur. Thus when a systolic murmur of MR is heard in conjunction with the diastolic murmur of aortic insufficiency, prognosis is much more guarded.

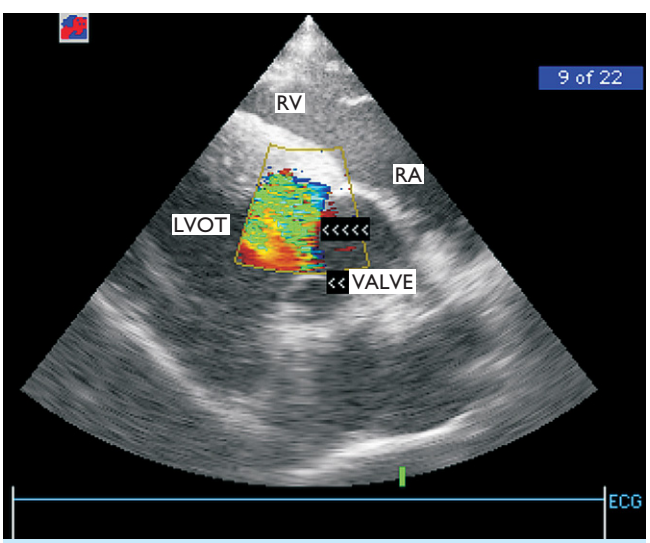


Fig. 33.34
Color flow Doppler study of aortic valve regurgitation in a 16-year-old Grand Prix dressage horse. The image shows a green jet of blood traveling from the center of the aortic valve towards the interventricular septum. The two-dimensional image showed valve leaflet thickening typical of nodular degeneration in the older horse. There was no evidence of exercise-induced arrhythmias and left ventricular dimensions were still within normal limits. The horse is subject to regular echocardiographic and electrocardiographic examinations as aortic valve degeneration is progressive. Currently he is able to remain in full competition, as there is no significant left ventricular dilation. LVOT, left ventricular outflow tract; RA, right atrium; RV, right ventricle.

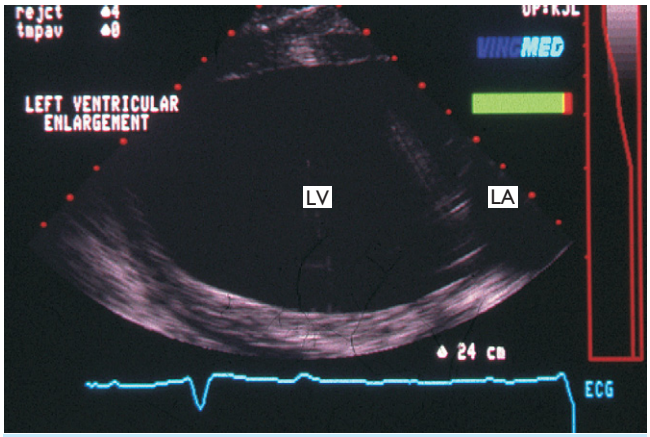


Fig. 33.35
Two-dimensional echocardiograph from the right hemithorax from an 11-year-old riding horse with a grade 5/6 murmur of aortic regurgitation. Note the rounded bloated appearance of the dilated left ventricle. Dilation results in increased afterload to the left ventricle and increases both myocardial work and oxygen demand. Coronary perfusion is simultaneously reduced as diastolic aortic pressure falls. Stretch and hypoxia increase the likelihood of ventricular arrhythmia and there is increasing risk of exercise-induced arrhythmias and sudden death. Severe volume overload also causes dilation of the mitral valve annulus resulting in secondary development of mitral regurgitation that can ultimately result in left-sided heart failure. LA, left atrium; LV, left ventricle. (Courtesy of Dr KJ Blissitt, Royal (Dick) School of Veterinary Studies, Edinburgh.)

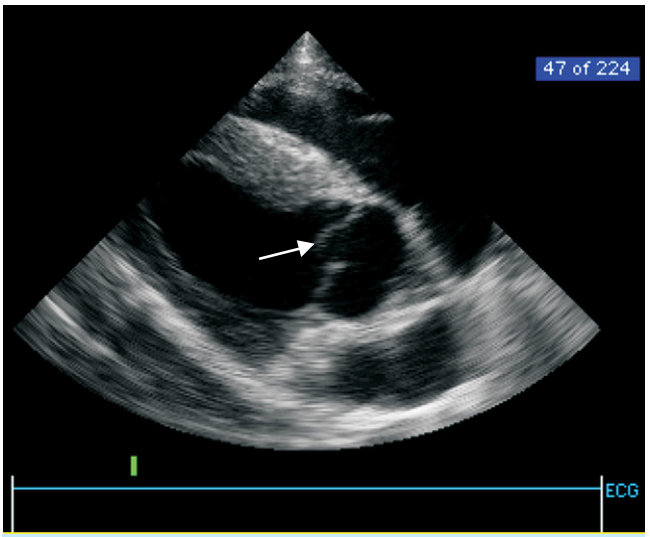


Fig. 33.36
Two-dimensional echocardiograph from a 9-year-old National Hunt race horse with a grade 3/6 murmur of aortic regurgitation. The image has been optimized to show the aortic valve (center). The non-coronary leaflet (arrow) has prolapsed into the left ventricular outflow tract. There is a bright echogenic nodule at the coaptation point of the valve, the usual site of nodular degeneration in older horses.

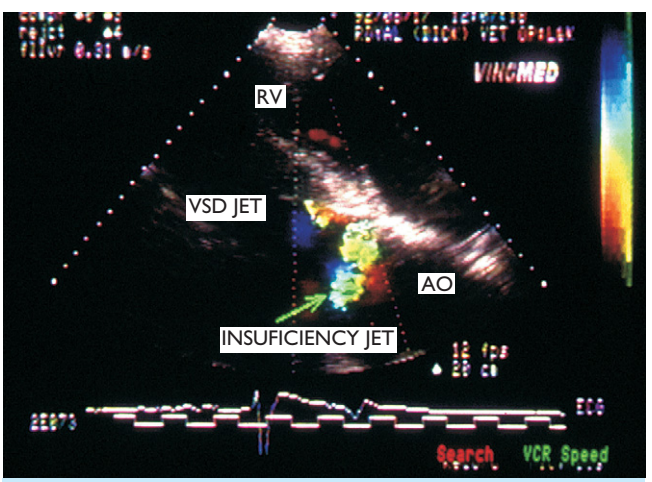


Fig. 33.37
Color flow Doppler study of the aorta and left ventricular outflow tract from the right hemithorax of a 7-year-old novice event horse during late diastole. The horse failed a pre-purchase examination after a grade 3/6 diastolic murmur was detected from the left heart base. The image shows two discrete regurgitant jets (labeled), one from the aortic valve and one from a small ventricular septal defect which closes when the ventricle shortens in systole. AO, aorta; RV, right ventricle; VSD, ventricular septal defect.

Special examination

Color flow Doppler echocardiography will confirm the presence of aortic regurgitation (Fig. 33.34). Pulsed or continuous wave Doppler techniques allow estimates of right and left ventricular stroke volume and regurgitant fraction to be made. Two-dimensional and M-mode echocardiography are used to evaluate cardiac chamber size and left ventricular wall motion. In severe aortic regurgitation, there is left ventricular dilation (Fig. 33.35) and secondary mitral regurgitation.

Careful examination of the aortic valve using 2D and color flow Doppler techniques may demonstrate the underlying cause of the valve dysfunction. Typical findings include valve leaflet prolapse (Fig. 33.36) and nodular degeneration, thickening of the valve leaflets, or evidence of a small ventricular septal defect (Fig. 33.37). There is often diastolic fluttering of the anterior mitral valve leaflet visualized by 2D or M-mode echocardiography.[83] In severe volume overload and secondary mitral regurgitation, premature closure of the mitral valve and septal hyperkinesis may also be a feature.[84]

In horses with mild–moderate aortic valve regurgitation and without evidence of heart failure, electrocardiographic examination during appropriate exercise is mandatory to ensure that there is an absence of exercise-induced ventricular arrhythmias.

Treatment

There is no specific treatment for aortic valve regurgitation available and in horses with compensated valve dysfunction,

none is indicated. When signs of left ventricular volume overload become evident (Fig. 33.35), or signs of heart failure are present, the horse must be immediately retired from ridden exercise. Palliative therapy focuses upon control of heart rate (digoxin), reduction of volume overload (diuretics), and reduction of cardiac afterload (angiotensin converting enzyme inhibitors). On the rare occasion that valve dysfunction is caused by endocarditis, targeted antibiotic therapy will be required.

Prognosis

Most commonly the condition arises due to normal progressive aging changes of the valve leaflets and when the murmur is detected in older horses the prognosis for life and performance is generally good. In such cases performance problems are rarely reported and the ultimate cause of death or euthanasia in these horses is usually noncardiac. In older horses, the condition usually progresses slowly and they are usually able to continue their normal activities, provided they are monitored regularly by echocardiography and ECG.

Aortic insufficiency also occurs sporadically in younger horses when the only abnormalities on echocardiography include leaflet prolapse, dilation of the aortic root, and premature degenerative changes (thickening or nodular degeneration). In these horses the condition might progress to heart failure during the course of the horse's athletic career. In some cases progression is very slow and the horse's career may not be noticeably compromised, but progression of regurgitation and volume overload is impossible to predict in individuals, so all affected cases must be carefully monitored. As a result when the murmur is encountered during a pre-purchase examination, although each patient must be considered individually, in general the murmur should be viewed with concern.

When a systolic murmur of mitral valve regurgitation is heard in conjunction with the diastolic murmur of aortic insufficiency, or there is hyperkinesis of peripheral pulses, it is likely that there is a large regurgitant fraction and that mitral valve regurgitation is secondary to severe volume overload. As a result prognosis is much more guarded and the horse must be retired from ridden duties.

Etiology and pathophysiology

Usually the condition arises due to nodular degeneration of the valve leaflets, a change that appears to be age related.[53,54] When a loud murmur of aortic insufficiency is detected in a horse under 15 years of age there has been premature progression of aortic valve disease and a complicating reason, other than normal aging processes, is implicated. Vegetative endocarditis, though very rare, can affect both aortic and mitral valves in horses,[70] and prognosis for performance and survival is poor. More commonly premature regurgitation is caused by prolapse of the noncoronary cusp of the aortic valve into a small ventricular septal defect (Fig. 33.37).[82] In many affected horses, the septal defect is not of hemodynamic significance per se, as there is little or no blood flow through it during systole as the heart contracts and shortens. Aortic valve regurgitation has also been implicated in the pathogenesis of aneurysm formation in the proximal aorta.[85]

When the regurgitant fraction is large, there is volume overload of the left ventricle (Fig. 33.35) and dilation of the mitral valve annulus resulting in mitral regurgitation. The severely dilated ventricle also becomes prone to exercise-induced ventricular arrhythmias. This increased susceptibility occurs due to increased cardiac work and myocardial oxygen demand caused by increased cardiac preload and the augmented afterload of cardiac dilation. These factors are coupled with reduced diastolic blood pressure and thence coronary perfusion pressure. The risk of arrhythmia is heightened when myocardial oxygen demand increases and diastole shortens during exercise. As a result, affected horses should be monitored regularly by echocardiography and exercising ECG as long as they remain in ridden work.

Epidemiology

In a population of 1159 horses comprising many retired animals, the presence of a diastolic murmur of aortic insufficiency was found to be significantly associated with age.[86] The murmur is only infrequently detected in race horses,[1–4] but the prevalence is greater in older National Hunt Thoroughbreds than in those engaged in flat racing (Tables 33.1, 33.2).

Complex congenital lesions

A wide variety of complex cardiac abnormalities have been reported in foals.[87–95] They are however uncommon[96] and often result in early signs of heart failure and cyanosis. Complex developmental abnormalities have a higher incidence in Arabian foals, but they can occur in all breeds, occasionally presenting at adulthood or adolescence[97] (Fig. 33.38). Complex congenital lesions are not compatible with athletic performance, but depending upon the amount of intracardiac shunting and venous admixture, can carry a surprisingly good prognosis for short- to medium-term survival.

Diseases of the myocardium

- Diseases of the myocardium are poorly understood in horses.
- They are characterized by loss of performance and arrhythmias at rest and during exercise.
- Measurement of serum or plasma concentration of cardiac troponin I and the isoenzymes of lactate

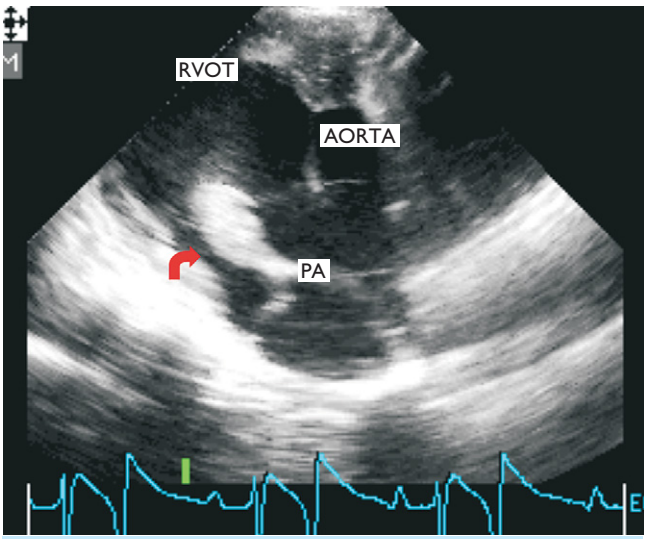


Fig. 33.38
Two-dimensional echocardiograph from the right hemithorax of an 18-month-old Thoroughbred with tetralogy of Fallot. This is a cranial short-axis view of the right ventricular outflow tract (RVOT). The outflow tract connects directly with a dilated aorta and a pulmonary artery (PA). Subvalvular pulmonic stenosis is severe (red arrow).

dehydrogenase will be elevated in severe acute cases of myocardial inflammation and necrosis.

- Dilated cardiomyopathy occurs rarely in athletic horses and has been associated with nutritional deficiencies in young horses and cattle.
- Occasionally toxic damage to myocytes occurs when a cardiotoxin is accidentally introduced into equine feed. The ionophores salinomycin and monensin have caused a number of such outbreaks throughout the world.[98–102]
- Horses that survive ingestion of cardiotoxins usually develop a dilated hypocontractile ventricle that mimics dilated cardiomyopathy.
- True inherited idiopathic cardiomyopathy, as occurs in other species, has not yet been identified in horses.

Recognition

History

Myocarditis has been linked to poor performance syndromes occurring in individuals, or in outbreaks in racing stables. Myocarditis may be the underlying cause of atrial and ventricular arrhythmia in athletic horses. In the acute phases of toxic damage to the myocardium, one or more horses may die suddenly from fatal ventricular arrhythmia.

Physical examination

In many mildly affected cases, the horse is normal on physical examination at rest. A cardiac rhythm disturbance may be present during auscultation, or during palpation of the apex beat or peripheral pulse. If cardiac function is severely compromised, the horse will present with signs of biventricular heart failure (see 'Mitral regurgitation' above).

Special examination

A definitive diagnosis of the origin of the ectopic complexes (atrial or ventricular) will be determined by electrocardiography (see 'Supraventricular premature systoles' and 'Ventricular premature systoles' above). In cases of poor performance an ECG during appropriate exercise is advisable.

In acute cases, measurement of serum cardiac troponin I and the isoenzymes of lactate dehydrogenase can sometimes provide a definitive diagnosis of myocardial inflammation and necrosis, though in most horses these analyses are not conclusive. It is important to appreciate that these laboratory tests are poorly validated in horses and that their sensitivity and specificity in this species have not yet been determined. In addition, they have been developed to assess acute ischemic events in people, when the amount of myocardial damage and necrosis is enormous. With the possible exception of toxic damage to the equine myocardium, in equine practice it is unlikely that such severe acute myocardial damage is likely to occur, so it is not surprising that in our hands these tests are frequently disappointing. In addition, when horses present with suspected myocardial dysfunction, it is quite possible that the acute insult to the heart or any causative agent were present considerably earlier, further reducing the power of serologic and biochemical testing methods. Of the biochemical tests currently available, cardiac troponin I probably has the highest specificity for myocardial injury and appears to be phylogenetically conserved between mammals. New markers of myocardial injury will undoubtedly continue to be developed for assessment of myocardial injury in human medicine. Unfortunately, for the reasons stated above, no matter how specific these tests become, it is unlikely that a biochemical marker will ever be able to definitively diagnose mild myocardial dysfunction in horses.

Echocardiography is also useful to assess the cardiac chambers and systolic function. Abnormal wall motion suggestive of localized myocardial damage may be present, or there may be extensive areas of fibrosis and calcification of the myocardium and endocardium.

The results of all these examinations may be unremarkable or equivocal, especially on horses with vague signs of poor performance or lone arrhythmia.

It has also been suggested that postexercise echocardiography may be a more sensitive method to detect mild ischemic damage to the myocardium in horses.[103,104] M-mode echocardiography is used within 60 seconds of exercise to fatigue in an attempt to mimic the stress echocardiography that is carried out during exercise in people to detect subclinical disease.[105] Unfortunately it is not practical to perform the examination during steady-state exercise in horses and the technique appears to have a very high coefficient of variation in normal horses.[106] Despite this

limitation, the method's advocates claim that the technique has been useful in horses undergoing performance evaluation on the treadmill.[104]

Treatment

Therapeutic aim

Treat underlying disease process and any life-threatening arrhythmia. Remove access to toxin. Improve nutritional status.

Therapy

In all suspected outbreaks, or in individual animals, thorough evaluation of previous medical history, bacteriologic or serologic examination and assessment of nutritional status of affected horses and, any horses in contact with the affected animals, should be undertaken.

In most cases of extensive myocardial damage or necrosis, treatment is ineffectual once clinical signs are apparent. Therapy is therefore aimed at the control of clinical signs and amelioration of cardiac failure with the use of appropriate antiarrhythmic drugs to treat life-threatening rhythm disturbances. Affected horses should always be completely rested to reduce myocardial oxygen demand.

In less severely affected cases with signs of poor performance or lone arrhythmia, rest and steroid therapy have been advocated (see 'Supraventricular premature systoles' above). When biochemical markers of myocardial damage are elevated at diagnosis, their levels can be used to monitor progress.

Prognosis

The prognosis for myocardial disease is dependent upon the severity of the underlying damage to the myocardium. In general the prognosis for return to athletic function is hopeless if there is echocardiographic evidence of reduced systolic function or marked chamber dilation. The prognosis for survival is also poor.

When myocarditis is suspected in horses presenting with poor performance and arrhythmia, and when there are no echocardiographic or biochemical abnormalities, prognosis is fair. A percentage of affected horses will return to their previous athletic performance following rest and/or steroid therapy. In the absence of a definitive test to diagnose myocarditis in horses, unfortunately it is questionable whether true myocardial inflammation was ever present in many of these cases. Myocardial biopsy is an invasive, high-risk procedure, and as a result it seems unlikely that our understanding of this condition will improve in the foreseeable future.

Etiology and pathophysiology

In most species the usual underlying cause of myocardial damage is ischemia resulting from coronary artery occlusion, usually arteriosclerosis. A similar etiology may underlie the condition in horses, as areas of focal fibrosis are common in the equine myocardium at post-mortem examination.[53–55] Cranley & McCullagh[55] also demonstrated a relationship between proximal aortic *Strongylus vulgaris* lesions and the presence of focal ischemic lesions in the myocardium and hypothesized that microembolization from parasitic lesions in the proximal aorta produced obstructive arteriosclerotic lesions in myocardial arterioles. In most horses, the areas of fibrosis are focal and do not penetrate the whole thickness of the ventricular myocardium,[53–55] but it is possible that during cell ischemia and death, before fibrosis occurs, these areas act as foci for arrhythmogenesis. In more severely affected horses, there may be sufficient damage to wide areas of myocardium to provoke extensive remodeling and lasting damage to cardiac function. Unfortunately in most post-mortem studies the fibrotic lesions cannot be correlated to clinical signs before death and in many cases the lesions appear inactive. In addition, improved anthelmintic management of equidae has resulted in a marked reduction in the incidence of thrombo-ischemic lesions associated with large strongyle infestations (Dr Ken Smith, personal communication), although minor intimal tracking consistent with strongyle damage remains a common incidental finding at post-mortem examination.[107] Although the precise etiology was uncertain, a number of authors have found post-mortem evidence of acute myocarditis in horses presenting with severe ventricular arrhythmia and poor performance.[61,63,108]

Ionophores such as monensin,[109,110] and salinomycin[98] and rattlesnake poison[111] cause direct damage to myocytes resulting in cell death, replacement fibrosis, arrhythmia, and loss of systolic function.

In the poor performance syndrome in racing yards, the cardiac signs are often observed some time after an outbreak of infectious respiratory disease, but despite extensive serologic and bacteriologic investigations, in most cases, a causative agent cannot be identified. More research is needed in this area. In humans, viruses are believed to be associated with dilated cardiomyopathy,[112] and during influenza virus epidemics there may be unexpected mortality of humans due to cardiovascular diseases.[113] The precise mechanism of viral damage to the myocardium is not fully understood, but may involve procoagulant effects.[113] It is possible that similar sporadic cases of virus-associated or postviral myocarditis occur in the equine population, but at the moment this is entirely speculative. There is, however, evidence that equine viruses, including equine viral arteritis, equine herpesvirus-1, and African horse sickness virus, replicate in epicardial or myocardial blood vessels in natural and experimental disease,[114–116] and myocarditis has been reported in horses infected with influenza virus.[117,118]

Idiopathic dilated cardiomyopathy in dogs and humans results from various genetic mutations of the proteins involved in cardiac contraction. There is reduced contractile function and ultimately cell death and fibrous remodeling

that result in a dilated poorly contractile ventricle and symptoms of heart failure and arrhythmia. There have been clinical and anecdotal reports of a similar syndrome in horses, based on the post-mortem or echocardiographic diagnosis of a large dilated heart. However it is important to appreciate that myocardial failure and dilation accompanies all types of heart failure in end-stages, so that echocardiographic evidence of dilated poorly contractile ventricle is not diagnostic of dilated cardiomyopathy.

Epidemiology

No epidemiologic information is currently available, as myocarditis is too poorly understood in horses.

Diseases of the pericardium

Recognition

History

Affected horses may present with general signs of malaise or evidence of heart failure including weakness and collapse.[119]

Presenting signs

In horses affected with bacterial pericarditis, there will be associated signs of infection and sepsis. Cardiovascular signs depend upon the volume of pericardial fluid. In cardiac tamponade (large effusion compressing the right atrium), jugular distension, subcutaneous edema, ascites, pleural effusion and abdominal enlargement will be evident. Peripheral pulse quality is poor and heart rate is increased. There may by muffling of the heart sounds with the presence of pericardial friction rubs in some cases.[119,120]

Special tests

Two-dimensional echocardiography will identify fluid in the pericardial space. There may be obvious compression of the right cardiac structures, depending upon the volume of effusate present.

Electrocardiography will reveal sinus tachycardia, but the QRS amplitude will be less than usual. Electrical alternans, as occurs in other species, is rare in horses.[119,120]

Hematology, bacteriology and analysis and culture of pericardial fluid are valuable in determining etiology and treatment in cases of septic pericarditis.

Therapy

Therapeutic aims

To release pressure on the right heart chambers and restore normal cardiac filling and to achieve bacteriological cure in cases of septic pericarditis

Treatment

Aggressive pericardial drainage and lavage have been recommended for effusions associated with cardiac compromise.[119] Additional antibiotic therapy as indicated by culture and sensitivity will also be indicated in bacterial pericarditis. In cases of nonseptic idiopathic pericarditis, corticosteroids are recommended.[119,120] Surgical pericardectomy was also attempted as a treatment for restrictive pericarditis in a horse, but the results were disappointing and the condition recurred.[121]

Prognosis

In a series of 18 cases described by Worth & Reef,[119] all 14 of the horses treated successfully returned to their previous athletic performance. Only one treated horse died in the series of 10 cases of idiopathic pericarditis described by Freestone and colleagues,[120] suggesting that with aggressive treatment prognosis is good. In contrast to other species, there are few reports of effusion returning repeatedly after drainage. If effusion results from sepsis, or trauma, the prognosis is more guarded and will depend upon the nature of the effusion and the response to antimicrobial agents.

Etiology and pathophysiology

In the series of 18 cases described by Worth & Reef,[119] pericarditis was defined as idiopathic in six horses. A bacterial cause was identified in five horses and the remaining horses had nonseptic pericarditis associated with bacterial (five horses) and viral respiratory disease (two horses). Laboratory analysis of pericardial fluid samples from 10 cases of idiopathic pericarditis classified six cases as aseptic serofibrinous, three cases as eosinophilic, and one case as histiocytic.[120]

The hemodynamic effect of pericardial effusion depends upon the volume of effusion and the amount of compression of the thin-walled right atrium. Increased pericardial pressure impedes ventricular filling and increases end-diastolic pressure. Reduced stroke volume of the right heart causes reduction in arterial blood pressure and activates the renin–angiotensin system resulting in massive retention of Na and water. Backward failure of the right ventricle rapidly occurs, resulting in jugular distension and abdominal, pleural and subcutaneous fluid accumulation. Low-output failure simultaneously results in weakness and exercise intolerance.

Epidemiology

Isolated cases of pericarditis occur only rarely in athletic horses and no specific epidemiologic information is available. In spring of 2001 in central Kentucky, outbreaks of pericarditis and uveitis were recognized in grazing yearlings. The outbreaks occurred concurrently with mare reproductive

loss syndrome on breeding establishments. The syndrome was only detected in horses at grass and as a result, athletic animals were not affected.[122] The precise etiology of the syndrome remains uncertain at this time.

Diseases of the vessels

Parasitic arteritis

General

Three general syndromes of large vessel disease are recognized in performance horses. These are: sudden death due to large vessel rupture; acute or recurrent colic due to arteritis and thrombosis of the cranial mesenteric arteries or renal arteries; and a vague history of increasingly poor performance and hind limb lameness with aortoiliacofemoral thrombosis.

Aortic and great vessel rupture

Recognition

History and presenting signs

Horses present with sudden death or sudden-onset pallor, tachycardia, and weakness, usually during exercise. Subacute cases may also present with ventricular arrhythmia, usually ventricular tachycardia.[57] Rapid weak pulses with pulse deficits are usually obvious. Horses are often in extreme distress and exhibit profuse sweating. They are frequently misdiagnosed as colic cases. There is usually a loud continuous cardiac murmur, the position of which varies according to the site of rupture.

Treatment

There is no specific treatment. Antiarrhythmic drugs may be used to control the ventricular rhythm disturbance for symptomatic relief. Response to drug therapy is variable, depending upon the extent of damage to the conduction tissues.

Prognosis

Death usually occurs acutely or very soon after vessel rupture due to ventricular arrhythmia or hypovolemic shock. When rupture is into the right heart, the horse may present subacutely with a sudden onset continuous heart murmur, ventricular arrhythmia, and/or acute distress. The prognosis for subacute cases depends on the site and size of the aortic rupture. Usually, but not invariably, they are also fatal.

Etiology and pathogenesis

Rupture of the aorta, at the level of the sinus of Valsalva, aortic arch, or the main pulmonary artery and its branches, can occur.[123–125] When a large vessel ruptures into the thoracic cavity, death is immediate through rapid hypovolemic shock. Aortic aneurysms are reported most frequently at or around the right coronary sinus up to the brachiocephalic trunk.[85,126–128] It seems likely that an aneurysmal weakness at the site of vessel rupture also underlies sudden death and rupture is most likely during strenuous exercise when arterial and pulmonary vascular pressure increases. These sites are also commonly affected with lesions associated with *Strongylus vulgaris* migration[55] and parasitic damage to arteries has been postulated to underlie great vessel rupture in horses. In subacute cases rupture of the aneurysm usually occurs at the level of the right coronary artery from whence it dissects into the interventricular septum,[57] pulmonary artery,[129] or the right heart.[130] When the aneurysm dissects through the interventricular septum, there is widespread damage of the cardiac conduction system resulting in the characteristic ventricular rhythm disturbances. Occasionally volume overload leads to right heart failure after rupture of the aneurysm into the right ventricle.[130]

Pulmonary artery aneurysm and vessel rupture can be associated with severe pulmonary hypertension in left heart failure.

Epidemiology

Large vessel rupture tends to occur most frequently, but not exclusively, in older performance horses.

Cranial mesenteric parasitic arteritis

History and presenting signs

Cranial mesenteric parasitic arteritis cases present with acute colic symptoms when mesenteric arterial occlusion is complete, or with chronic weight loss, diarrhea and intermittent recurrent colic if occlusion is partial.[131]

Special tests

Peritoneal fluid aspiration and rectal examination will be necessary to establish a diagnosis.

Therapy

Therapeutic aims

Therapy is usually palliative but aims to restore normal nutrition, hydration and electrolyte status, and normal gut function.

Treatment

Larvicidal anthelmintics are recommended. For thromboembolic colic, laparotomy and resection of devitalized bowel

may be required. Fluid therapy and analgesic administration may also be required in cases of acute and chronic colic.

Prognosis

Depends on the severity of the presenting signs in colic cases, but repeated bouts of colic can continue until an acute ischemic episode occurs.

Etiology and pathophysiology

During migration, *Strongylus vulgaris* larvae damage the arterial endothelium. This results in activation of inflammatory mediators, disruption of the normal integrity of the vessel wall, and intimal thickening.[107] The resulting turbulence and expression of inflammatory mediators promotes platelet adhesion, fibrin deposition, and thrombus formation. Lesions are most likely to form at vessel branches, where eddy formation and turbulence naturally occur.

Epidemiology

Parasitic arteritis is most likely to occur in horses with a history of inadequate or inappropriate anthelmintic use.

Aortoiliacofemoral thrombosis

Presenting signs

Clinical signs vary from mild hind limb stiffness that reduces performance to more severe unilateral or bilateral hindlimb lameness induced by strenuous exercise. Fairly commonly, increasingly poor performance is often noted before the onset of more dramatic clinical signs. The affected limb may feel cooler after fast exercise. Affected horses may also become distressed and unpredictable and sweat profusely immediately following very strenuous work. There may be reduced saphenous venous refill time in the affected limb after exercise and the affected limb may feel cooler. In longstanding cases there may be unilateral hind limb muscle atrophy.[132,133]

Special tests

Aortoiliacofemoral thrombosis may be diagnosed by careful rectal palpation revealing vessel occlusion/aneurysm at the bifurcation of the caudal aorta. Two-dimensional ultrasonography is the most practical method to make a definitive diagnosis,[134] although Doppler and nuclear scintigraphic methods[135] have also been used. In athletic horses, the thrombus is usually only partially occlusive at presentation and flow limitation occurs initially at maximal exercise. As the thrombus increases in size, flow limitation occurs with progressively less strenuous activity.

Therapy

Therapeutic aims

To relieve signs of hindlimb ischemia by restoring limb blood flow. Strategies include preventing further thrombus formation, encouraging thrombolysis, providing analgesia, and allowing a collateral circulation to develop.

Treatment

Specific treatments with various anticoagulant agents[136] and surgical removal of thrombus have been described. None have been critically assessed and recovery will always depend upon the development of collateral circulation and prevention of further clot formation. In athletic horses, daily administration of aspirin is often recommended, but its efficacy is unknown.[132] Monthly administration of ivermectin coupled with twice daily administration of phenylbutazone has also been suggested, but the efficacy of this regime is also difficult to assess as improvements in clinical signs may result from the development of collateral circulation alone.[137]

Prognosis

The prognosis for return to previous levels of athletic performance after aortoiliacofemoral thrombosis is poor.

Etiology and pathophysiology

Characteristically organized lesions are found at the aortic quadrification and extend into the distal portions of the femoral and internal iliac arteries. The lesions may be partially or completely occlusive and consist of well-organized and well-vascularized fibrous tissue, occasionally containing hemorrhagic or degenerate areas. Proximal to the organized masses, thrombi are often present.[138] The pathogenesis of the lesions remains unclear. *Strongylus vulgaris* larval damage has been implicated, but actual larvae or inflammatory cells are not usually present in the lesions[138] and the larvae rarely migrate to such caudal arterial locations.[107] In addition, the disease is most frequently reported in athletic animals with a good standard of management. Others have suggested that the condition may be similar to arteriosclerosis obliterans in humans when intimal damage, expression of inflammatory mediators, thrombus formation and fibrosis result in progressive vessel occlusion.[138] It has been proposed that equine iliac arteries may be predisposed to damage because of vessel branching that results in turbulent flow at a location that is already predisposed to damage because of large forces of locomotion and tight fascial attachments to surrounding tissues.[137]

Epidemiology

The condition has been documented in horses of all ages and sexes, but clinical signs are more frequently reported in male

performance horses.[138] It is possible this observation reflects the higher proportion of males engaged in strenuous activity rather than a true sex difference in prevalence of arterial damage. The average age of horses in a series of 15 cases was 5.2 years.[138]

Jugular vein thrombosis

Recognition

History

This condition is often associated with prolonged intravenous catheterization following surgical procedures. Horses with endotoxemia or septicemia are at increased risk.[139] Venous thrombosis and thrombophlebitis also follow repeated jugular venepuncture, particularly when the drugs being administered are irritant, or intravenous technique is poor.

Presenting signs When one vein is affected there may be no obvious clinical signs except localized firmness and cording of the vessel. When both vessels are affected, there will be proximal engorgement of vessels coupled with subcutaneous and local edema. Head and laryngeal swelling can occur in extreme cases. Head swelling is always exacerbated when the head is lowered, e.g. during grazing. When a long length of vein is occluded by thrombus, there may be bacterial colonization resulting in pyrexia, depression, neck stiffness, heat, and pain. Inadvertent perivascular deposition of irritant drugs such as phenylbutazone, guiaphenesin, thiopentone and hypertonic solutions also results in heat, swelling and localized pain. If sufficiently severe, the initial chemical irritation may be followed by a marked inflammatory response, tissue necrosis, and skin sloughing.

Special examination

Two-dimensional ultrasound examination is useful to assess the extent of the thrombus, or check jugular vein patency in cases of severe perivascular inflammation and swelling. An echodense cavitating thrombus is usually present within the jugular vein. The appearance of brightly echogenic areas within the thrombus suggests that gas-forming bacteria are present and that aggressive treatment will be required. Hematologic and biochemical investigation usually demonstrates leucocytosis, neutrophilia, and hyperfibrinoginemia.

Treatment

Therapeutic aims

Therapy is focused upon the need to discourage further thrombus formation and the control and prevention of infection, thus reducing the chances of septic embolization and systemic complications. In mild or unilateral cases treatment may not be required as spontaneous recanalization occurs in many affected horses.

Therapy

Prolonged systemic antibiotic therapy will be required when bacterial infection is present. All intravenous catheters must be removed and further venepuncture cease. Surgical excision and removal of the affected vein may be required when the lesion is extensive and infected.[140–142] Concurrent administration of nonsteroidal anti-inflammatory drugs, hot packing, and massage may also provide analgesia and relief during the acute phase.

When inadvertent perivascular injection of a known irritant has occurred, the drug should be diluted by instilling large volumes (at least 1 L) of isotonic electrolyte solution around the site. Local anesthetic agents (without epinephrine) can be added to the diluent solution to provide analgesia.

Prognosis

In most cases prognosis is good and normal jugular filling returns after recanalization occurs. If there is infection and septic embolization, the prognosis is more guarded. If early aggressive treatment is not performed after perivascular injection of a known irritant, there may be extensive necrosis and sloughing of neck skin that ultimately requires reconstructive surgery. Occasionally there may be damage to the recurrent laryngeal nerves, carotid artery, ventral neck muscles, and the vago-sympathetic trunk.

Etiology and pathogenesis

Localized or diffuse vascular endothelial damage exposes endothelial collagen and promotes platelet and fibrin adhesion and thrombus formation. When the thrombus is occlusive there is increased venous pressure resulting in swelling and edema in dependent areas. When thrombus or thrombophlebitis is complicated by sepsis there will be pyrexia and the possibilty of septic emboli causing disease in other body systems. Horses with a hypercoagulable state, or with endotoxemia and sepsis, are at a higher risk of thrombosis and thrombophlebitis.[139] Although the jugular vein is most commonly affected, thrombosis of other systemic veins has also been reported.[143]

Epidemiology

Jugular thrombosis and thrombophlebitis occur sporadically in performance horse and are usually iatrogenic associated with administration of drugs or intravenous catheterization.

Immune-mediated vasculitis

History

Immune-mediated vasculitis is associated with previous and ongoing infections including *Streptococcus equi* (strangles),

equine viral arteritis, ehrlichiosis, equine infectious anemia, and equine influenza. Occasionally the syndrome occurs after other systemic diseases including neoplasia and colitis.[144] As a result the condition is rare in athletic horses.

Presenting signs, treatment, and prognosis

Immune-mediated vasculitis usually results in cutaneous lesions (crusting, ulceration), edema, erythema, pyrexia, reluctance to move, depression, and inappetance. Treatment depends upon the underlying cause, although corticosteroids are recommended in the absence of active infection. Prognosis depends on the underlying cause, speed of recognition of clinical signs, and patient response to early aggressive treatment.

References

1. Kriz NG, Hodgson DR, Rose RJ. Prevalence and clinical importance of heart murmurs in race horses. J Am Vet Med Assoc 2000; 216:1441–1445.
2. Patteson MW, Cripps PJ. A survey of cardiac auscultatory findings in horses. Equine Vet J 1993; 25:409–417.
3. Young LE, Wood JLN. The effects of age and training on murmurs of atrioventricular valvular regurgitation in young Thoroughbreds. Equine Vet J 2000; 32:195–199.
4. Young LE, Wood JLN. Effect of age and training on thoroughbred valvular competence. In: *Proceedings of the 19th Annual Veterinary Medical Forum, Denver*. 2001; 347–348.
5. Martin BB Jr, Reef VB, Parente EJ, et al. Causes of poor performance of horses during training, racing, or showing: 348 cases (1992–1996). J Am Vet Med Assoc 2000; 216:554–558.
6. Naylor JM, Yadernuk LM, Pharr JW, et al. An assessment of the ability of diplomates, practitioners, and students to describe and interpret recordings of heart murmurs and arrhythmia. J Vet Intern Med 2001; 15:507–515.
7. Patteson DF, Detweiler DK, Glendenning SA. Heart sounds and murmurs of the normal horse. Ann N Y Acad Sci 1965; 127:242–305.
8. Welker FH, Muir WW. An investigation of the second heart sound in the normal horse. Equine Vet J 1990; 22:403–407.
9. Scheffer CW, Robben JH, Sloet van Oldruitenborgh-Oosterbaan MM. Continuous monitoring of ECG in horses at rest and during exercise. Vet Rec 1995; 137:371–374.
10. Hall MC, Steel JD, Stewart GA. Cardiac monitoring during exercise tests in the horse. 2. Heart rate responses to exercise. Aust Vet J 1976; 52:1–5.
11. Holmes JR. Equine electrocardiography: some practical hints on technique. Equine Vet J 1984; 16:477–479.
12. Physick-Sheard PW, Hendren CM. Heart score: physiological basis and confounding variables. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology 1. Cambridge: Burlington Press; 1998; 121–134.
13. Patteson MW. Equine cardiology. 1st edn. Oxford: Blackwell Science; 1996.
14. Hamlin RL, Klepinger WL, Gilpin KW, et al. Autonomic control of heart rate in the horse. Am J Physiol 1972; 222:976–978.
15. Raekallio M. Long term ECG recording with Holter monitoring in clinically healthy horses. Acta Vet Scand 1992; 33:71–75.
16. Reef VB, Clark ES, Oliver JA, et al. Implantation of a permanent transvenous pacing catheter in a horse with complete heart block and syncope. J Am Vet Med Assoc 1986; 189:449–452.
17. Reef VB, Levitan CW, Spencer PA. Factors affecting prognosis and conversion in equine atrial fibrillation. J Vet Intern Med 1988; 2:1–6.
18. Deem DA, Fregin GF. Atrial fibrillation in horses: a review of 106 clinical cases, with consideration of prevalence, clinical signs, and prognosis. J Vet Intern Med 1982; 180:261–265.
19. Bonagura JD. Equine heart disease. An overview. Vet Clin North Am Equine Pract 1985; 1:267–274.
20. Reimer JM, Reef VB, Sweeney RW. Ventricular arrhythmias in horses: 21 cases (1984–1989). J Am Vet Med Assoc 1992; 201:1237–1243.
21. Cornick JL, Seahorn TL. Cardiac arrhythmias identified in horses with duodenitis/proximal jejunitis: six cases (1985–1988). J Am Vet Med Assoc 1990; 197:1054–1059.
22. Buntenkotter S, Deegen E. Behaviour of the heart rate of horses with auricular fibrillation during exercise and after treatment. Equine Vet J 1976; 8:26–29.
23. Maier-Bock H, Ehrlein HJ. Heart rate during a defined exercise test in horses with heart and lung diseases. Equine Vet J 1978; 10:235–242.
24. Fregin GF, Deem DA. Epistaxis in horses with atrial fibrillation. Proc Am Assoc Equine Pract 1980; 26:431–433.
25. Holmes JR, Henigan M, Williams RB, et al. Paroxysmal atrial fibrillation in race horses. Equine Vet J 1986; 18:37–42.
26. Rose RJ, Davis PE. Paroxysmal atrial fibrillation in a race horse. Aust Vet J 1977; 53:545–549.
27. Gelzer AR, Moise NS, Vaidya D, et al. Temporal organization of atrial activity and irregular ventricular rhythm during spontaneous atrial fibrillation: an in vivo study in the horse. J Cardiovasc Electrophysiol 2000; 11:773–784.
28. Packer M. How should physicians view heart failure? The philosophical and physiological evolution of three conceptual models of the disease. Am J Cardiol 1993; 71:3C–11C.
29. Smith TW, Braunwald E, Kelly RA. The management of heart failure. In: Braunwald E, ed. Heart disease: a textbook of cardiovascular medicine. Philadelphia: WB Saunders: 1992; 464–520.
30. McGuirk SM, Muir WW. Diagnosis and treatment of cardiac arrhythmias. Vet Clin North Am Equine Pract 1985; 1:353–370.
31. Reef VB, Reimer JM, Spencer PA. Treatment of atrial fibrillation in horses: new perspectives. J Vet Intern Med 1995; 9:57–67.
32. Muir WW, Reed SM, McGuirk SM. Treatment of atrial fibrillation in horses by intravenous administration of quinidine. J Vet Intern Med 1990; 197:1607–1610.
33. Marr CM. Treatment of arrhythmias and cardiac failure. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: WB Saunders: 1997; 250–259.
34. Miller MR, McNamara RL, Segal JB, et al. Efficacy of agents for pharmacologic conversion of atrial fibrillation and subsequent maintenance of sinus rhythm: a meta-analysis of clinical trials. J Fam Pract 2000; 49:1033–1046.
35. Naccarelli GV, Dorian P, Hohnloser SH, et al. Prospective comparison of flecainide versus quinidine for the treatment of paroxysmal atrial fibrillation/flutter. The Flecainide Multicenter Atrial Fibrillation Study Group. Am J Cardiol 1996; 77:53A–59A.
36. Ohmura H, Hiraga A, Aida H, et al. Determination of oral dosage and pharmacokinetic analysis of flecainide in horses. J Vet Med Sci 2001; 63:511–514.

37. Ohmura H, Nukada T, Mizuno Y, et al. Safe and efficacious dosage of flecainide acetate for treating equine atrial fibrillation. J Vet Med Sci 2000; 62:711–715.
38. Cobbe SM. Using the right drug. A treatment algorithm for atrial fibrillation. Eur Heart J 1997; 18(suppl C):C33–C39.
39. van Loon G, Jordaens L, Muylle E, et al. Intracardiac overdrive pacing as a treatment of atrial flutter in a horse. Vet Rec 1998; 142:301–303.
40. Opie LH. Drugs for the heart, 4th edn. Philadelphia: WB Saunders, 1995.
41. Fagbemi SO, Chi L, Lucchesi BR. Antifibrillatory and profibrillatory actions of selected class I antiarrhythmic agents. J Cardiovasc Pharmacol 1993; 21:709–719.
42. Wang J, Bourne GW, Wang Z, et al. Comparative mechanisms of antiarrhythmic drug action in experimental atrial fibrillation. Importance of use-dependent effects on refractoriness. Circulation 1993; 88:1030–1044.
43. Reef VB, Marr CM. Holter monitoring in the management of atrial fibrillation following conversion. In: Proceedings of the 11th Annual Veterinary Medical Forum Washington; 1993; 610–613.
44. Moore EN, Spear JF. Electrophysiological studies on atrial fibrillation. Heart Vessels Suppl 1987; 2:32–39.
45. Nattel S. New ideas about atrial fibrillation 50 years on. Nature 2002; 415(6868):219–226.
46. Coumel P. Management of atrial fibrillation. Isr J Med Sci 1996; 32:871–872.
47. Coumel P, Thomas O, Leenhardt A. Drug therapy for prevention of atrial fibrillation. Am J Cardiol 1996; 77:3A–9A.
48. Muir WW, McGuirk SM. Hemodynamics before and after conversion of atrial fibrillation to normal sinus rhythm in horses. J Am Vet Med Assoc 1984; 184:965–970.
49. Collatos C, Clark ES, Reef VB, et al. Septicemia, atrial fibrillation, cardiomegaly, left atrial mass, and *Rhodococcus equi* septic osteoarthritis in a foal. J Am Vet Med Assoc 1990; 197:1039–1042.
50. Gelberg HB, Smetzer DL, Foreman JH. Pulmonary hypertension as a cause of atrial fibrillation in young horses: four cases (1980–1989). J Am Vet Med Assoc 1991; 198:679–682.
51. Else RW, Holmes JR. Pathological changes in atrial fibrillation in the horse. Equine Vet J 1971; 3:56–64.
52. Petch MC. Atrial fibrillation: bad news for man and horse? Equine Vet J 1986; 18:3–4.
53. Else RW, Holmes JR. Cardiac pathology in the horse. 2. Microscopic pathology. Equine Vet J 1972; 4:57–62.
54. Else RW, Holmes JR. Cardiac pathology in the horse. 1. Gross pathology. Equine Vet J 1972; 4:1–8.
55. Cranley JJ, McCullagh KG. Ischaemic myocardial fibrosis and aortic strongylosis in the horse. Equine Vet J 1981; 13:35–42.
56. Button C, Scrutchfield WL, Clark RG, et al. Multiple atrial dysrhythmias in a horse. J Am Vet Med Assoc 1980; 177:714–719.
57. Marr CM, Reef VB, Brazil TJ, et al. Aorto-cardiac fistulas in seven horses. Vet Radiol Ultrasound 1998; 39:22–31.
58. Leroux AJ, Schott HC, Hines MT. Ventricular tachycardia associated with exhaustive exercise in a horse. J Am Vet Med Assoc 1995; 207:335–337.
59. Grubb TL, Muir-WW III. Anaesthetic emergencies and complications – Part 1. Equine Vet Educ 1998; 10:98–109.
60. Opie LH. Electricity out of control: ventricular arrhythmias. In: Opie LH, ed. The heart: physiology from cell to circulation. New York: Lippincott/Raven; 1998; 589–609.
61. Kiryu K, Machida N, Kashida Y, et al. Pathologic and electrocardiographic findings in sudden cardiac death in race horses. J Vet Med Sci 1999; 61:921–928.
62. Traub-Dargatz JL, Schlipf JW Jr, Boon J, et al. Ventricular tachycardia and myocardial dysfunction in a horse. J Am Vet Med Assoc 1994; 205:1569–1573.
63. Machida N, Nakamura T, Kiryu K, et al. Cardiopathological observation on a case of persistent ventricular tachycardia in a pony mare. J Vet Med Sci 1992; 54:1213–1216.
64. van Loon G, Fonteyne W, Rottiers H, et al. Dual-chamber pacemaker implantation via the cephalic vein in healthy equids. J Vet Intern Med 2001; 15:564–571.
65. van Loon G, Laevens H, Deprez P. Temporary transvenous atrial pacing in horses: threshold determination. Equine Vet J 2001; 33:290–295.
66. Hamir AN, Reef VB. Complications of a permanent transvenous pacing catheter in a horse. J Comp Pathol 1989; 101:317–326.
67. Reef VB. Heart murmurs in horses: determining their significance with echocardiography. Equine Vet J Suppl 1995; 19:71–80.
68. Reef VB, Bain FT, Spencer PA. Severe mitral regurgitation in horses: clinical, echocardiographic and pathological findings. Equine Vet J 1998; 30:18–27.
69. Young LE. Cardiac responses to training in 2-year-old Thoroughbreds: an echocardiographic study. Equine Vet J Suppl 1999; 30:195–198.
70. Maxson AD, Reef VB. Bacterial endocarditis in horses: ten cases (1984–1995). Equine Vet J 1997; 29:394–399.
71. Buergelt CD, Cooley AJ, Hines SA, et al. Endocarditis in six horses. Vet Pathol 1985; 22:333–337.
72. Ewart S, Brown C, Derksen F, et al. *Serratia marcescens* endocarditis in a horse. J Am Vet Med Assoc 1992; 200:961–963.
73. McCormicK BS, Peet RL, Downes K. *Erysipelothrix rhusiopathiae* vegetative endocarditis in a horse. Aust Vet J 1985; 62:392.
74. Dedrick P, Reef VB, Sweeney RW, et al. Treatment of bacterial endocarditis in a horse. J Am Vet Med Assoc 1988; 193:339–342.
75. Long KJ. Doppler echocardiography – clinical applications. Equine Vet Educ 1993; 5:161–166.
76. Long KJ. Echocardiographic studies of valvular and ventricular function in horses. PhD thesis, University of Edinburgh; 1993; 221–238.
77. Pollak SJ, McMillan SA, Knopff WD, et al. Cardiac evaluation of women distance runners by echocardiographic color Doppler flow mapping. J Am Coll Cardiol 1988; 11:89–93.
78. Davis JL, Gardner SY, Schwabenton B, et al. Congestive heart failure in horses: 14 cases (1984–2001). J Am Vet Med Assoc 2002; 220:1512–1515.
79. Holmes JR, Miller PJ. Three cases of ruptured mitral valve chordae in the horse. Equine Vet J 1984; 16:125–135.
80. Reef VB. Mitral valvular insufficiency associated with ruptured chordae tendineae in three foals. J Am Vet Med Assoc 1987; 191:329–331.
81. Marr CM, Love S, Pirie HM, et al. Confirmation by Doppler echocardiography of valvular regurgitation in a horse with a ruptured chorda tendinea of the mitral valve. Vet Rec 1990; 127:376–379.
82. Reef VB. Evaluation of ventricular septal defects in horses using two-dimensional and Doppler echocardiography. Equine Vet J Suppl 1995; 19:86–96.

83. Reef VB, Spencer P. Echocardiographic evaluation of equine aortic insufficiency. Am J Vet Res 1987; 48:904–909.
84. Bonagura JD, Pipers FS. Echocardiographic features of aortic valve endocarditis in a dog, a cow, and a horse. J Am Vet Med Assoc 1983; 182:595–599.
85. Sleeper MM, Durando MM, Miller M, et al. Aortic root disease in four horses. J Am Vet Med Assoc 2001; 219:491–496.
86. Horn JNR. Sympathetic nervous control of cardiac function and its role in equine heart disease. PhD thesis, University of London; 2002; 1–193.
87. Reppas GP, Canfield PJ, Hartley WJ, et al. Multiple congenital cardiac anomalies and idiopathic thoracic aortitis in a horse. Vet Rec 1996; 138:14–16.
88. Zamora CS, Vitums A, Nyrop KA, et al. Atresia of the right atrioventricular orifice with complete transposition of the great arteries in a horse. Anat Histol Embryol 1989; 18:177–182.
89. Bayly WM, Reed SM, Leathers CW, et al. Multiple congenital heart anomalies in five Arabian foals. J Am Vet Med Assoc 1982; 181:684–689.
90. Vitums A, Bayly WM. Pulmonary atresia with dextroposition of the aorta and ventricular septal defect in three Arabian foals. Vet Pathol 1982; 19:160–168.
91. Critchley KL. An interventricular septal defect, pulmonary stenosis and bicuspid pulmonary valve in a Welsh pony foal. Equine Vet J 1976; 8:176–178.
92. Muylle E, De Roose P, Oyaert W, et al. An interventricular septal defect and a tricuspid valve insufficiency in a trotter mare. Equine Vet J 1974; 6:174–176.
93. Prickett ME, Reeves JT, Zent WW. Tetralogy of fallot in a thoroughbred foal. J Am Vet Med Assoc 1973; 162:552–555.
94. Vitums A, Grant BD, Stone EC, et al. Transposition of the aorta and atresia of the pulmonary trunk in a horse. Cornell Vet 1973; 63:41–57.
95. Gumbrell RC. Atresia of the tricuspid valve in a foal. N Z Vet J 1970; 18:253–256.
96. Crowe MW, Swerczek TW, Ward Crowe M. Equine congenital defects. Am J Vet Res 1985; 46:353–358.
97. Vanloon G, Deprez P. Echographic diagnosis of complex congenital cardiac anomalies in 2 adult horses. Vlaams Diergeneesk Tijdschr 1998; 67:288–292.
98. Guthrie AJ, Killeen VM, Mulders SG, et al. Use of the cardiopulmonary flow index to evaluate cardiac function in Thoroughbred horses. J South Afr Vet Assoc 1991; 62:43–47.
99. Bila CG, Perreira CL, Gruys E. Accidental monensin toxicosis in horses in Mozambique. J South Afr Vet Assoc 2001; 72:163–164.
100. Bezerra PS, Driemeier D, Loretti AP, et al. Monensin poisoning in Brazilian horses. Vet Hum Toxicol 1999; 41:383–385.
101. Sarcey G, Lorgne G. Les intoxications par les antibiotiques ionophores chez les equides. [Equine intoxications by polyether antibiotics.] Prat Vet Equine 1993; 23:45–50.
102. Doonan GR, Brown CM, Mullaney TP, et al. Monensin poisoning in horses – an international incident. Can Vet J 1989; 30:165–169.
103. Reef VB. Stress echocardiography and its role in performance assessment. Vet Clin North Am Equine Pract 2001; 17:179–189.
104. Reef VB. Electocardiography and echocardiography in the exercising horse. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: WB Saunders; 1997; 234–239.
105. Feigenbaum H. Evolution of stress testing. Circulation 1992; 85:1217–1218.
106. Durnado MM, Reef VB, Birks EK. Right ventricular pressure dynamics: relationship to stress echocardiography. Equine Vet J Suppl 2002; 34:472–477.
107. Morgan SJ, Stromberg PC, Storts RW, et al. Histology and morphometry of *Strongylus vulgaris*-mediated equine mesenteric arteritis. J Comp Pathol 1991; 104:89–99.
108. Fisher EW, Pirie HM, Andrew H. Clinical–pathological correlation of an equine cardiac arrhythmia. Vet Rec 1970; 86:499–502.
109. Blomme EAG, Perle Kl, Wilkins PA, et al. Ionophore toxicity in horses. Equine Vet Educ 1999; 11:153–158.
110. Matsuoka T, Novilla MN, Thomson TD, et al. Review of monensin toxicosis in horses. J Equine Vet Sci 1996; 16:8–15.
111. Dickinson CE, Traub-Dargatz JL, Dargatz DA, et al. Rattlesnake venom poisoning in horses: 32 cases (1973–1993). J Am Vet Med Assoc 1996; 208:1866–1871.
112. Opie LH. Heart failure and neurohumoral responses. In: Opie LH, ed. The heart: physiology from cell to circulation. New York: Lippincott/Raven; 1998; 475–511.
113. Visseren FL, Bouwman JJ, Bouter KP, et al. Procoagulant activity of endothelial cells after infection with respiratory viruses. Thromb Haemost 2000; 84:319–324.
114. Del Piero F. Equine viral arteritis. Vet Pathol 2000; 37:287–296.
115. Brown CC, Meyer RF, Grubman MJ. Presence of African horse sickness virus in equine tissues, as determined by in situ hybridization. Vet Pathol 1994; 31:689–694.
116. Machida N, Taniguchi T, Nakamura T, et al. Cardio-histopathological observations on aborted equine fetuses infected with equid herpesvirus 1 (EHV–1). J Comp Pathol 1997; 116:379–385.
117. Powell DG. Equine infectious respiratory disease. Vet Rec 1995; 96:30–34.
118. Wilson WD. Equine influenza. Vet Clin North Am, Equine Pract 1993; 9:257–282.
119. Worth LT, Reef VB. Pericarditis in horses: 18 cases (1986–1995). J Am Vet Med Assoc 1998; 212:248–253.
120. Freestone JF, Thomas WP, Carlson GP, et al. Idiopathic effusive pericarditis with tamponade in the horse. Equine Vet J 1987; 19:38–42.
121. Hardy J, Robertson JT, Reed SM. Constrictive pericarditis in a mare: attempted treatment by partial pericardiectomy. Equine Vet J 1992; 24:151–154.
122. Dwyer RM, Garber L, Traub DJ, et al. An epidemiological investigation of mare reproductive loss syndrome: breaking ground on a new disease. In: *Society for Veterinary Epidemiology and Preventive Medicine Twentieth Anniversary Proceedings, Cambridge, UK*; 2002.
123. Platt H. Sudden and unexpected deaths in horses: a review of 69 cases. Br Vet J 1982; 138:417–429.
124. Gelberg HB, Zachary JF, Everitt JI, et al. Sudden death in training and racing Thoroughbred horses. J Am Vet Med Assoc 1985; 187:1354–1356.
125. Brown CM, Kaneene JB, Taylor RF. Sudden and unexpected death in horses and ponies: an analysis of 200 cases. Equine Vet J 1988; 20:99–103.
126. Derksen FJ, Reed SM, Hall CC. Aneurysm of the aortic arch and bicarotid trunk in a horse. J Am Vet Med Assoc 1981; 179:692–694.
127. Reef VB, Klumpp S, Maxson AD, et al. Echocardiographic detection of an intact aneurysm in a horse. J Am Vet Med Assoc 1990; 197:752–755.
128. Shirai W, Momotani E, Sato T, et al. Dissecting aortic aneurysm in a horse. J Comp Pathol 1999; 120: 307–311.

129. Holmes JR, Rezakhani A, Else RW. Rupture of a dissecting aortic aneurysm into the left pulmonary artery in a horse. Equine Vet J 1973; 5:65–70.
130. Roby KA, Reef VB, Shaw DP, et al. Rupture of an aortic sinus aneurysm in a 15-year-old broodmare. J Am Vet Med Assoc 1986; 189:305–308.
131. Hillyer MH, Mair TS. Recurrent colic in the mature horse: a retrospective review of 58 cases. Equine Vet J 1997; 29:421–424.
132. Dyson SJ, Worth LT. Aortoiliacofemoral thrombosis. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: WB Saunders; 1997; 267–268.
133. Maxie MG, Physick-Sheard PW. Aortic-iliac thrombosis in horses. Vet Pathol 1985; 22:238–249.
134. Reef VB, Roby KA, Richardson DW, et al. Use of ultrasonography for the detection of aortic-iliac thrombosis in horses. J Am Vet Med Assoc 1987; 190:286–288.
135. Boswell JC, Marr CM, Cauvin ER, et al. The use of scintigraphy in the diagnosis of aortic-iliac thrombosis in a horse. Equine Vet J 1999; 31:537–541.
136. Branscomb BL. Treatment of arterial thrombosis in a horse with sodium gluconate. J Am Vet Med Assoc 1968; 152:1643–1646.
137. Harris PA. Musculoskeletal system. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders, 1998; 371–426.
138. Maxie MG, Physick-Sheard PW. Aortic-iliac thrombosis in horses. Vet Pathol 1985; 22:238–249.
139. Lankveld DPK, Ensink JM, Dijk PV, et al. Factors influencing the occurrence of thrombophlebitis after post-surgical long-term intravenous catheterization of colic horses: a study of 38 cases. J Vet Med Ser A 48:545–552.
140. Rijkenhuizen ABM, Swieten HV, Van Swieten HA. Reconstruction of the jugular vein in horses with post thrombophlebitis stenosis using saphenous vein graft. Equine Vet J 1998; 30:236–239.
141. Wiemer P, Ugahary F. Chirurgische behandeling van een oblitererende trombose van de vena jugularis van een paard. Gebruik van een synthetische vaatprothose. [Surgical treatment of obliterating jugular vein thrombosis in a horse, using a synthetic vascular prosthesis.] Tijdschrift Diergeneeskunde 1998; 123:40–44.
142. Ben Chehida N, Bellagha A, Bardi K. Traitement d'une thrombophlebite chez un cheval par une prothese en polytetrafluoroethylene (PTFE). [Treatment of thrombophlebitis in a horse using a polytetrafluoroethylene (PTFE) prosthesis.] Prat Vet Equine 1994; 26:169–173.
143. Brianceau P, Divers TJ. Acute thrombosis of limb arteries in horses with sepsis: five cases (1988–1998). Equine Vet J 2001; 33:105–109.
144. Morris DD. Cutaneous vasculitis in horses: 19 cases (1978–1985). J Am Vet Med Assoc 1987; 191:460–464.

CHAPTER 34

Metabolic responses to exercise and training

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Introduction

The superior performance capacity of horses may have its roots in evolution as the means for a horse to escape its predators, and natural selection has led to the survival of the fastest individuals. Several physiologic factors contribute to the horse's athletic prowess. Aerobic capacity, as indicated by maximal oxygen uptake,[1–3] is more than twice that of elite human athletes. This exceptional oxygen uptake is made possible by a high cardiac output and capillary and mitochondrial density in skeletal muscle, and also by the splenic reservoir of 4–12 L of red blood cells released into circulation at the beginning of exercise. Several studies in horses and other species have shown that the augmentation in oxygen-carrying capacity resultant from increased red cell volume markedly increases aerobic capacity.[4–6] The horse is also advantaged by high muscle glycogen stores[7,8] that provide a readily available pool of substrate for ATP synthesis, thereby avoiding limitations to performance associated with inadequate substrate supply. In addition, equine skeletal muscle has higher buffering capacity compared to other species[9] which allows the horse to tolerate high muscle lactate concentrations during exercise.[10–12] Not only is the muscle able to tolerate high concentrations of lactate, but also the behavior of equine red blood cells (RBC) appears to differ from that of other athletic species. In horses, but not in other species studied so far, RBC appear to function as a lactate sink which may contribute to the efflux of lactate from contracting skeletal muscle.[13–16]

Skeletal muscle is well adapted for upregulation of metabolic rate with increasing intensity of exercise. For example, oxygen uptake, which at rest may be as low as 4 mL/kg/min,[6] increases in exercising horses up to 160–200 mL/kg/min.[1–3] In Standardbred horses running at 100% of $\dot{V}O_{2max}$, total muscle blood flow has been estimated at 226 L/min or approximately 78% of total cardiac output.[17] Therefore, the increase in metabolic rate is even greater in contracting skeletal muscle and oxygen consumption may approach 250 mL/per kg muscle per min.[18] This change in oxygen uptake indicates acceleration of aerobic pathways for energy

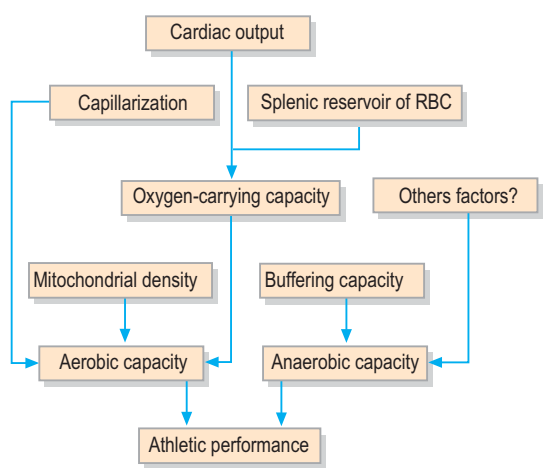

Fig. 34.1
Athletic performance from a metabolic viewpoint is a sum of aerobic and anaerobic capacities. When energy sources are not limiting, aerobic capacity depends both on the availability of oxygen and the ability of muscle tissue to use oxygen for energy. Much less is known about the factors, other than buffering capacity, that influence anaerobic capacity.

transduction, but during high-intensity exercise the rate of anaerobic metabolism also increases. Adenosine triphosphate (ATP) content in muscle remains nearly constant over a large range of changes in muscle activity,[19–22] indicating that ATP demand for muscle contraction is balanced by adenosine diphosphate (ADP) rephosphorylation. During maximal exercise or due to shortage of glycogen and other fuels, the rate of ATP utilization may exceed the rate of production, with resultant activation of the enzyme myokinase and eventually loss of adenine nucleotides. In human skeletal muscle, energy consumption may be up to 3 mmol ATP/kg muscle per s[23] and if it is assumed that similar maximal rates occur in equine muscle during intense exercise, it is evident that ATP resynthesis from the aerobic oxidation of glucose or fatty acids will not meet energy demands during maximal exercise.[24] The remainder must be derived from anaerobic processes, mainly glycolysis of glucose to lactate.

Integration of various body systems

Exercise requires the co-ordinated function of the central nervous, respiratory, cardiovascular, hematologic and musculoskeletal systems. At the onset of exercise, the rapid and pronounced effects on the cardiovascular system and overall metabolic rate are initiated and controlled by neuroendocrine mechanisms with the catecholamines norepinephrine and epinephrine being the primary regulators. These hormones are synthesized and secreted by the adrenal medulla; norepinephrine also by postganglionic sympathetic neurons. In horses, high plasma concentrations of epinephrine during exercise suggest that the adrenal medulla plays a more important role in the sympathoadrenal response than in other species.[25] Heart rate increases from the resting level of 30–40 beats per minute (bpm) up to 200–250 bpm.[26] In addition, cardiac contractility increases and systole is shortened. Together, these changes result in an up to 10-fold increase in cardiac output, which in horses during exercise may be over 300 L/min, a value that is 2–3 higher than in steers of the same size.[27] Catecholamines also cause contraction of the spleen and thus the release of 4–12 L of red blood cells into circulation.[4,28] Due to neural factors, hypoxia and hormones such as atrial natriuretic peptide, arginine vasopressin and hormones of the renin–angiotensin system, vasodilation occurs in muscles, thereby reducing total peripheral resistance.[29] Simultaneous vasoconstriction and reduction in blood flow to other tissues allows blood flow in skeletal muscle to increase by 70–76-fold,[26] while an 80% reduction in renal blood flow has been reported.[18,29–31]

The rate of respiration, which in galloping horses is coupled to stride frequency, also increases. Catecholamines are involved in the stimulation of respiration rate and also contribute to an increase in minute ventilation via relaxation of bronchioles.[32]

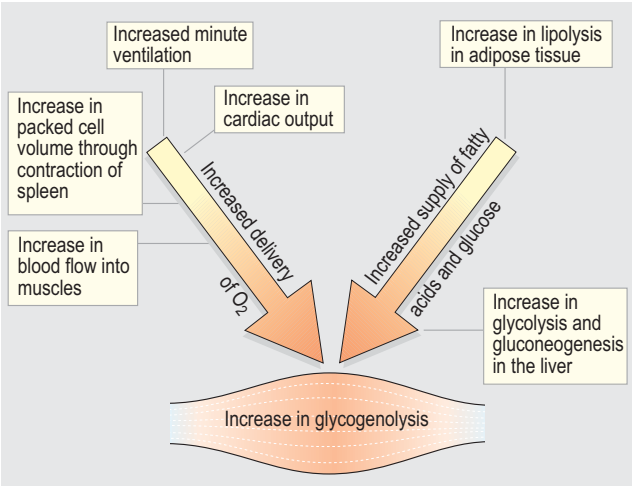

Fig. 34.2
Exercise-induced changes in various body systems. Delivery of oxygen to working muscles is increased due to the effects of catecholamines and other hormones on the lungs, heart, spleen and blood vessels. Simultaneously, catecholamines together with other catabolic hormones increase the supply of energy substrates via circulation and through increased breakdown of muscle glycogen.

Hormonal mechanisms are also important for the mobilization and utilization of energy substrates. The catecholamines together with insulin and cortisol increase the availability of fuels for energy transduction. In muscle, rapid degradation of glycogen is induced through activation of glycogen phosphorylase and inhibition of glycogen synthesis. Similar changes in the liver lead to release of glucose into circulation, which is further augmented through stimulation of gluconeogenesis. In adipose tissue, catecholamines activate hormone-sensitive lipase, which results in an increase in the plasma concentration of free fatty acids. The inhibitory effect of insulin on lipolysis is attenuated as epinephrine decreases the release of insulin from pancreas (Fig. 34.2).

Methods of assessing metabolic responses to exercise

Exercise testing

To allow day-to-day or horse-to-horse comparisons, conditions for exercise testing should be standardized, which usually means the use of a high-speed treadmill. Modern, high-speed treadmills are capable of speeds in excess of 17 m/s. However, for safety reasons exercise tests involving maximal effort are often performed at lower speed with the treadmill set at an incline of up to 6° (10% grade). The advantages of treadmill testing are obvious – the speed and duration of exercise bouts can be controlled and the ambient

Fig. 34.3
A horse running on a high-speed treadmill. (Courtesy of Yrjö Tuunanen.)

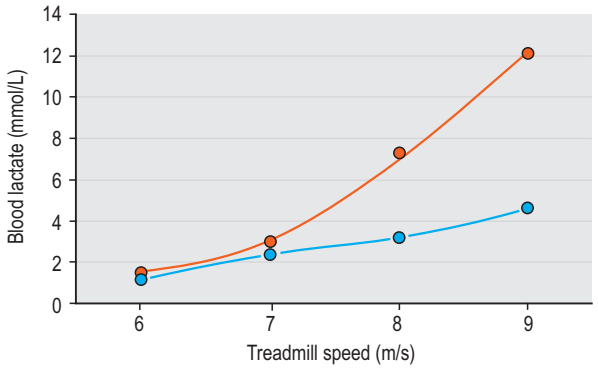

Fig. 34.4
Blood lactate response to submaximal treadmill exercise depends on the aerobic capacity of the horse. In untrained horses (orange circles) 2-minute steps at speeds indicated on the *x*-axis induce a rapid increase in blood lactate concentration, while the higher aerobic capacity of trained horses (blue circles) allows energy transduction without accumulation of lactic acid.

temperature can be kept constant. Furthermore, in countries where the ambient temperature and humidity are usually low, a climate-controlled treadmill laboratory facilitates exercise testing under conditions of high temperature and/or humidity.[33–35] Equally important is that while the horse is moving, blood samples can be taken through a catheter placed in a vein or an artery either with a syringe or constantly with the help of a peristaltic pump and a fraction collector.[36] Heart rate can be monitored with a pulse meter or by calculating it from an electrocardiogram and activity of different muscles can be recorded by electromyography.[37] Furthermore, the horse can be equipped with a mask that allows measurement of respiratory gases. Additional weight may be placed on the horse to simulate the weight of a rider or the horse can actually be mounted by an experienced rider.[38] The treadmill is also a suitable tool to study locomotion, because the horse is not moving forward and thus it is possible to film movements with a high-speed camera (Fig. 34.3).

Several types of treadmill tests have been developed since 1960s when Professor Sune Persson in Sweden designed a submaximal standardized exercise test,[4] modifications of which are nowadays frequently used all over the world. In the original test the horse runs four successive 2-minute intervals with the aim of reaching a heart rate of 200 bpm at the highest speed. Blood samples are taken at the end of each 2-min bout that is long enough to allow the heart rate to level off at each speed. This test and its modifications, which include differences in the incline and the duration of exercise intervals, are very useful, for example, for determination of lactate threshold and other indices of aerobic capacity. A typical result from such an exercise test for two horses, one well trained and the other less trained, is shown in Figure 34.4.

In tests to determine maximum heart rate and oxygen uptake ($\dot{V}O_{2max}$) the intervals are usually shorter, often 1 min, up to a speed when the horse is no longer able to keep up with the treadmill. Treadmill tests are also well suited for endurance-type exercise. The speed may be constant throughout the test or may include faster and slower phases. The duration of the test is either determined in advance or the test is continued until the onset of fatigue. The test may also be designed to simulate a specific type of event, such as the competition exercise test that simulates the endurance test of a three-day event.[39] It is also possible to load the horse with additional weights in a system that simulates draught work.[40] Because some indices of exercise capacity, such as V_{La4} (the running speed that elicits a blood lactate concentration of 4 mmol/l) or V_{200} (the running speed that elicits a heart rate of 200 bpm), may be influenced by apprehension, the horses should be acclimatized to the treadmill, a procedure that usually takes 1–2 exposures.[41]

The main drawback of treadmill exercise testing is the expensive equipment needed. Therefore horses are often tested on a track, where it is possible to simulate any type of competition but more difficult to control the speed and take blood samples when compared to treadmill testing procedures. Also the testing conditions may vary from one testing occasion to another, because ambient temperature, wind, track surface and other extraneous factors in the vicinity of the track may influence the results. Furthermore, the horse has to be stopped every time a blood sample is taken and therefore the speed cannot be increased as smoothly as on a treadmill. The stop, although short, may also influence the concentrations of metabolites in blood. Several studies show, however, that track tests are reproducible and reliable,[42–44] but comparison to treadmill tests is difficult.[45]

Samples and measurements to study the effects of exercise

Blood samples are often used to estimate the effects of exercise, as they are easier to collect and less invasive than muscle

samples. From a metabolic viewpoint, the most interesting samples would be those taken from veins coming directly from exercising muscles, especially if combined with arterial samples. These would allow for calculation of oxygen uptake, the consumption of various fuels and the efflux of catabolic products. However, for practical reasons samples are most often taken from the jugular vein, which represents mixed venous blood. For some metabolites, the concentrations in jugular venous blood are similar to those in arterial blood,[46] while others such as lactate differ.[47] It should, however, be kept in mind that concentration of any substance in blood is a sum of its release into and its disappearance from the blood and the analysis of blood samples gives information only about the very moment the sample is taken, but does not tell anything about the rates of events.

Metabolites, such as non-esterified fatty acids (NEFA), are usually analyzed from blood plasma or serum but for some analysis, especially glucose and lactate, whole blood can also be used. The analysis of lactate is complicated because equine RBC appear to function as a lactate sink and up to 50% of blood lactate may be in RBC.[13,48] Although there is a close correlation between whole-blood and plasma lactate concentrations,[13,49] this is not true on an individual basis because the uptake of lactate into RBC varies interindividually.[15,48] On the basis of lactate transport activity, Standardbred horses can be divided into two populations: one with high and the other with low lactate transport activity in their RBC.[15,50] Lactate transport capacity appears to be inherited with the high capacity being caused by the dominant allele.[50] Because of this interindividual variation in lactate distribution and differences in arterial and venous lactate concentrations,[47] it is extremely important to standardize the sampling and the treatment of samples when, for example, lactate threshold values are measured. To demonstrate the effects of RBC lactate transport activity on the interpretation of blood lactate data, the following example is given. Two horses had the same blood lactate concentration of 18.7–18.8 mmol/L after exercise. One of the horses with high lactate transport activity in its RBC had a plasma lactate concentration of 21.4 mmol/L, while the other with low lactate transport activity in RBC had a plasma lactate concentration of 29.6 mmol/L. Thus, if lactate threshold was calculated on the basis of blood lactate concentrations the two horses would have had the same value, but if the determination was based on plasma values a significant difference would have been recorded.[24]

As stated above, the blood samples are not suitable to measure rates or fluxes. To study these isotope techniques are available. When a small amount of a substrate labeled with a radioactive, e.g. ^{14}C, or a stable, non-radioactive, e.g. ^{13}C, isotope is infused into the circulation, the disappearance of the isotope can subsequently be analyzed from serial blood samples and the rate of substrate utilization can be calculated. Of these alternatives, the use of stable, non-radioactive isotopes is safer but the disadvantages are the high price of stable-isotope labeled substrates as well as the complexity of the analysis techniques, which also requires special apparatus.[51–53] Recent equine studies have employed stable isotope tracer techniques in exercise studies. Geor et al,[54–57] Jose-Cunilleras et al[58] and Pagan et al[59] used a constant-rate infusion of a stable isotopically labeled tracer of glucose in order to quantify rates of glucose production and utilization during sustained exertion. From concurrent calculations of whole-body rates of carbohydrate (CHO) oxidation and the rate of plasma glucose disappearance (glucose R_d), it was also possible to estimate the contribution by plasma glucose and intramuscular CHO (glycogen and lactate) to total CHO use. The latter calculations were based on the assumption that the glucose R_d was equal to actual plasma glucose oxidation rate. This assumption has been validated in human subjects during exercise[60] but not yet verified in horses.

Metabolic changes in muscle are determined by analysis of biopsy samples, which are usually taken from the middle gluteal muscle at the depth of 2, 4 or 6 cm.[61–65] If samples are taken before exercise and immediately after exercise, it is possible to estimate the consumption of glycogen and accumulation of lactate. Muscle samples are also useful to follow the recovery of energy stores and to evaluate training effects, because in addition to the changes in fuels and metabolites, it is also possible to determine the muscle fiber composition, capillarization and mitochondrial density and to measure activity of enzymes.

Muscle samples can be analyzed as a mixed sample containing all fiber types or on a single fiber or fiber-type basis. For practical reasons most biochemical analyses are performed on mixed muscle samples because of the substantially greater amount of work required for isolation of single fibers. A semiquantitative alternative is the use of histochemical analysis, e.g. for the analysis of glycogen in single fibers. The differences in the results between mixed muscle and single fiber analysis may be enormous. Concerning glycogen analysis, a 50–60% decline may be observed in homogenates of mixed muscle obtained after exercise, but examination of individual fibers from the same sample may reveal complete depletion of glycogen in some fibers and minimal change in others.[66–69] The same is true for ATP. The concentrations of ATP in some fibers are extremely low after maximal exercise, while in other fibers from the same sample the levels are close to resting values.[70,71]

Lactate threshold (V_{La4}) and the speed of the horse at a heart rate of 200 bpm (V_{200}) are useful indicators of aerobic capacity and frequently used in the evaluation of fitness and state of training. These indices are easy to measure, can be determined both on a track and a treadmill and do not require any expensive equipment. Metabolically, lactate threshold is said to represent the maximal work intensity at which ATP is produced aerobically, i.e. there exists a steady-state situation in blood lactate concentration, wherein lactate is released (mainly from muscles) into circulation at the same rate as it is used by other tissues. Based on studies in humans, it has been shown that blood lactate concentration starts to increase exponentially around a concentration of 4 mmol/L. Similarly, in horses lactate threshold is expressed as the speed of the treadmill or the speed of the horse on a track when blood lactate concentration is 4 mmol/L.

The speed at a heart rate of 200 bpm (V_{200}) has been suggested to indicate both the cardiovascular and metabolic capacities of a horse.[72] Aerobic capacity, measured as maximum oxygen uptake ($\dot{V}o_{2max}$), correlates with the running speed over 2000 m.[73] $\dot{V}o_{2max}$ is also useful, because thereafter it is possible to express workloads as a percentage of $\dot{V}o_{2max}$.[74] Rose et al[75] used different exercise protocols to determine $\dot{V}o_{2max}$ and found that the test itself did not markedly influence the results and the close correlation between maximum oxygen uptake and maximum heart rate allows estimation of the former on the basis of the latter variable.[76]

Anaerobic capacity is far more difficult to estimate and many of the tests used to evaluate anaerobic power of human athletes are not suitable for horses. So far, the only test that can be applied from human sports medicine is the measurement of maximal accumulated oxygen deficit (MAOD), which is calculated from the difference of calculated O_2 demand and maximum oxygen uptake.[77]

The expired gases, oxygen and carbon dioxide, can additionally be used to calculate the respiratory exchange ratio (R), i.e. the ratio of carbon dioxide produced over oxygen consumed. Using stoichiometric equations for the combustion of CHO and fat, values for R can be used to estimate the relative contribution of these substrates to energy expenditure during exercise. It should be noted, however, that these estimates are invalid at high work intensities wherein a portion of expired CO_2 is derived from the bicarbonate buffer system (the buffering of lactic acid) and values for R may be greater than 1.0.

Sources of metabolic fuel

Fuel for ATP synthesis in skeletal muscle is either stored in the muscle cells or taken up from the circulation. The utilization of fuels is limited by their availability, activity of oxidative enzymes and the availability of oxygen for their complete oxidation and/or the density of mitochondria in the muscle. Major fuels stored in the muscle fibers are glycogen, triglycerides and phosphocreatine and the fuels from circulation are fatty acids and glucose. Because water content of the muscle cells may change during exercise, the concentrations of muscle substrates are often expressed as mmoles (or μmoles) per kg dry muscle.

Equine skeletal muscle has a high capacity to store glycogen; in trained horses, typical values are around 600–650 mmol/kg dry muscle.[66,68,78–80] In human muscle, similar high values are reached only after successful carbohydrate loading procedures. The hydrolyzable carbohydrate content of typical feeds for athletic horses is already high and additional carbohydrate supplementation only slightly increases muscle glycogen content.[81–83] The content of triglycerides in equine skeletal muscle is highly variable.[83,84] The third form of fuel stored is phosphocreatine (PCr), a high-energy phosphate. Although the content of PCr is enough to support ATP production for a few seconds only, it is important both in the beginning and at the end of maximal effort.

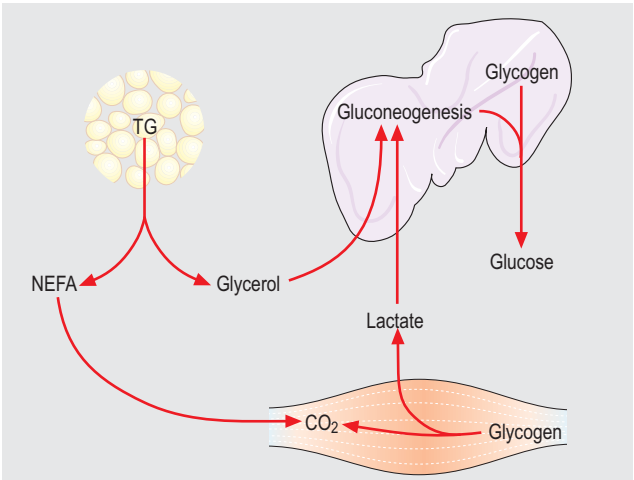

Fig. 34.5 During exercise, energy stores in muscle, liver and adipose tissue are mobilized by the action of catecholamines and other hormones. Fatty acids (NEFA) are released from triglycerides (TG) in adipose tissue and transported by circulation to the working muscles. Muscle glycogen is the body's main store of carbohydrates, but additional glucose from liver glycogen and gluconeogenesis is provided via circulation.

The main energy stores outside the muscle tissue are adipose tissue for lipids and liver for glucose, the latter derived from hepatic glycogenolysis and gluconeogenesis. During exercise, an increase in epinephrine concentration contributes to the mobilization of these energy stores. Glucose is released from liver, through the action of glucose–6-phosphatase, and lipids from adipose tissue enter circulation as non-esterified fatty acids (NEFA). Additional glucose may be produced in the liver from glycerol that is a byproduct of lipolysis as well as lactate and alanine formed in the muscle (Fig. 34.5).

The release of nutrients from the gastrointestinal tract depends on pre-exercise feeding regimens (see below). In general, equine diets are rich in carbohydrates (e.g. hemicellulose) that are not degraded by salivary and pancreatic amylase, but rather are subjected to bacterial fermentation in the cecum and colon. Short-chain (or volatile) fatty acids, mainly acetate, propionate and butyrate, are produced via this process. It has been shown that, at rest, acetate may provide approximately 30% of the energy utilized by the hindlimb,[85] while propionate is used mainly for gluconeogenesis.[86,87] The direct contribution of these substrates to energy use during exercise is not known.

Major metabolic pathways for energy transduction

ATP for muscle contraction may be produced by aerobic and anaerobic pathways. It has to be kept in mind that ATP is not a storage form of energy. Rather, it is the 'metabolic currency'

for cellular processes such as muscle contraction and because cellular stores are small, the rate of ATP synthesis must keep pace with utilization.

Equine skeletal muscle has a high oxidative capacity and, in trained horses, all type I and type IIA fibers are rich in mitochondria and the activities of oxidative enzymes such as citrate synthase (CS) and 3-hydroxyacyl-CoA dehydrogenase (HAD) are high.[88–91] Both carbohydrates and fatty acids can be used as substrates for aerobic energy transduction, the proportion of which varies with the intensity of exercise. During a 400 m Quarter Horse race, about 40% of energy is derived from aerobic metabolism, while aerobic metabolism accounts for 70–80% of the energy used by Thoroughbreds and Standardbreds in races of 1600–2100 m.[92] During endurance events, nearly all energy metabolism is aerobic.[92]

At rest, when the plasma concentration of fatty acids is low, blood glucose may account for about 80% of oxygen consumed by the hindlimb.[85] The capacity of aerobic metabolism is limited by oxygen delivery or the capacity of muscle fibers to use oxygen. The main anaerobic pathway of energy metabolism is glycolysis for which glucose is either derived from blood or from the glycogen stored in muscle. Although the yield of ATP per one mole of glucose degraded is only 2–3 moles, muscle has a high glycolytic capacity. On the basis of glycolytic enzyme activities measured in equine[79,90,93] and human[23] skeletal muscle, the capacity for anaerobic energy transduction is well in excess of the maximal rate of energy consumption. The disadvantage of this mechanism is the excessive production of lactic acid which eventually will lead to fatigue (Fig. 34.6).

Mechanisms of fatigue

Both high- and low-intensity exercise eventually result in fatigue, but the mechanisms are completely different: the accumulation of lactic acid and other metabolic byproducts during intense exercise versus substrate depletion (fuel shortage) during longer duration exercise at low or moderate intensity. After high-intensity exercise, lactic acid concentrations in muscle range from 100 to 200 mmol/kg dry muscle.[10–12,19,22,94] The accompanying increase in proton concentration results in a marked decrease in muscle pH, with values as low as 6.5–6.3 measured in horses following intense, fatiguing exercise.[19,95] The decrease in pH may be the single most important factor in the development of fatigue during intense exercise. Low pH disturbs calcium release and especially calcium uptake by the sarcoplasmic reticulum, and thus the relaxation phase of muscle contraction cycle is slowed. ATP synthesis is also compromised because the key regulatory enzyme of glycolysis, phosphofructokinase, is inhibited by protons. Furthermore, acidification changes the structure of myosin heads such that the efficiency of ATP binding decreases.[96]

The means to prevent intramuscular acidosis include buffers, the most important of which are proteins, the bicarbonate system, phosphate and carnosine.[96,97] Although buffering capacity of equine muscle is higher than in other species, it is still not enough to prevent acidosis.[9,98] The second mechanism for regulation of cell pH is the transport of protons out of the cell.[99,100] Only the acid form, lactic acid, is able to diffuse through cell membranes; both protons and lactate anions require a transporter for transmembrane movement. In skeletal muscle, there are two carriers that may facilitate the efflux of protons: the Na^+/H^+ exchange protein and monocarboxylate transporters.[99,100] During Na^+/H^+ exchange, one Na^+ is transported into the cell and simultaneously one H^+ is carried out from the cell. There are no studies on the activity of Na^+/H^+ exchange in equine muscle, but in human muscle this carrier plays a minor role and monocarboxylate transporters (MCT), which simultaneously transport one proton together with one lactate anion, are responsible for most proton efflux.[99,100] Several isoforms

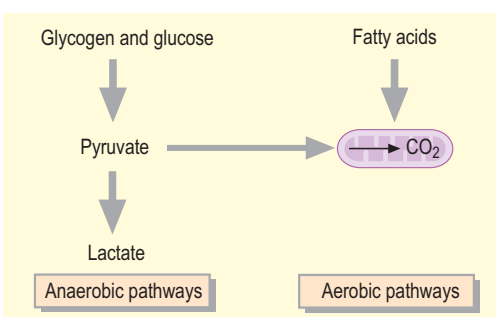

Fig. 34.6 The capacity (indicated by the breadth of the arrows) of glycolytic enzymes to produce energy by anaerobic metabolism is high in comparison to aerobic pathways from glucose and fatty acids. The latter are limited by transport of substrates across cell membranes, the number of mitochondria, the activity of mitochondrial enzymes and the availability of oxygen.

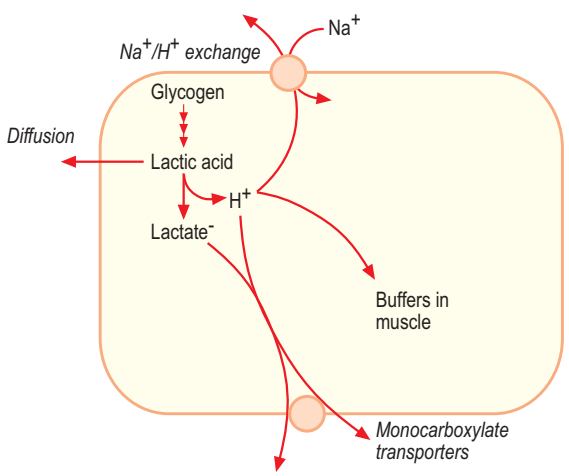

Fig. 34.7
Lactic acid formed via anaerobic glycolysis is almost completely dissociated into a lactate anion and a proton. The means to prevent acidification of the cell include different buffer systems and transport of hydrogen ions out from the muscle cell. Most hydrogen ions are transported by the monocarboxylate transporter (MCT) with Na^+/H^+ exchange playing a minor role.

of MCTs have been characterized, but only two or three are expressed in skeletal muscle. The main isoforms in muscle are MCT1 and MCT4 and, in some species, MCT2 is also expressed.[101–103] MCT1 and MCT4 have also been found in equine skeletal muscle (Koho N, Hyyppä S, Pösö AR, unpublished observation). In human athletes, MCT1, which is the main lactate carrier in oxidative muscles, is upregulated by exercise. On the other hand, the content of MCT4, which is the dominant isoform in glycolytic fibers, increases only with high-intensity training.[105,106] In human subjects, the endurance training-associated decrease in muscle lactate accumulation during exercise is associated with an increase in skeletal muscle MCT content,[107] demonstrating the importance of MCTs for the regulation of intramuscular pH (Fig. 34.7).

During high-intensity exercise acidification may be the main reason for fatigue, but a reduction in energy stores may be another contributing factor. After maximal exercise (e.g. trotting races), some muscle fibers appear to be completely devoid of glycogen and studies of single fibers demonstrate marked ATP depletion.[66,68,70,71] In rats, there is a linear relationship between ATP degradation in skeletal muscle and the development of fatigue during high-intensity exercise[108] and depletion of ATP during maximal tests suggests that a similar relationship may also exist in horses.[11,109]

During endurance exercise, the intensity is usually low to moderate and there is no marked accumulation of lactic acid.[67,79,110,111] Therefore, acidification is not a major cause of fatigue. From a metabolic viewpoint, the major contributing factor to the development of fatigue is a shortage of fuel, especially depletion of glycogen stores,[79,83] as demonstrated by a correlation between the extent of glycogen depletion and the duration of exercise.[112] Low blood glucose concentration also may contribute as it limits the glucose availability to the central nervous system. In addition, central fatigue may be due to increased formation of serotonin in the central nervous system.[113]

During endurance exercise, factors not related to substrate supply may be more important in the development of fatigue. These include the loss of electrolytes in sweat which may disturb the neuronal control of muscle contractions, loss of water in sweat that may hamper oxygen and substrate supply via the circulation, and hyperthermia.

Responses and mechanisms

Responses in metabolite concentrations in plasma

During exercise, the major hormonal change in blood is an increase in the concentrations of norepinephrine and epinephrine that, in addition to their effects on the cardiovascular and respiratory systems, induce metabolic changes in muscle, liver and adipose tissue. The increase in catecholamine concentrations occurs at the onset of exercise and is proportional to exercise intensity. In horses during maximal effort, the responses are several fold greater than in humans.[25,114,115] Other hormonal changes with metabolic implications include a decrease in insulin and increases in cortisol and glucagon.[54,111,116–118]

Due to the above-mentioned hormonal changes, concentrations of metabolic fuels such as NEFA and glucose are increased in circulation. NEFA is released from the adipose tissue together with glycerol. It has been suggested that of these two, glycerol is a more reliable indicator of lipolysis.[119,120] The background to this suggestion lies in the fact that muscle tissue, which accounts for about 40% of the bodyweight, is the main user of NEFA and thus even small changes in the oxidation of fatty acids in the muscle will greatly influence the concentration of NEFA in plasma. On the other hand, the concentration of glycerol is not influenced by changes in muscle metabolism as it is mainly utilized by the liver. This is demonstrated by studies in which NEFA and glycerol concentrations have been measured in tests where the intensity of exercise varies. The results show that NEFA concentration decreases significantly during intense exercise, while glycerol concentration increases steadily.[80,120,121] Especially during low-to-moderate intensity exercise, there is a progressive increase in lipid oxidation with increasing exercise duration.[82,122] Horses differ from other athletic animals in that there is an increase in the circulating triglycerides (TG) during exercise.[121] TG are released from the liver as very low density lipoproteins (VLDL),[121] and may have been synthesized in response to increased delivery of NEFA to the liver. Lipoprotein lipase located on the outer side of the endothelial membranes in muscle capillaries will release fatty acids from circulating VLDL-TG for oxidation in muscles.

Changes in blood glucose concentration depend on the type of exercise. Plasma glucose concentration tends to decrease during prolonged exercise (> 3 hours), but during short, intense exercise both decreases and increases have been recorded,[67,118,120,123,124] depending on exercise intensity and training and feeding status of the horse. The regulation of blood glucose during exercise is complex, but changes in prevailing hormone concentrations are important. The exercise-associated increase in hepatic glucose output is mainly mediated via a decrease in the insulin:glucagon ratio, whereas the rate of uptake and utilization in exercising muscle is restrained by increases in circulating epinephrine.[56]

As discussed earlier, lactate is the end-product of anaerobic metabolism and lactate concentrations in blood increase during high-intensity exercise. Lactate concentrations after different types of competitions and exercise tests are shown in Table 34.1. Usually, the highest lactate concentrations are seen 2–10 minutes after exercise. In equine blood, a significant amount of lactate may be in RBC; uptake is rapid and depends on the activity of MCT on the RBC membrane.[48]

As a result of ATP degradation during high-intensity exercise, breakdown products of purine nucleotides such as ammonia, hypoxanthine, uric acid and allantoin appear in blood.[14,22,109,127,134] In horses, the predominant end-products of purine catabolism are uric acid and allantoin. The time to peak concentration varies individually and peak

Table 34.1 Maximal lactate concentrations after exercise (values are means ± standard error of the mean)

	Distance/time	Blood lactate (mmol/L)	Plasma lactate (mmol/L)	References
Endurance races	80–100 km	1.6 ± 0.1	0.50 ± 0.2	111,116,126
Standardbred races (trotting)	2100 m	21.6 ± 0.9	24.5 ± 0.7	13,91
Standardbred races (pacing)	1760–2160 m		20.9 ± 4.1	130
Thoroughbred races	1100–3800 m	29.6 ± 4.7	33 ± 1.9	47,126–129
Three-day event, cross-country	6200 m		19.1 ± 4.2	126,131
Showjumping			9.0 ± 0.9	132
Polo			9.2 ± 1.2	125
Donkey after exercise			10 ± 1.4	133

concentrations are reached as late as 30 min after exercise.[134,135] Marked accumulation of uric acid, allantoin and ammonia is seen mainly after intense exercise and the breakdown of adenine nucleotides is probably triggered by accumulation of ADP and the decrease in muscle pH.[127,135,136] In horses, the threshold value for accumulation of these breakdown products is a muscle pH of 6.8, which represents a lactate concentration of 80 mmol/kg dry weight in muscle and about 12 mmol/L in blood.[22,134] It has been suggested that the peak concentration of uric acid or ammonia is useful as an indicator of ATP degradation in muscles.[135]

Changes in muscle

In muscle, the most prominent changes are a decrease in glycogen content, accumulation of lactic acid and degradation of ATP and phosphocreatine (PCr). Glycogen, which is stored as macro- and proglycogen molecules, is the target for glycogen phosphorylase that is activated by muscle contraction and epinephrine. From the molecular weight it can be calculated that macroglycogen has about 2100 non-reducing ends from which the release of glucose may begin simultaneously.[137] Proglycogen, on the other hand, has a much smaller molecular weight and the number of non-reducing ends in this type of glycogen is only 64–128 per molecule.[137] In humans, proglycogen appears to be more readily available for degradation and in the early phases of exercise, especially when exercise intensity is low to moderate, glycogen breakdown occurs from proglycogen molecules only.[138,139] In horses during an endurance race, macroglycogen is utilized to a greater extent than proglycogen.[140] Breakdown of macroglycogen is activated only at high-intensity exercise in humans,[138] but in horses during intense exercise both pro- and macroglycogen seem to contribute equally to glycogenolysis.[141] Although the physiological roles and regulation of macro- and proglycogen metabolism are far from clear, subcellular location and the density of branches in the outer tiers of the molecules may be involved.[139]

As mentioned, during fatiguing high-intensity exercise muscle glycogen concentration decreases by up to 50%. Although fatigue during such exercise is often ascribed to accumulation of lactic acid and depletion of PCr and ATP,[69,109] depletion of glycogen in individual fibers may also contribute.[66,69] After endurance rides a more complete depletion of glycogen is seen and, in some horses, muscle biopsy samples may be completely devoid of glycogen.[67,110]

Marked accumulation of lactate in muscle is seen only when the intensity of exercise exceeds the anaerobic threshold. After a near-maximal exercise test, lactate accumulation in muscle correlates with the amount of glycogen utilized.[142] Accumulation depends also on the oxidative capacity of muscle,[94,142] and thus horses that have a high proportion of type IIB fibers with low oxidative capacity have higher lactate concentrations in their muscles after high-intensity exercise.[94] In addition, muscle hemodynamics[100,143] and the activity of monocarboxylate transporters[107] (i.e. the rate of lactate efflux) will influence the extent of lactate accumulation in muscle. Muscle lactate concentrations up to 200 mmol/kg dry weight have been measured in equine muscle.[12,22]

The changes in muscle TG content with exercise are more difficult to estimate because interindividual variation, both in TG content and utilization rate, is high.[83,84,142] In middle gluteal muscle, TGs are stored mainly in type I fibers and type IIB fibers have the lowest content.[79] A decrease in muscle TG content is more evident in association with endurance-type exercise,[79,82,122] but a decrease also may occur after short, near-maximal exercise.[142]

Phosphocreatine (PCr), a high-energy phosphate stored in muscle, is depleted during high-intensity exercise.[21,109,135,144] The synthesis of PCr after exercise is very rapid and thus results are greatly influenced by the time of sampling in relation to end of exercise. ATP concentration starts to decline and ADP begins to accumulate when ATP consumption exceeds the capacity of ADP rephosphorylation. The myokinase reaction (ADP + ADP → ATP + AMP) is activated to keep the concentration of ADP low. To drive this reaction towards formation of ATP, AMP is further deaminated to inosine monophosphate (IMP). The accumulation of IMP closely mirrors the loss of ATP.[127] This reaction cascade eventually leads to loss of adenine nucleotides and fatigue will follow.

Partitioning of energy supply at different workloads

The relative contribution of different substrates (i.e. carbohydrate, fat, protein) to fuel metabolism during exercise is determined by a number of factors, including the intensity and duration of exercise, muscle composition (i.e. fiber types), training status, diet and the type of food consumed before exercise (the effects of habitual diet and pre-exercise feeding on metabolic response are further discussed below). At rest when energy transduction is fully aerobic, muscle may use volatile fatty acids, lipids and carbohydrates. Equine diets are usually low in lipids and plasma NEFA concentration is also low at rest. Thus, during periods of inactivity the utilization of lipids for energy may be limited by their low concentration. The main energy sources are acetate, which is formed by bacterial fermentation in the colon and cecum, and glucose.[85]

Contemporary metabolic studies in horses have utilized stable isotope tracer methodology in combination with indirect calorimetry (O_2 uptake measurements and respiratory exchange ratio) for calculation of substrate oxidation rates during exercise at different intensities.[54–56,59,59] Figure 34.8 depicts the estimated relative contributions of lipid, plasma glucose and muscle glycogen to energy expenditure in horses during exercise at 30% and 60% of $\dot{V}O_{2max}$. During the early phases of moderate-intensity exercise (35–55% $\dot{V}O_{2max}$), use of carbohydrate (plasma glucose, muscle glycogen) predominates[145] but if exercise is continued for longer periods there is increased utilization of fats as indicated by a progressive decrease in the respiratory exchange ratio.[54,82,122] However, the utilization of plasma glucose and muscle glycogen continues, and is reflected by lowered blood glucose concentrations and depletion of muscle glycogen after endurance exercise.[67,79,110,111]

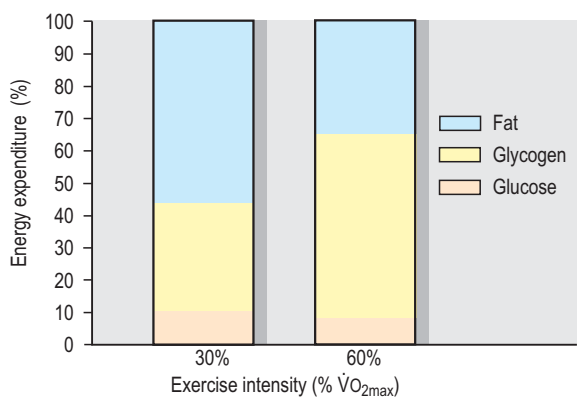

Fig. 34.8
The estimated relative contributions of lipid, plasma glucose and muscle glycogen to energy expenditure in horses during exercise at approximately 30% and 60% of maximum aerobic capacity ($\dot{V}O_{2max}$). When compared to exercise at 30% $\dot{V}O_{2max}$, there is increased reliance on muscle glycogen (and a decreased energy contribution from fat) for energy transduction during exercise at 60% $\dot{V}O_{2max}$. (Adapted from Geor et al.[56])

The main energy source at maximal performance is muscle glycogen. This is directly demonstrated in studies which show diminished anaerobic power in horses that perform high-intensity exercise after glycogen depletion.[146] Lipids are also used during intense exercise as demonstrated by decreases in NEFA concentrations during intense exercise bouts.[80,120,121]

Effects of ambient temperature

Exercise causes a decrease in plasma volume[28] and if exercise is undertaken in high temperature and humidity, high rates of sweat fluid loss will exacerbate the reduction in plasma volume.[35] In extreme conditions, sweating rate may be 10–15 L/h[147] and during the cross-country phase of a three-day event a horse may lose 2–4% of bodyweight, while a 10% loss of bodyweight may be incurred during endurance rides.[147,148] If the horse is unacclimatized, exercise in hot, humid conditions will decrease maximum oxygen uptake and increase lactate production, i.e. the primary change being a decrease in aerobic capacity with increased reliance on anaerobic metabolism.[149]

The opposite, exercise in cold, dry conditions (–25°C), does not change indices of aerobic capacity. However, respiratory rate is lower during exercise in cold when compared to thermoneutral ambient conditions.[150] Resting metabolic rate may increase by 70% from the values at thermoneutrality in cold-stressed horses.[151]

Effects of warm-up

The purpose of a warm-up is to adjust the body to transition from rest to exercise and thereby gain the dual benefits of enhanced performance and reduced risk of injury by a gradual increase in exercise intensity. An active warm-up increases body and muscle temperature by about 1°C as a result of the heat generated during muscular activity. Warm-up improves tissue oxygenation, because epinephrine and norepinephrine released during warm-up increase respiratory rate, tidal volume and heart rate, cause the spleen to contract and release stored RBC into the circulation, and increase blood flow to skeletal muscles. Catecholamines also activate glycogenolysis and lipolysis and thus increase the supply of energy fuels to the muscle, while elevated temperature decreases the activation energy of metabolic reactions. A higher temperature also increases elasticity of muscles, tendons and ligaments, which may reduce the risk of injury and allow for full range of motion in the joints.

Two equine studies have demonstrated that a brief period (5–10 min) of warm-up exercise, completed 5 min before the start of treadmill exercise at 115–120% of $\dot{V}O_{2max}$, results in a significant acceleration in $\dot{V}O_2$ kinetics, i.e. the rate of rise in $\dot{V}O_2$ after exercise onset.[152,153] This change in oxygen uptake kinetics enhances the ability of muscle to work aerobically and reduces lactate accumulation during high-intensity exercise.[152–154] In one study, both a low- and a high-intensity

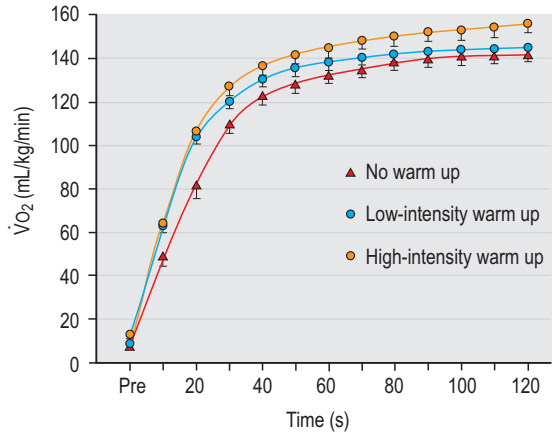

Fig. 34.9
Effects of a low- and high-intensity warm-up on oxygen consumption ($\dot{V}O_2$) in six horses during 2 minutes of intense exercise (~ 115% of maximum aerobic capacity). Note the acceleration in the rate of rise in $\dot{V}O_2$ when exercise was preceded by a warm-up. (Adapted from Geor et al.[153])

warm-up resulted in a significant increase in the run time to fatigue during intense treadmill exercise when compared to exercise undertaken without prior warm-up[154] (Fig. 34.9)

The ideal duration and intensity of warm-up exercise is not known and likely depends on the nature of the subsequent exercise task and the prevailing ambient conditions. On the one hand, if the warm-up period is too brief to allow time for the rise in body temperature the desired effect is not gained, whereas if exercise intensity during warm-up is too high significant lactate accumulation will be present at the onset of performance exercise. The studies by Tyler et al[152] and Geor et al[153] demonstrated that even a low-intensity warm-up (5 min of trotting exercise) is beneficial in terms of an enhancement in aerobic energy metabolism during subsequent galloping exercise. The benefits of warm-up are likely diminished if the rest period between warm-up and performance is extended so that the horse cools down.

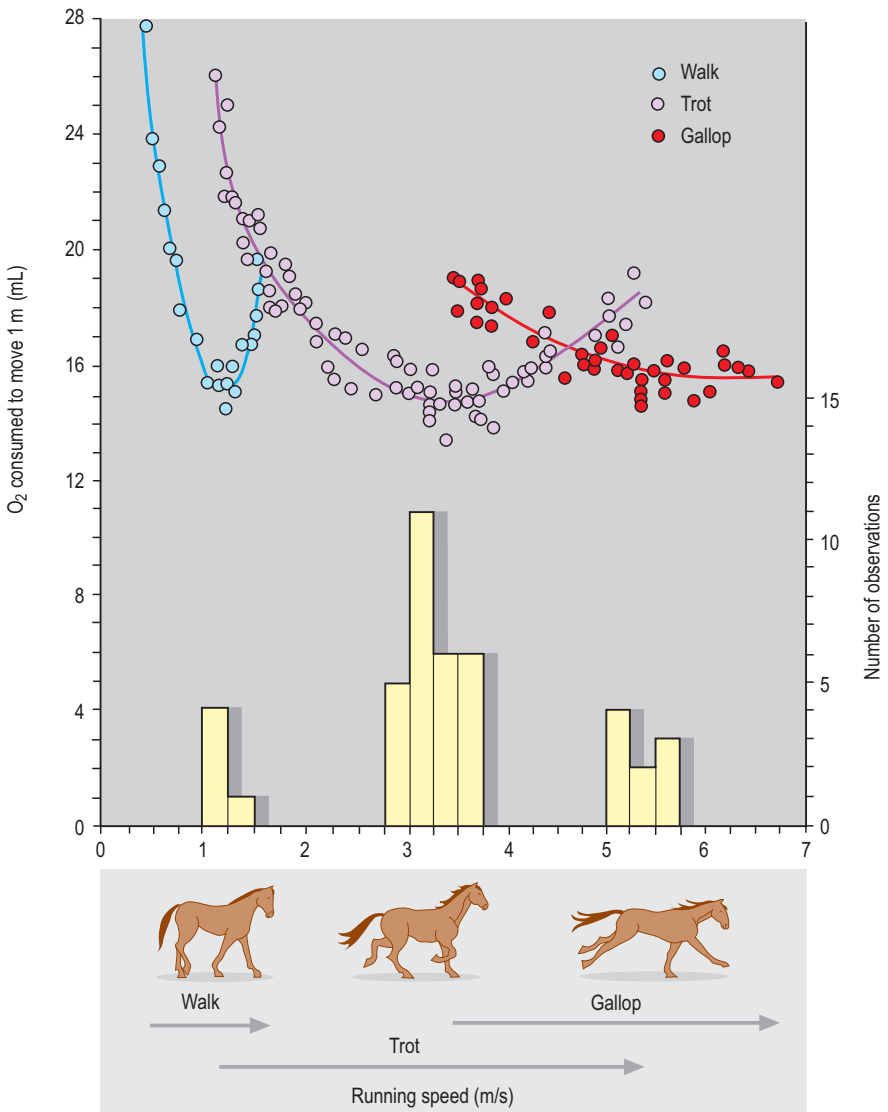

Fig. 34.10 The relationship between net energy cost, expressed as mL O_2 consumed to move 1 m, and speed at the walk, trot and gallop in small horses. Notice that the minimum energy cost is similar for all gaits. If allowed to do so, the horse changes gait at the speed where energy cost of the two adjacent gaits is the same. (Figure originally published by Hoyt & Taylor[155] and reprinted with the permission of Nature Publishing Group.)

Economy of locomotion

Stride length and stride frequency are the main determinants of running speed. Net energy cost, which is expressed as mL O_2 consumed over distance covered, varies minimally over a great variety of speeds because as speed increases horses change gait (walk, trot, canter, gallop) to an energetically more efficient one. Within a given gait, energy cost changes with increasing speed along a U-shaped curve which overlaps with the respective curve for the adjacent gait.[155,156] The change in gait occurs at the crossover point where net energy cost is the same for the two gaits, e.g. walk and trot or trot and gallop. This relationship has been described in detail by Hoyt & Taylor (see Fig. 34.12).[155] When allowed to choose gaits, the horse has a tendency to voluntarily utilize a relatively narrow set of speeds around the nadir of the energy cost curve. Possible explanations for this behavior include minimizing musculoskeletal stresses and maximizing metabolic economy.[157] Locomotion pattern also depends on other factors, the most important of these being muscle composition.[158,159] These factors may have performance implications, especially in Standardbred events (trotting or pacing) where the horse is forced to maintain a certain gait for an extended period of time and at speeds that are not energetically optimal for the gait in question (Fig. 34.10).

Differences between breeds

Thoroughbreds have higher maximum oxygen uptake than other breeds (Table 34.2) and thus their aerobic capacity is also higher than in other breeds. Another basis for differences in metabolic responses is muscle fiber composition. In faster breeds, such as Thoroughbreds, the percentage of type I fibers in locomotor muscles is lower than in Standardbreds, which again have lower percentages of type I fibers than horses used for endurance events, such as Arabs.[160] The breeds with a high percentage of type I fibers are more suited for aerobic, long-lasting work while horses with a high percentage of type II fibers are best suited for exercise in which high-intensity bursts are needed. Within a single breed, the variation in the slow-twitch:fast-twitch (type I:type II) ratio is less marked than between breeds, and training-induced differences are mainly seen in the type IIA:type IIB ratio. Exact comparisons are, however, difficult because horses from different breeds are used for different purposes and they hardly ever perform comparable exercises. This is evident when maximal lactate concentrations after different events are compared (see Table 34.1). For faster breeds, it is possible to compare the metabolic effects of races (e.g. Thoroughbred or Standardbred racing) that may be considered as maximal effort, although differences in gait complicate these comparisons.

Table 34.2 Maximum oxygen uptake ($\dot{V}O_{2max}$) in different breeds (values are means ± standard error of the mean)

Breed	$\dot{V}O_{2max}$ (mL/kg/min)	References
Thoroughbred	133 ± 10, 135.8 ± 5.9; 154 ± 3	161–163
Standardbred	143.9 ± 10.7, 151 ± 2; 164.9 ± 4.3	164–166
Arab	129 ± 2.5	163
Pony	107.8 ± 12.8	166
Donkey	110 ± 2	133

Metabolism during recovery from exercise

Lactate removal

After cessation of exercise, the rate of oxygen consumption remains elevated[167] and blood lactate concentration continues to increase, with peak concentrations attained 2–10 min post exercise. Lactate is an excellent energy source because it contains more than 90% of the energy in glucose. During exercise the main tissues that use lactate are the liver, which converts lactate back to glucose, and the heart in which lactate is used directly for energy. There also may be some utilization of lactate by type I muscle fibers. However, during recovery the major consumer of lactate is, due to its large mass, skeletal muscle with oxidation of lactate by all fiber types.[168]

The rate of lactate removal from blood depends on the metabolic state. At rest the need for energy is low, but even light exercise increases the oxygen consumption of muscles and thereby the oxidation of lactic acid.[168–170] Following high-speed treadmill exercise, the half-life of lactate is decreased by 50% in horses that exercise lightly in comparison to those that remain stationary.[169] The rate of lactate disappearance is independent of concentration which implies that the rate-limiting step in the process is saturable[169] (Fig. 34.11).

Glycogen synthesis

Recovery from exercise is metabolically characterized by resynthesis of energy stores depleted during exercise, especially that of glycogen. In horses, recovery of glycogen is typically slow; during the first 24 hours practically no repletion occurs and full recovery after exhausting exercise may take up to 3 days.[78,80,110,112] In horses, glycogen resynthesis appears to start in type IIB fibers,[112] and among the two glycogen forms, synthesis of proglycogen is favored during the early phase of recovery in both humans and horses.[141,171] In human athletes, consumption of a high carbohydrate diet enhances the rate of glycogen resynthesis, but similar abrupt changes in feed, especially the addition of soluble carbohydrates, are not practical in the horse because they may cause gastrointestinal dysfunction or even laminitis. The only means that has so far been found to enhance the rate of muscle glycogen synthesis is the intravenous administration of large doses of glucose (6 g/kg over 12 hours).[146,172]

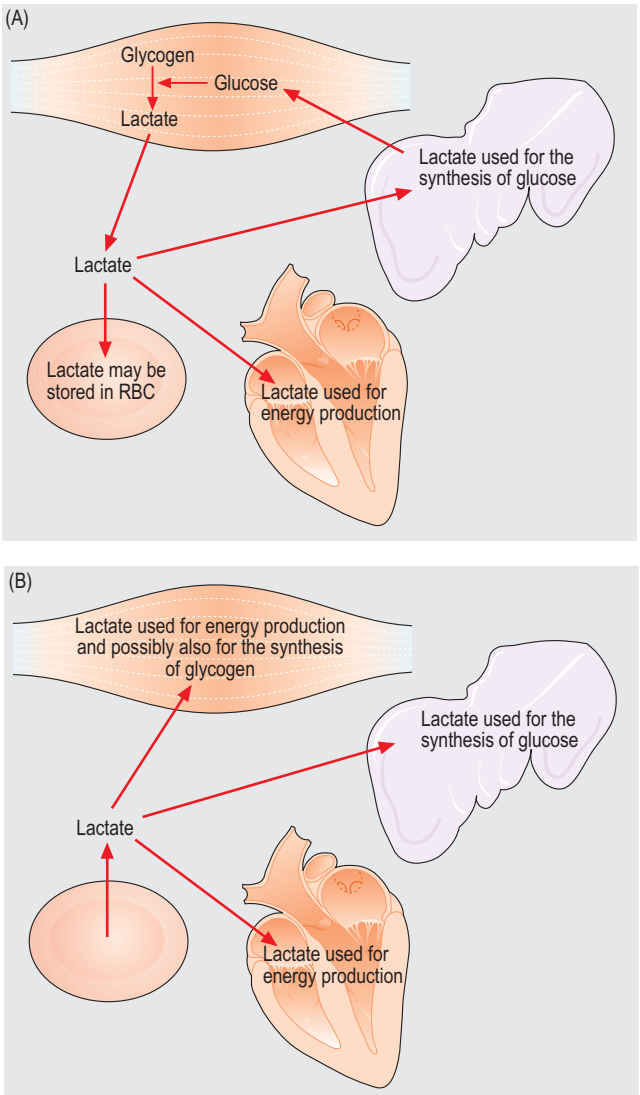

Fig. 34.11
During exercise (A) lactate is formed in the working muscles and the flow of lactate is from muscle cells into blood plasma and further into tissues such as heart and liver that may use lactate for energy or glucose production. In horses, a substantial proportion of lactate produced in muscle may also be taken up by red blood cells (RBC). During recovery (B) the direction of lactate flow is reversed, i.e. from RBC to plasma, and the main user of lactic acid is skeletal muscle. Light exercise during the recovery period that increases muscle energy requirements will also increase the rate of lactate disappearance.

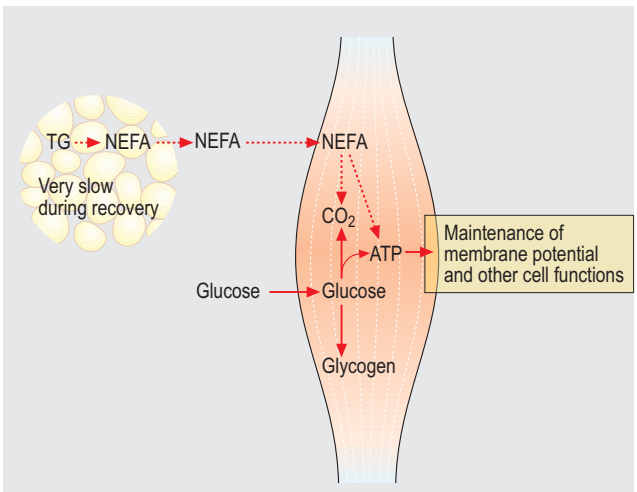

Fig. 34.12
During recovery the rate of lipolysis decreases, leading to low concentrations of fatty acids (NEFA) in plasma. Therefore, the predominant substrate for muscle metabolism is blood glucose. The use of glucose in the maintenance of cell functions will affect the availability of glucose for the resynthesis of glycogen.

The reasons for the slow rate of glycogen synthesis in the horse are not known, but in general the hormonal status immediately after exercise does not favor anabolic processes, such as the resynthesis of glycogen. During exercise, the concentration of insulin is reduced.[117,118] As insulin contributes to the activation of glycogen synthase as well as the transport of glucose into muscle by the insulin-activated glucose transporter (GLUT-4), low insulin status during the postexercise period does not favor glycogen resynthesis. Another possible factor may be a shortage of fuel during recovery. Skeletal muscle has to maintain its normal functions and only the available substrate (glucose) in excess of these demands is available for the resynthesis of glycogen. After exercise, catecholamine concentrations decrease within minutes and consequently lipolysis is inhibited and the plasma concentration of NEFA decreases to a very low level.[80] Therefore, the predominant substrate available for muscle will be glucose (Fig. 34.12).

Metabolic responses to training

Exercise training affects aerobic and anaerobic capacity and thus training effects are seen at both submaximal and maximal exercise intensities. Changes in aerobic capacity reflect increases in maximum oxygen consumption,[74,162,166,173,174] blood volume and red cell volume in young horses,[4] capillarization of all fiber types,[175] and increases in the mitochondrial density and activities of oxidative enzymes such as CS and HAD.[88,160,176–181] Such increases in aerobic capacity mean that the trained horse is able to run faster before the lactate threshold is reached and accumulation of lactate begins when compared to an untrained animal.[142]

The primary change in muscle fiber composition is from IIB/IIX → IIA and further training also may result in an increase in type I fibers.[177,180,182–184] Histochemical analysis show an increase in type IIA fibers, but recent use of myosin-

specific antibodies has revealed that after training muscles contain a high proportion of IIXA fibers.[185] The best Standardbred trotters have the highest type IIA:IIB fiber ratios and also the cross-sectional area of type II fibers tends to be smaller when compared to less well-performing horses.[175] In contrast, successful endurance horses have a high percentage of type I fibers with a large cross-sectional area.[186] Very intense training has been reported to increase the cross-sectional area of type II fibers.[187] The most important changes that describe training effects in skeletal muscle are increases in type I fiber area and capillarization, particularly the number of capillaries in contact with type I and type IIA fibers, and an increase in the oxidative capacity of type IIB fibers.[188,189] Some studies have also demonstrated an increase in muscle glycogen and triglyceride content after endurance training.[184]

Because of increased oxidative capacity, less glycogen is used and respiratory exchange ratio decreases during both high-[190] and moderate-intensity[57] exercise. Also due to high aerobic capacity, lactate accumulation in plasma at a given submaximal work level is lower.[91,] Studies in humans also demonstrate that the exercise-induced increase in muscle lactate concentration is mitigated by training[107] due to increased lactate efflux out of the muscle and a training-associated increase in plasma volume.

The changes in anaerobic capacity are more difficult to measure, but an increase in maximal accumulated oxygen deficit (MAOD) and lower accumulation of lactate in skeletal muscle were found in trained horses after a maximal sprint to fatigue, providing indication of an increase in anaerobic capacity with training.[162] These changes were accompanied by a significant increase in run time to fatigue during sprinting. The effects of training on blood lactate concentrations after maximal effort are controversial. Some studies show no differences[162] while others show significantly higher lactate concentrations after training.[91,120] As previously mentioned, studies in human athletes have demonstrated that training increases the quantity of MCTs on muscle membranes.[105,106] This increase in muscle MCT could contribute to higher blood lactate concentrations after training. Another factor that could modify blood lactate concentrations after training is an increase in muscle buffering capacity. Studies in horses have reported both an increase and no change in muscle buffering capacity with training.[162,176,191]

Training intensity and duration

Significant training effects are apparent even when the intensity of training exercise is low or moderate, but these changes mainly reflect an increase in aerobic capacity and reactions related to aerobic metabolism. Decreases in the rate of glycogenolysis, increases in oxidative enzymes and increases in oxygen extraction by tissues are evident after as little as 2 weeks of training,[173,174] sometimes even before any measurable changes in indices of muscle oxidative capacity can be detected.[190] In general, most of the training-induced increase in aerobic capacity occurs during the initial 6-week period of training.[165] However, further increments in $\dot{V}O_{2max}$ occur if a training stimulus is maintained.[165] The study by Hinchcliff et al,[162] however, clearly shows that high-intensity training is necessary for improvements in anaerobic capacity. It is possible that intense exercise is also necessary for maximum improvements in aerobic capacity because adaptive changes in aerobic processes appear to require hypoxia as an inducer of gene activity, e.g. the induction of erythropoiesis, capillary growth and the synthesis of glycolytic enzymes appear to be regulated by hypoxia.[192]

Detraining

Most of the changes in metabolism require synthesis of new proteins and thus require days or weeks to develop; these adaptations also persist for several weeks after the cessation of regular physical activity (detraining).[193,194] In general, adaptive training responses in skeletal muscle persist for 5–6 weeks after the cessation of regular physical activity.[180,184] Similarly, there is minimal change in maximum oxygen uptake after 2–4 months of detraining.[165,194] However, in the study by Butler et al,[194] lactate accumulation during intense exercise was higher after a 15-week period of detraining, indicating a decrease in aerobic capacity. The fiber type changes during detraining occur in reverse order to the changes during training.[180,184]

Effects of diet on metabolic responses

The chemical energy (i.e. ATP) required for muscle contraction is ultimately provided in the diet. Therefore, inasmuch as diet can influence the storage of glycogen and TG in muscle, there is an obvious relationship between dietary intake and skeletal muscle exercise metabolism. Indeed, studies in human athletes have unequivocally demonstrated that a high-CHO, low-fat diet will result in higher muscle glycogen concentration when compared to a more conventional, lower CHO diet.[195] Furthermore, there is a direct relationship between initial muscle glycogen stores and performance during moderate intensity (50–80% of $\dot{V}O_{2max}$) endurance exercise in humans.[196] Thus, for human athletes, dietary strategies that boost muscle glycogen stores enhance exercise performance. Conversely, a low-CHO, high-fat diet impairs endurance exercise performance, in part due to lower initial muscle glycogen concentrations.

Although there has been extensive study of the metabolic responses to exercise in horses, relatively few studies have examined the effects of diet composition on substrate metabolism and exercise performance. Traditionally, the high energy requirements of athletic horses have been met by diets high in hydrolyzable CHO (i.e. grains). In the past decade, however, there has been increased emphasis on use of alternative energy sources, such as fat and beet pulp, in equine rations and some data are available regarding the effects of such diets on the metabolic response to exercise.

High carbohydrate diets

As mentioned, only a modest increase in the glycogen content of muscle has been observed in horses fed diets rich in hydrolyzable CHO.[81–83] For example, Essén-Gustavsson et al[83] reported a 12% increase in the resting muscle glycogen content of Standardbred horses fed a diet containing approximately 2 kg of starch and sugar when compared to an isocaloric diet that provided about 1.3 kg hydrolyzable CHO per day. However, no beneficial effect on performance has been shown in horses after CHO-rich diets.[81–83] On the contrary, higher HR and blood lactate accumulation is observed during intense exercise in horses fed CHO-rich diets.[81,82] The underlying mechanisms of these responses are unknown but may be related to alterations in sympathetic outflow and circulating catecholamine concentrations. Interestingly, Jansson et al[197] reported higher HR during submaximal exercise in horses fed 1.5 kg of barley sugar per day when compared to an oat-based diet, suggesting that the form of CHO also may influence the HR response during exercise. There is also evidence that diets comparatively high in starch and sugar increase HR and excitability of horses at rest.[198]

Fat-supplemented diets

The inclusion of fat (as vegetable oil) in diets for athletic horses is now widespread and it is common for horses to receive up to 20% of total daily digestible energy (DE) from fat. However, the effects of dietary fat supplementation in horses on exercise metabolism and performance are somewhat controversial, in part because of the wide variability in the design and results of studies examining various physiological responses to dietary fat.

Fat supplementation in horses is characterized by an increase in plasma phospholipids and cholesterol and a decrease in plasma TGs.[199,200] Changes in the activities of lipoprotein lipase and the enzymes of β-oxidation also suggest that horses adapted to a fat-supplemented diet have increased capacity for the uptake and oxidation of fatty acids in muscle. Indeed, some recent studies have shown lower respiratory exchange ratio in fat-adapted horses during low and moderate-intensity exercise.[59,201] Pagan et al[59] also reported a decrease in glucose flux during low-intensity exercise in horses adapted to a diet providing 25% of DE from corn oil. Thus, fat supplementation enhances lipid oxidation and spares the use of endogenous CHO (plasma glucose, muscle glycogen) during moderate exercise. Theoretically, such a glycogen-sparing effect could improve exercise performance. However, the actual effects of fat supplementation on endurance exercise performance have not been reported.

The minimum (or optimum) level of dietary fat necessary for expression of these metabolic adaptations has not been established. Most studies have fed diets containing 3–12% fat (total diet on a dry matter basis) and in one study a dose–response relationship was detected between fat intake (3.0–10.8% fat) and heparin-released plasma lipoprotein lipase activity.[202]

The length of time required for metabolic adaptation to dietary fat is a somewhat contentious issue. Some nutritionists believe that a minimum of 10–12 weeks is required for adaptation.[217] However, metabolic adaptations to fat supplementation have been observed as early as 3–5 weeks after the start of supplementation.[59,199] Thus, whereas a 2–3 month period may be required for complete adaptation to a fat-supplemented diet, some of the metabolic responses are evident much earlier. In one study, the metabolic responses to fat supplementation were abolished within 5 weeks of withdrawal of the oil-supplemented diet.[199] Thus, the putative benefits of fat-supplemented diets in horses are dependent on continued use of such rations.

There is some evidence that fat supplementation also improves the performance of horses undertaking higher intensity exercise (e.g. race horses). Harkins et al[203] reported improved racetrack performance in Thoroughbreds fed a fat-supplemented diet and attributed this improvement to increased muscle glycogen content and glycogen utilization rate during exercise. Furthermore, Eaton et al[204] reported that a fat-supplemented diet resulted in a small but statistically significant increase in run time to fatigue and MAOD in horses undertaking treadmill exercise at an intensity equivalent to 120% of $\dot{V}O_{2max}$. However, in this study there was no corresponding change in resting muscle glycogen content or glycogen utilization rate during exercise. The mechanism for enhancement of high-intensity exercise performance with fat supplementation is unclear, although increased activation of glycolysis and glycogenolysis is a possibility, the data of Eaton and colleagues[204] notwithstanding.

Fat-supplemented diets for horses have lower hydrolyzable CHO (starch and sugar) content when compared to grain-based rations. These diets therefore provide less substrate (glucose) for muscle glycogen synthesis. However, although a drastic reduction in the soluble CHO content of the diet (< 10% of DE from starch and sugar) is associated with marked reductions in muscle glycogen content,[81] it appears that muscle glycogen content is largely unchanged when horses are fed diets containing moderate amounts of fat (up to 7.5% of total dry matter or 20% of DE).[84,198] However, in horses not adapted to a fat-supplemented diet, consumption of meals containing 7.5% fat (rapeseed oil) slows the rate of muscle glycogen replenishment.[84]

Sugar beet pulp

Non-starch carbohydrate feeds, such as sugar beet pulp (SBP) and soya hulls, are now commonly added to diets for athletic horses. The carbohydrate fraction of these feeds is devoid of starch, but rich in non-starch polysaccharides (fiber). SBP contains major fractions of pectins, arabinans and galactans that are extensively fermented in the hindgut.[205] Up to 3.0 g SBP per kg bodyweight have been fed to adult horses without any adverse effects on overall nutrient utilization or performance.[206] Replacing oats with plain SBP will reduce the glycemic and insulinemic responses to a meal.[206] However, when oats were replaced by molassed SBP there was no appreciable change in glycemic response although the postprandial increase in insulin was mitigated.[207]

Replacing oats with SBP also mitigates the rate of muscle glycogenolysis and the increases in muscle and plasma lactate in Standardbred trotters performing a treadmill exercise test that simulated a race.[207] Similarly, replacing oats with barley sugar resulted in a significant reduction in muscle glycogen utilization during intense exercise.[197] Therefore, a reduction in dietary starch, with replacement by SBP or barley sugar, modifies the muscle glycogenolytic response to high-intensity exercise. The mechanism of this apparent glycogen-sparing effect when oat starch is replaced by barley sugar or SBP is not known. Potentially, an increase in sugar intake results in enhanced use of plasma glucose for energy with a concomitant decrease in energy transduction from muscle glycogen.

Dietary protein

Studies in humans and in dogs have indicated that protein is an unimportant substrate during exercise, although under some circumstances amino acid oxidation may account for up to 5–10% of energy expenditure.[195] The contribution of protein to energy expenditure in horses during exercise is unknown, but it has generally been assumed that carbohydrate and fat oxidation predominate. On the other hand, the effects of dietary protein level on exercise metabolism and performance have received some attention. In one study of racetrack feeding practices, there was an inverse correlation between dietary protein level and race performance; for every 1 kg of crude protein (CP) ingested over recommended levels, there was a 1–3 s increase in race time.[208] However, these conclusions are questionable as the statistical analysis of the data was inappropriate. Subsequent laboratory investigations comparing metabolic responses in horses fed moderate (~10% CP; recommended levels) versus high (~18% CP) protein diets have yielded equivocal results. Miller et al[209] and Pagan et al[82] reported attenuated blood lactate accumulation during exercise in horses fed a high-protein diet. However, a subsequent study by Miller-Graber and colleagues[210] did not detect an effect of dietary protein level on lactate accumulation or muscle glycogenolysis during exercise.

More recently, Graham-Thiers and colleagues[211] have evaluated the effects of a restricted protein diet (7.5% CP with added lysine and threonine) on acid–base responses in horses subjected to repeated bouts of high-intensity exercise. When compared to a 14.5% CP diet, the restricted protein diet mitigated exercise-associated acidemia. However, quantitatively the effects were very small and the physiological significance remains to be determined (for further discussion, see Chapter 39).

Effects of pre-exercise feeding

The timing and composition of a meal consumed before exercise can influence metabolic response. Most notably, the hyperglycemia and insulinemia associated with the digestion and absorption of grain meals affect the mix of substrates utilized during a bout of exercise. Insulin is a potent inhibitor of lipolysis and fatty acid oxidation in skeletal muscle and also promotes glucose uptake into muscle via recruitment of the transporter protein GLUT-4 to the sarcolemma. Thus, hyperinsulinemia at exercise onset will suppress NEFA availability and lipid oxidation and increase reliance on carbohydrate stores (including plasma glucose) for energy transduction.

Accordingly, several equine studies have demonstrated that a grain meal (1–3 kg of oats, corn or a mixture of the two) consumed 3 hours or less before exercise results in hyperglycemia, hyperinsulinemia and decreased plasma NEFA concentration at the start of exercise, and a subsequent marked decrease in plasma glucose concentration during the initial period of exercise.[212–215] This decrease in plasma glucose concentration tends to be short-lived such that during prolonged moderate-intensity exercise (e.g. 60 min at 50% of $\dot{V}O_{2max}$), the plasma glucose concentration of grain-fed horses is not substantially different from horses fasted before exercise. On the other hand, plasma NEFA remains lower when compared to the fasted state throughout exercise. Jose-Cunilleras and colleagues[58] utilized isotopic tracer methods and indirect calorimetry to determine the effects of hay (alfalfa cubes; ~3 kg) and starch (cracked corn; 1.7 kg) feeding on glucose flux and substrate oxidation during exercise. The alfalfa cubes were consumed between 2 and 3 hours before exercise, while the cracked corn was ingested 90 min pre-exercise. Feeding corn before exercise resulted in increased utilization of blood-borne glucose and whole-body carbohydrate oxidation when compared to a meal of alfalfa or not feeding (Fig. 34.13).

The effects of pre-exercise grain feeding on endurance exercise performance in horses have not been reported. In humans, carbohydrate ingestion during exercise unequivocally improves performance during prolonged (more than 2 hours) moderate-intensity (> 50–60% of $\dot{V}O_{2max}$) exercise,

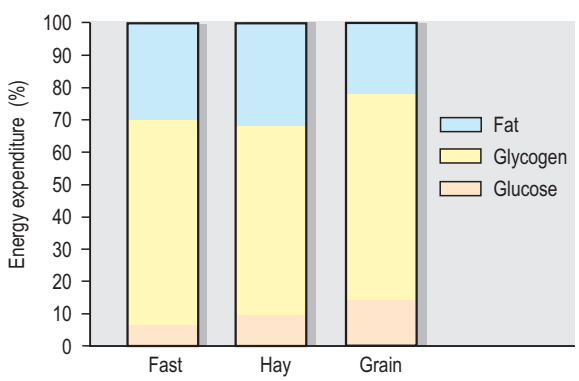

Fig. 34.13
Effects of pre-exercise feeding on the partitioning of energy expenditure in horses during the 5–30 min period of exercise at 50% of maximum oxygen uptake. Horses were either fasted or fed cracked corn or alfalfa cubes 2 hours before exercise. Grain feeding resulted in a significant increase in the caloric contribution from oxidation of glucose when compared to the fast and hay feeding trials. (From Jose-Cunilleras et al.[58])

presumably by maintaining glucose supply in skeletal muscle at a time when glycogen stores are depleted. On the other hand, the performance effects of pre-exercise glucose feedings in human athletes are more equivocal. For horses performing endurance exercise, the acceleration in carbohydrate oxidation (and suppression of fat oxidation) associated with grain feeding may result in premature fatigue as a result of carbohydrate depletion.

As demonstrated in the study by Jose-Cunilleras et al,[58] together with the results of earlier studies by Pagan & Harris,[215] forage meals (< 2–3 kg) consumed 2–3 hours before exercise have minimal effect on substrate availability and oxidation during sustained exertion. However, free choice consumption of hay in the 12–24-hour period before exercise may adversely affect performance because of an increase in bodyweight (gut fill). Large meals (hay or grain or a combination) consumed near the start of exercise also may result in a decrease in plasma volume as a result of fluid shifts into the gastrointestinal tract.[215] Such reductions in plasma volume could compromise cardiovascular and thermoregulatory function during exercise.

There is some evidence that a short-term reduction in forage intake is beneficial in horses undertaking high-intensity exercise. When compared to ad libitum hay consumption, restricting hay intake to ~ 1% of bodyweight for a 3-day period before a treadmill exercise test (2 min at 115% $\dot{V}O_{2max}$) resulted in a 2% decrease in bodyweight and a reduction in anaerobic energy expenditure during exercise, as evidenced by reduced oxygen deficit and plasma lactate concentrations. The reduction in bodyweight was attributed to a reduction in gut fill.[216]

In summary, small forage meals consumed 2–3 hours before exercise have minimal effect on substrate metabolism during exertion. However, meals containing hydrolyzable carbohydrate (starch and sugar) consumed within 3 hours of the start of exercise accelerate carbohydrate utilization and decrease lipid oxidation. Although the performance effects of these feeding practices are not known, this suppression in lipid oxidation may be detrimental during endurance exercise (e.g. endurance races; speed and endurance test of a three-day event).

References

1. Evans DL, Rose RJ. Determination and repeatability of maximum oxygen uptake and other cardiorespiratory measurements in the exercising horse. Equine Vet J 1988; 20:94–98.
2. Rose RJ, Hodgson DR, Kelso TB, et al. Maximum O_2 uptake, O_2 debt and deficit, and muscle metabolism in Thoroughbred horses. J Appl Physiol 1988; 64:781–788.
3. Langsetmo I, Weigle GE, Fedde MR, et al. $\dot{V}O_2$ kinetics in the horse during moderate and heavy exercise. J Appl Physiol 1997; 83:1235–1241.
4. Persson SGB. On blood volume and working capacity in horses. Acta Vet Scand 1967; 19(Suppl):1–189.
5. Simon TL. Induced erythrocythemia and athletic performance. Semin Hematol 1994; 31:128–133.
6. Fenger CK, McKeever KH, Hinchcliff KW, et al. Determinants of oxygen delivery and hemoglobin saturation during incremental exercise in horses. Am J Vet Res 2000; 61:1325–1332.
7. Jones WE. Equine sports medicine. Philadelphia, PA: Lea and Febiger; 1989; 121–136.
8. Derman KD, Noakes TD. Comparative aspects of exercise physiology. In: Hodgson DR, Rose RJ, eds. The athletic horse. Philadelphia, PA: Saunders; 1994; 13–25.
9. McCutcheon LJ, Kelso TB, Bertocci LA, et al. Buffering and aerobic capacity in equine muscles: variation and effect of training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 348–358.
10. Snow DH, Harris RC, Gash SP. Metabolic response of equine muscle to intermittent maximal exercise. J Appl Physiol 1985; 58:1689–1697.
11. Schuback K, Essén-Gustavsson B. Muscle anaerobic response to a maximal treadmill exercise test in Standardbred trotters. Equine Vet J 1998; 30:504–510.
12. Valberg S, Macleay JM, Billstrom JA, et al. Skeletal muscle metabolic response to exercise in horses with 'tying-up' due to polysaccharide storage myopathy. Equine Vet J 1999; 31:43–47.
13. Pösö AR, Lampinen KJ, Räsänen LA. Distribution of lactate between red blood cells and plasma after exercise. Equine Vet J 1995; 18(Suppl):231–234.
14. Räsänen LA, Lampinen KJ, Pösö AR. Responses of blood and plasma lactate and plasma purine concentrations to maximal exercise and their relation to performance in Standardbred trotters. Am J Vet Res 1995; 56: 1651–1656.
15. Väihkönen LK, Pösö AR. Interindividual variation in total and carrier mediated lactate influx into red blood cells. Am J Physiol Reg Integr Comp Physiol 1998; 274: R1121–R1128.
16. Väihkönen LK, Heinonen OJ, Hyyppä S, et al. Lactate transport activity in red blood cells of trained and untrained individuals from four racing species. Am J Physiol Reg Integr Comp Physiol 2001; 281:R19–R24.
17. Armstrong RB, Essén-Gustavsson B, Hoppeler H, et al. O_2 delivery at $\dot{V}O_{2max}$ and oxidative capacity in muscles of standardbred horses. J Appl Physiol 1992; 73: 2274–2282.
18. Manohar M. Furosemide and systemic circulation during severe exercise. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 132–147.
19. Lovell DK, Reid TA, Rose RJ. Effects of maximal exercise on equine muscle: changes in metabolites, pH and temperature. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 312–320.
20. Hodgson DR, Kelso TB, Bayly WM, et al. Responses to repeated high intensity exercise: influence on muscle metabolism. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 302–311.
21. Valberg S, Essén-Gustavsson B, Lindholm A, et al. Blood chemistry and skeletal muscle metabolic responses during and after different speeds and durations of trotting. Equine Vet J 1989; 21:91–95.
22. Sewell DA, Harris RC. Adenine nucleotide degradation in the thoroughbred horses with increasing exercise duration. Eur J Appl Physiol 1992; 65:271–277.
23. Newsholme EA, Leech AR. Biochemistry for the medical sciences. Chichester, UK: John Wiley; 1986; 357–381.

24. Pösö AR. Monocarboxylate transporters and lactate metabolism in equine athletes. Acta Vet Scand 2002; 43:63–74.
25. Snow DH, Harris RC, MacDonald IA, et al. Effect of high-intensity exercise on plasma catecholamines in the Thoroughbred horse. Equine Vet J 1992; 24:462–467.
26. Rose RJ, Evans DL. Cardiovascular and respiratory function in the athletic horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 1–24.
27. Hoppeler H. What makes horses superior athletes? In: Kallings P, ed. Proceedings of the International Conference on Equine Sports Medicine. Uppsala, Sweden: Almqvist and Wiksell; 1990; 7–13.
28. McKeever KH, Hinchcliff KW, Reed SM, et al. Role of decreased plasma volume in hematocrit alterations during incremental exercise in horses. Am J Physiol 1993; 265:R404–408.
29. Manohar M. Respiratory muscle perfusion during strenous exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 1–8.
30. Parks CM, Manohar M. Distribution of blood flow during moderate and strenous exercise in ponies (*Equus caballus*). Am J Vet Res 1983; 44:1861–1866.
31. Manohar M, Goetz TE, Saupe B, et al. Thyroid, renal, and splanchnic circulation in horses at rest and during short-term exercise. Am J Vet Res 1995; 56:1356–1361.
32. Irvine CHG. The role of hormones in exercise physiology. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 377–388.
33. Harris PA, Marlin DJ, Scott CM, et al. Electrolyte and total protein changes in nonheat acclimated horses performing treadmill exercise in cool (20 degrees C/40%RH), hot, dry (30 degrees C/40% RH) or hot, humid (30 degrees C/80% RH) conditions. Equine Vet J 1995; 20(Suppl):85–96.
34. Hyyppä S, Saastamoinen M, Pösö AR. Restoration of water and electrolyte balance in horses after repeated exercise in hot and humid conditions. Equine Vet J 1996; 22(Suppl):108–112.
35. Jansson A, Nyman S, Morgan K, et al. The effect of ambient temperature and saline loading on changes in plasma and urine electrolytes Na^+ and K^+ following exercise. Equine Vet J 1995; 20(Suppl):147–152.
36. Baragli P, Tedeschi D, Gatta D, et al. Application of a constant blood withdrawal method in equine exercise physiology studies. Equine Vet J 2001; 33:543–546.
37. von Wessum R, Sloet van Oldruitenborgh-Oosterbaan M, Clayton HM. Electromyography in the horse in veterinary medicine and in veterinary research – a review. Vet Quart 1999; 21:3–7.
38. Sloet van Oldruitenborgh-Oosterbaan M, Barneveld A, Schamhardt HC. Effects of weight and riding on workload and locomotion during treadmill exercise. Equine Vet J 1995; 18(Suppl):413–417.
39. Marlin DJ, Harris RC, Harris PA, et al. Objectives of the Animal Health Trust Acclimatisation Study, including the design of a treadmill based simulated Competition Exercise Test. In: Clarke AF, Jeffcott LB, eds. On to Atlanta '96. Guelph, Canada: University of Guelph; 1994; 23–24.
40. Gottlieb M, Essén-Gustavsson B, Lindholm A, et al. Cardio-respiratory and muscle metabolic responses to draught work on a treadmill in Standardbred horses. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 384–392.
41. King CM, Evans DL, Rose RJ. Acclimation to treadmill exercise. Equine Vet J 1995; 18(Suppl):453–456.
42. Dubreucq C, Chatard JC, Couroucé A, et al. Reproducibility of a standardised exercise test for Standardbred trotters under field conditions. Equine Vet J 1995; 18(Suppl): 08–112.
43. Kobyashi M, Kuribara K, Amada A. Application of V200 values for evaluation of training effects in the young Thoroughbred under field conditions. Equine Vet J 1999; 30(Suppl):159–162.
44. Couroucé A. Field exercise testing for assessing fitness in French Standardbred trotters. Vet J 1999; 157: 112–122.
45. Couroucé A, Geffroy O, Barrey E, et al. Comparison of exercise tests in French trotters under training track, racetrack and treadmill conditions. Equine Vet J 1999; 30(Suppl):528–532.
46. Russell MA, Rodiek AV, Lawrence LM. Effects of exercise, training and sampling location on selected plasma free amino acids in horses. Can J Anim Sci 1986; 66:827–831.
47. Harris PA, Snow DH. The effects of high intensity exercise on the plasma concentration of lactate, potassium and other electrolytes. Equine Vet J 1988; 20:109–113.
48. Väihkönen LK, Hyyppä S, Pösö AR. Factors affecting accumulation of lactate in red blood cells. Equine Vet J 1999; 30(Suppl):443–447.
49. Persson SGB, Essén-Gustavsson B, Funkquist P, et al. Plasma, red cell and whole blood lactate concentrations during prolonged treadmill exercise at V_{LA4}. Equine Vet J 1995; 18(Suppl):104–107.
50. Väihkönen LK, Ojala M, Pösö AR. Age-related changes and inheritance of lactate transport activity in red blood cells. Equine Vet J 2002; 34(Suppl):568–572.
51. Schulze E, Fuhrmann H, Neitzel ES, et al. Glucose entry rate in dairy cattle as determined by stable isotope ^{13}C-labelled glucose at different stages of reproduction. Comp Biochem Physiol B 1991; 100:167–171.
52. Bonnaire Y, Dehennin L, Plou P, et al. Testosterone administration to mares: criteria for detection of testosterone abuse by analysis of metabolites in plasma and urine. J Analyt Toxicol 1995; 19:175–181.
53. Klein H-J, Schulze E, Deegen E, et al. Metabolism of naturally occurring [^{13}C]glucose given orally to horses. Am J Vet Res 1988; 49:1259–1262.
54. Geor RJ, Hinchcliff KW, Sams RA. Glucose infusion attenuates hepatic glucose production and enhances glucose use in horses during low intensity exercise. J Appl Physiol 2000; 88:1765–1776.
55. Geor RJ, Hinchcliff KW, McCutcheon LJ, et al. Epinephrine inhibits exogenous glucose utilization in exercising horses. J Appl Physiol 2000; 88:1777–1790.
56. Geor RJ, Hinchcliff KW, Sams RA. β-Adrenergic blockade augments glucose utilization in horses during graded exercise. J Appl Physiol 2000; 89:1086–1098.
57. Geor RJ, McCutcheon LJ, Hinchcliff KW, et al. Training-induced alterations in glucose metabolism during moderate intensity exercise. Equine Vet J 2002; 34(Suppl):2 2–28.
58. Jose-Cunilleras E, Hinchcliff KW, Sams RA, et al. Glycemic index of a meal fed before exercise alters substrate use and glucose flux in exercising horses. J Appl Physiol 2002; 92:117–128.
59. Pagan JD, Geor RJ, Harris PA, et al. Effects of fat adaptation on glucose kinetics and substrate oxidation during low intensity exercise. Equine Vet J 2002; 34(Suppl):33–38.
60. Jeukendrup AE, Raben A, Gijsen A, et al. Glucose kinetics during prolonged exercise in highly trained human subjects: effect of glucose ingestion. J Physiol 1999; 515: 579–589.

61. Lindholm A, Piehl K. Fibre composition, enzyme activities and concentrations of metabolites and electrolytes in muscles of Standardbred horses. Acta Vet Scand 1974; 15:287–309.
62. Snow DH, Guy PS. Percutaneous needle muscle biopsy in the horse. Equine Vet J 1976; 8:150–155.
63. Kline KH, Lawrence LM, Novakofski J, et al. Changes in muscle fiber type variation within the middle gluteal of young and mature horses as a function of sampling depth. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 271–277.
64. Bruce VL, Turek RJ, Schurg WA. Muscle fibre compartmentalisation in the gluteus medium of the horse. Equine Vet J 1993; 25:69–72.
65. Valette JP, Barrey E, Jouglin M, et al. Standardisation of muscular biopsy of gluteus medius in French trotters. Equine Vet J 1999; 30(Suppl):342–344.
66. Lindholm A, Bjerneld H, Saltin B. Glycogen depletion pattern in muscle fibres of trotting horses. Acta Physiol Scand 1974; 90:475–484.
67. Snow DH, Baxter P, Rose RJ. Muscle fibre composition and glycogen depletion in horses completing in an endurance ride. Vet Rec 1981; 108:374–378.
68. Valberg S. Glycogen depletion patterns in the muscle of Standardbred tortters after exercise of varying intensities and duration. Equine Vet J 1986; 18:479–484.
69. Gottlieb M. Muscle glycogen depletion patterns during draught work in Standardbred horses. Equine Vet J 1989; 21:110–115.
70. Essén-Gustavsson B, Ronéus N, Pösö AR. Metabolic response in skeletal muscle fibres of Standardbred trotters after racing. Comp Biochem Physiol 1997; 117B:431–436.
71. Harris DB, Harris RC, Wilson AM, et al. ATP loss with exercise in muscle fibres of the gluteus medius of the thoroughbred horse. Res Vet Sci 1997; 63:231–237.
72. Persson SGB. Analysis of fitness and state of training. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 441–457.
73. Harkins JD, Beadle RE, Kamerling SG. The correlation of running ability and physiological variables in Thoroughbred racehorses. Equine Vet J 1993; 25:53–60.
74. Evans DL, Rose RJ. Maximum oxygen uptake in racehorses: changes with training state and prediction from submaximal cardiorespiratory measurements. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 51–67.
75. Rose RJ, Hodgson DR, Bayly WM, et al. Kinetics of $\dot{V}o_2$ and $\dot{V}co_2$ in the horse and comparison of five methods for determination of maximum oxygen uptake. Equine Vet J 1990; 9(Suppl):39–42.
76. Eaton MD, Evans DL, Hodgson DR, et al. Effect of treadmill incline and speed on metabolic rate during exercise in Thoroughbred horses. J Appl Physiol 1995; 79: 951–957.
77. Eaton MD, Evans DL, Hodgson DR, et al. Maximal accumulated oxygen deficit in thoroughbred horses. J Appl Physiol 1995; 78:1564–1568.
78. Snow DH, Harris RC, Harman JC, et al. Glycogen repletion following different diets. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 701–710.
79. Essén-Gustavsson B, Karlström K, Lindholm A. Fibre types, enzyme activities and substrate utilisation in skeletal muscles of horses competing in endurance rides. Equine Vet J 1984; 16:197–202.
80. Hyyppä S, Räsänen LA, Pösö AR. Resynthesis of glycogen in skeletal muscle from Standardbred trotters after repeated bouts of exercise. Am J Vet Res 1997; 58:162–166.
81. Topliff DR, Potter GD, Dutson TR, et al. Diet manipulation and muscle glycogen in the equine. Lexington, KY: Proceedings of the Equine Nutrition and Physiology Symposium; 1983; 119–124.
82. Pagan JD, Essén-Gustavsson B, Lindholm A, et al. The effect of dietary energy source on exercise performance in Standardbred horses. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 686–700.
83. Essén-Gustavsson B, Blomstrand E, Karlström K, et al. Influence of diet on substrate metabolism during exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 288–298.
84. Hyyppä S, Saastamoinen M, Pösö AR. Effect of post exercise fat-supplemented diet on muscle glycogen repletion. Equine Vet J 1999; 30(Suppl):493–498.
85. Pethick DW, Rose RJ, Bryden WL, et al. Nutrient utilisation by the hindlimb of Thoroughbred horses at rest. Equine Vet J 1993; 25:41–44.
86. Ford EJH, Simmons HA. Gluconeogenesis from caecal propionate in the horse. Br J Nutr 1985; 53:55–60.
87. Simmons HA, Ford EJH. Gluconeogenesis from propionate produced in colon of the horse. Br Vet J 1991; 147:340–345.
88. Essén-Gustavsson B, Lindholm A. Muscle fibre characteristics in active and inactive Standardbred horses. Equine Vet J 1985; 17:434–438.
89. Pösö AR, Essén-Gustavsson B, Persson SGB. Metabolic responses to standardised exercise test in Standardbred trotters with red cell hypervolaemia. Equine Vet J 1993; 25:527–531.
90. Ronéus M, Lindholm A, Åsheim Å. Muscle characteristics of Thoroughbreds of different ages and sexes. Equine Vet J 1991; 23:207–210.
91. Ronéus N, Essén-Gustavsson B, Lindholm A, et al. Plasma lactate response to submaximal and maximal exercise tests with training, and its relationship to performance and muscle characteristics in standardbred trotters. Equine Vet J 1994; 26:117–121.
92. Eaton MD. Energetics and performance. In: Hodgson DR, Rose RJ, eds. The athletic horse. Philadelphia, PA: Saunders; 1994; 49–61.
93. Cutmore CMM, Snow DH, Newsholme EA. Activities of key enzymes of aerobic and anaerobic metabolism in middle gluteal muscle from trained and untrained horses. Equine Vet J 1993; 17:354–356.
94. Valberg S, Essén-Gustavsson B. Metabolic response to racing determined in pools of type I, II A and II B fibers. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 290–301.
95. Harris RC, Snow DH, Katz A, et al. Effect of freeze-drying on measurements of pH in biopsy samples of the middle gluteal muscle of the horse: comparison of muscle pH to the pyruvate and lactate content. Equine Vet J 1989; 21:45–47.
96. Hyyppä S, Pösö AR. Fluid, electrolyte and acid-base responses to exercise in racehorses. Vet Clin North Am Equine Pract 1988; 14:121–136.
97. Harris RC, Dunnett M, Snow DH. Muscle carnosine content is unchanged during maximal intermittent exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 257–261.

98. Sewell DA, Harris RC, Dunnett M. Carnosine accounts for most of the variation in physico-chemical buffering in equine muscles. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 276–280.
99. Juel C. Lactate/proton co-transport in skeletal muscle: regulation and importance for pH homeostasis. Acta Physiol Scand 1996; 156:369–374.
100. Juel C. Muscle pH regulation: role of training. Acta Physiol Scand 1998; 162:359–366.
101. Halestrap AP, Price NT. The proton-linked monocarboxylate transporter (MCT) family: structure, function and regulation. Biochem J 1999; 343:281–299.
102. Bonen A. Lactate transporters (MCT proteins) in heart and skeletal muscles. Med Sci Sports Exerc 2000; 32:778–789.
103. Fishbein WN, Merezhinskaya N, Foellmer JW. Relative distribution of three major lactate transporters in frozen human tissues and their localization in unfixed skeletal muscle. Muscle Nerve 2002; 26:101–112.
104. Sepponen K, Koho N, Puolanne E, et al. Distribution of monocarboxylate transporter isoforms MCT1, MCT2 and MCT4 in porcine muscles. Acta Physiol Scand 2003; 177:79–86.
105. Pilegaard H, Domino K, Noland T, et al. Effect of high-intensity exercise training on lactate/H^+ transport capacity in human skeletal muscle. Am J Physiol 1999; 276:E255–E261.
106. Dubouchaud H, Butterfield GE, Wolfer EE, et al. Endurance training, expression, and physiology of LDH, MCT1, and MCT4 in human skeletal muscle. Am J Physiol 2000; 278:E571–E579.
107. Green H, Halestrap A, Mockett C, et al. Increases in muscle MCT are associated with reductions in muscle lactate after a single exercise session in humans. Am J Physiol Endocrinol Metab 2002; 282:E154–E160.
108. Dehaan A, Koudijs JCM. A linear relationship between ATP degradation and fatigue during high-intensity dynamic exercise in rat skeletal muscle. Exp Physiol 1994; 79:865–868.
109. Schuback K, Essén-Gustavsson B, Persson SGB. Incremental treadmill exercise until onset of fatigue and its relationship to metabolic response and locomotion pattern. Equine Vet J 1999; 30(Suppl):337–341.
110. Snow DH, Kerr MG, Nimmo MA, et al. Alterations in blood, sweat, urine and muscle composition during prolonged exercise in the horse. Vet Rec 1982; 110:377–384.
111. Lucke JN, Hall GN. Further studies on the metabolic effects of long distance riding: Golden Horseshoe Ride 1979. Equine Vet J 1980; 12:189–192.
112. Hodgson DR, Rose RJ, Allen JR. Muscle glycogen depletion and repletion patterns in horses performing various distances of endurance exercise. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 229–236.
113. Farris JW, Hinchcliff KW, McKeever KH, et al. Effect of tryptophan and of glucose on exercise capacity of horses. J Appl Physiol 1998; 85:807–816.
114. Nagata S, Takeda F, Kurosawa M, et al. Plasma adrenocorticotropin, cortisol and catecholamines responses to various exercises. Equine Vet J 1999; 30(Suppl): 570–574.
115. Kokkonen U-M, Pösö AR, Hyyppä S, et al. Exercise-induced changes in atrial natriuretic peptides in relation to other neuroendocrine responses and fluid balance in the horse. J Vet Med Assoc 2002; 49:144–150.
116. Dybdal NO, Gribble D, Madigan JE, et al. Alterations in plasma corticosteroids, insulin and selected metabolites in horses used in endurance rides. Equine Vet J 1980; 12:137–140.
117. Rose RJ, Snow DH. Hormonal changes associated with long distance exercise. Equine Vet J 1981; 13:195–197.
118. Pösö AR, Hyyppä S. Muscle and hormonal changes after exercise in relation to muscle glycogen concentrations. Equine Vet J 1999; 30(Suppl):332–336.
119. Havel RJ, Carlson LA, Ekelund LG, et al. Turnover rate and oxidation of different free fatty acids in man during exercise. J Appl Physiol 1964; 19:613–618.
120. Snow DH, MacKenzie G. Some metabolic effects of maximal exercise in the horse and adaptations with training. Equine Vet J 1977; 9:134–140.
121. Pösö AR, Viljanen-Tarifa E, Soveri T, et al. Exercise-induced transient hyperlipidemia in the racehorse. J Vet Med Assoc 1989; 36:603–611.
122. Rose RJ, Knight PK, Bryden WL. Energy use and cardiorespiratory responses to prolonged submaximal exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 281–287.
123. Rose RJ, Purdue RA, Hensley W. Plasma biochemistry alterations in horses during an endurance ride. Equine Vet J 1977; 9:122–126.
124. Pösö AR, Soveri T, Oksanen HE. The effect of exercise on blood parameters in standardbred and Finnish-bred horses. Acta Vet Scand 1983; 24:170–184.
125. Geiser DR, Andrews F, Sommerdahl C, et al. Electrolyte and acid-base changes in combined training horses after the cross-country event. Equine Pract 1994; 16:20–25.
126. Desmecht D, Linden A, Amory H, Art T. Relationship of plasma lactate production to cortisol release following completion of different types of sporting events in horses. Vet Res Commun 1996; 20:371–379.
127. Sewell DA, Harris RC, Hanak J, et al. Muscle adenine nucleotide degradation in the thoroughbred horse as a consequence of racing. Comp Biochem Physiol 1992; 101B:375–382.
128. Keenan DM. Changes of blood metabolites in horses after racing, with particular reference to uric acid. Aust Vet J 1979; 55:54–57.
129. Kelso TB, Hodgson DR, Witt EH, et al. Bicarbonate administration and muscle metabolism during high-intensity exercise: In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 438–447.
130. Evans DL, Priddle TL, Davie AJ. Plasma lactate and uric acid responses to racing in pacing Standardbreds and relationships with performance. Equine Vet J 2002; 34(Suppl):131–134.
131. White SL, Williamson LH, Maykuth P, et al. Heart rate and lactate concentration during two different cross country events. Equine Vet J 1995; 18(Suppl):463–467.
132. Art T, Amory H, Desmecht D, et al. Effect of show jumping on heart rate, blood lactate and other plasma biochemical values. Equine Vet J 1990; 9(Suppl):78–82.
133. Mueller PJ, Jones MT, Rawson RE, et al. Effect of increasing work rate on metabolic responses of the donkey (*Equus asinus*). J Appl Physiol 1994; 77:1431–1438.
134. Räsänen LA, Wiitanen PAS, Lilius E-M, et al. Accumulation of uric acid in plasma after repeated bouts of exercise in the horse. Comp Biochem Physiol 1996; 114B:139–144.
135. Harris RC, Marlin DJ, Snow DH, et al. Muscle ATP loss and lactate accumulation at different work intensities in the exercising Thoroughbred horse. Eur J Appl Physiol Occup Physiol 1991; 61:235–244.

136. Essén-Gustavsson B, Valberg S. Blood and muscle ammonia concentrations in horses during treadmill work and after racing. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 456–463.
137. Puolanne E, Pösö AR, Ruusunen M, et al. Lactic acid in muscles and its effects on meat quality. Proceedings of the 55th Reciprocal Meat Conference 2002; 55–62.
138. Graham TE, Adamo KB, Shearer J, et al. Pro- and macroglycogenolysis: relationships with excersise intensity and duration. J Appl Physiol 2001; 90:873–879.
139. Shearer J, Marchand I, Tarnopolsky MA, et al. Pro- and macroglycogenolysis during repeated exercise: roles of glycogen content and phosphorylase activation. J Appl Physiol 2001; 90:880–888.
140. Essén-Gustavsson B, Jensen-Waern M. Effect of an endurance race on muscle amino acid, pro- and macroglycogen and triglycerides. Equine Vet J 2002; 34(Suppl):209–213.
141. Bröjer J, Jonasson R, Schuback K, et al. Pro-and macroglycogenolysis in skeletal muscle during maximal treadmill exercise. Equine Vet J 2002; 34(Suppl):205–208.
142. Valberg S, Essén-Gustavsson B, Lindholm A, et al. Energy metabolism in relation to skeletal muscle fibre properties during treadmill exercise. Equine Vet J 1985; 17:439–444.
143. Pilegaard H, Bangsbo J, Henningsen P, et al. Effect of blood flow on muscle lactate release studied in perfused rat hindlimb. Am J Physiol Endocrinol Metab 1995; 269:E1044–E1051.
144. Ronéus N, Essén-Gustavsson B. Skeletal muscle characteristics and metabolic response to exercise in young Standardbreds. Am J Vet Res 1997; 58:167–170.
145. Hodgson DR, Rose RJ, McCutcheon LJ, et al. Effects of acetazolamide on cardiorespiratory and metabolic responses to submaximal exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 343–352.
146. Lacombe VA, Hinchcliff KW, Geor RJ, et al. Muscle glycogen depletion and subsequent replenishment affect anaerobic capacity of horse. J Appl Physiol 2001; 91:1782–1790.
147. Flaminio MJBF, Rush BR. Fluid and electrolyte balance in endurance horses. Vet Clin North Am Equine Pract 1998; 14:147–158.
148. White SL. Fluid, electrolyte, and acid-base balance in endurance horses. Vet Clin North Am Equine Pract 1998; 14:137–145.
149. Art T, Lekeaux P. Respiratory adjustments in unacclimatised horses exercised under hot, humid conditions. Equine Vet J 1995; 18(Suppl):289–293.
150. Dahl L-G, Gillespie JR, Kallings P, et al. Effects of cold environment on exercise tolerance in the horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 235–242.
151. Cymbaluk NF. Thermoregulation of horses in cold, winter weather: a review. Livestock Product Sci 1994; 40:65–71.
152. Tyler CM, Hodgson DR, Rose RJ. Effect of warm-up on energy supply during high intensity exercise in horses. Equine Vet J 1996; 28:117–120.
153. Geor RJ, McCutcheon LJ, Hinchcliff KW. Effects of warm-up intensity on kinetics of oxygen uptake and carbon dioxide production in horses during high-intensity exercise. Am J Vet Res 2000; 61:638–645.
154. McCutcheon LJ, Geor RJ, Hinchcliff KW. Effects of prior exercise on muscle metabolism during sprint exercise in horses. J Appl Physiol 1999; 87:1914–1922.
155. Hoyt DF, Taylor CF. Gait and energetics of locomotion in horses. Nature 1981; 292:239–240.
156. Wickler SJ, Hoyt DE, Cogger EA, et al. The cost of transport in an extended trot. Equine Vet J 2002; 34(Suppl): 126–130.
157. Wickler SJ, Hoyt DF, Cogger EA, et al. Effect of load on preferred speed and cost of transport. J Appl Physiol 2001; 90:1548–1551.
158. Persson SGB, Essén-Gustavsson B, Lindholm A. Energy profile and the locomotor pattern of trotting on an inclined treadmill. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 231–238.
159. Ronéus N, Essén-Gustavsson B, Johnston C, et al. Lactate response to maximal exercise on track: relation to muscle characteristics and kinematic variables. Equine Vet J 1995; 18(Suppl):191–194.
160. Snow DH. Skeletal muscle adaptations. A review. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 160–183.
161. Langsetmo I, Weigle GE, Fedde MR, et al. $\dot{V}o_2$ kinetics in the horse during moderate and heavy exercise. J Appl Physiol 1997; 83:1235–1241.
162. Hinchcliff KW, Lauderdale MA, Dutson J, et al. High intensity exercise conditioning increases accumulated oxygen deficit in horses. Equine Vet J 2002; 34:9–16.
163. Prince A, Geor R, Harris P, et al. Comparison of the metabolic responses of trained Arabians and Thoroughbreds during high- and low-intensity exercise. Equine Vet J 2002; 34(Suppl):95–99.
164. Gauvreau GM, Staempfli H, McCutcheon LJ, et al. Comparison of aerobic capacity between racing standardbred horses. J Appl Physiol 1995; 78:1447–1451.
165. Tyler CM, Golland LC, Evans DL, et al. Changes in maximum oxygen uptake during prolonged training, overtraining and detraining. J Appl Physiol 1996; 81:2244–2249.
166. Katz LM, Bayly WM, Roeder MJ, et al. Effects of training on maximum oxygen consumption of ponies. Am J Vet Res 2000; 61:986–991.
167. Langsetmo I, Poole DC. $\dot{V}o_2$ recovery kinetics in the horse following moderate, heavy, and severe exercise. J Appl Physiol 1999; 86:1170–1177.
168. Lovell DK, Rose RJ. Effects of postexercise activity on recovery from maximal exercise. Equine Vet J 1995; 18(Suppl): 188–190.
169. Marlin DJ, Harris RC, Harman JC, et al. Influence of post-exercise activity on rates of muscle and blood lactate disappearance in the Thoroughbred horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 321–331.
170. Hubbell JAE, Hinchcliff KW, Muir WW, et al. Cardiorespiratory and metabolic effects of walking, standing, and standing with a splint during the recuperative period from maximal exercise in horses. Am J Vet Res 1997; 58:1003–1009.
171. Adamo KB, Tarnopolsky MA, Graham TE. Dietary carbohydrate and postexercise synthesis of proglycogen and macroglycogen in human skeletal muscle. Am J Physiol Endocrinol Metab 1998; 275:E229–E234.
172. Davie AJ, Evans DL, Hodgson DR, et al. Effects of intravenous dextrose infusion on muscle glycogen resynthesis after intense exercise. Equine Vet J 1995; 18(Suppl):195–198.
173. Knight PK, Sinha AK, Rose RJ. Effects of training intensity on maximum oxygen uptake. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 77–82.
174. Eaton MD, Hodgson DR, Evans DL, et al. Effects of low- and moderate-intensity training on metabolic responses to

exercise in thoroughbreds. Equine Vet J 1999; 30(Suppl): 521–527.
175. Henckel P. Training and growth induced changes in the middle gluteal muscle of young Standardbred trotters. Equine Vet J 1983; 14:134–140.
176. Sinha AK, Ray SP, Rose RJ. Effect of training intensity and detraining on adaptations in different skeletal muscles. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 223–230.
177. Lovell DK, Rose RJ. Changes in skeletal muscle composition in response to interval and high intensity training. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 215–222.
177. Ronéus M, Essén-Gustavsson B, Lindholm A, et al. Skeletal muscle characteristics in young trained and untrained Standardbred trotters. Equine Vet J 1992; 24:292–294.
179. Ronéus M. Muscle characteristics in Standardbreds of different ages and sexes. Equine Vet J 1993; 25:143–146.
180. Serrano AL, Quiroz-Rothe E, Rivero JL. Early and long-term changes of equine skeletal muscle in response to endurance training and detraining. Pflugers Arch Eur J Physiol 2000; 441:263–274.
181. McGowan CM, Golland LC, Evans DL, et al. Effects of prolonged training, overtraining and detraining on skeletal muscle metabolites and enzymes. Equine Vet J 2002; 34(Suppl):257–263.
182. Wilson RG, Thornton JR, Inglis S, et al. Skeletal muscle adaptation in racehorses following high intensity interval training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 367–375.
183. Rivero JL, Serrano AL. Skeletal myosin heavy chain composition and carriage training. Equine Vet J 1999; 30(Suppl):318–323.
184. Serrano AL, Rivero JLL. Myosin heavy chain profile of equine *Gluteus medius* muscle following draught-exercise training and detraining. J Muscle Res Cell Motil 2000; 21:235–245.
185. Linnane L, Serrano AL, Rivero JLL. Distribution of fast myosin heavy chain-based muscle fibers in the gluteus medius of untrained horses: mismatch between antigenic and ATPase determinations. J Anat 1999; 194:363–372.
186. Rivero JL, Serrano AL, Henckel P, et al. Muscle fiber type composition and fiber size in successfully and unsuccessfully endurance-raced horses. J Appl Physiol 1993; 75:1758–1766.
187. Tyler CM, Golland LC, Evans DL, et al. Skeletal muscle adaptations to prolonged training, overtraining and detraining in horses. Pflugers Arch Eur J Physiol 1998; 436:391–397.
188. Lopez-Rivero JL, Morales-Lopez JL, Galisteo A-M, et al. Muscle fiber type composition in untrained and endurance-trained Andalusian and Arab horses. Equine Vet J 1991; 23:91–93.
189. Rivero JL. Muscle biopsy as a tool for assessing muscular adaptation to training in horses. Am J Vet Res 1996; 57:1412–1416.
190. Geor RJ, McCutcheon LJ, Shen H. Muscular and metabolic responses to moderate-intensity short-term training. Equine Vet J 1999; 30(Suppl):311–317.
191. Fox G, Henckel P, Juel C, et al. Skeletal muscle buffer capacity changes in Standardbred horses: effects of growth and training. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 341–347.
192. Boutilier RG, St-Pierre J. Surviving hypoxia without really dying. Comp Biochem Physiol A 2000; 126:481–490.
193. Essén-Gustavsson B, McMiken D, Karlström K, et al. Muscular adaptation of horses during intensive training and detraining. Equine Vet J 1989; 21:27–33.
194. Butler PJ, Woakes AJ, Anderson LS, et al. The effect of cessation of training on cardiorespiratory variables during exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 71–76.
195. Spriet LL, Peters SJ. Influence of diet on the metabolic response to exercise. Proc Nutr Soc 1998; 57:25–33.
196. Bergström J, Hermansen L, Hultman E, et al. Diet, muscle glycogen and physical performance. Acta Physiol Scand 1967; 71:140–150.
197. Jansson A, Nyman S, Lindholm A, et al. Effects on exercise metabolism of varying dietary starch and sugar proportions. Equine Vet J 2002; 34(Suppl):17–21.
198. MacLeay JJM, Valberg S, Pagan JD et al. Effect of diet on Thoroughbred horses with recurrent exertional rhabdomyolysis performing a standardised exercise test. Equine Vet J 1999; 30(Suppl):458–462.
199. Orme CE, Harris RC, Marlin DJ, et al. Metabolic adaptation to a fat-supplemented diet by the Thoroughbred horse. Br J Nutr 1997; 78:443–458.
200. Geelen SN, Sloet van Oldruitenborgh-Oosterbaan MM, Beynen AC. Dietary fat supplementation and equine plasma lipid metabolism. Equine Vet J 1999; 30(Suppl): 475–478.
201. Dunnett CE, Marlin DJ, Harris RC. Effect of dietary lipid on response to exercise: relationship to metabolic adaptation. Equine Vet J 2002; 34(Suppl):75–80.
202. Geelen SN, Jansen WL, Sloet van Oldruitenborgh-Oosterbaan MM, et al. Fat feeding increases equine heparin-released lipoprotein lipase activity. J Vet Intern Med 2001; 15:478–481.
203. Harkins JD, Morris GS, Tulley RT, et al. Effect of added dietary fat on racing performance in Thoroughbred horses. J Equine Vet Sci 1992; 12:123–129.
204. Eaton MD, Hodgson DR, Evans DL, et al. Effect of a diet containing supplementary fat on the capacity for high intensity exercise. Equine Vet J 1995; 18(Suppl): 353–356.
205. Sunvold GD, Hussein HS, Fahey Jr GC, et al. In vitro fermentation of cellulose, beet pulp, citrus pulp and citrus pectin using fecal innoculum from cats, dogs, horses, humans, and pigs and ruminal fluid from cattle. J Anim Sci 1995; 73:3639–3648.
206. Lindberg JE, Palmgren Karlsson C. Effect of replacing oats with sugar beet pulp and maize oil on nutrient utilisation in horses. Equine Vet J 2001; 33:585–590.
207. Palmgren Karlsson C, Jansson A, Essén-Gustavsson B, et al. Effect of molassed sugar beet pulp on nutrient utilisation and metabolic parameters during exercise. Equine Vet J 2002; 34(Suppl):44–49.
208. Glade MJ. Nutrition and performance of racing Thoroughbreds. Equine Vet J 1983; 15:31–36.
209. Miller PA, Lawrence LM. The effect of dietary protein level on exercising horses. J Anim Sci 1988; 66:2185–2192.
210. Miller-Graber PA, Lawrence LM, Foreman JH, et al. Dietary protein level and energy metabolism during treadmill exercise in horses. J Nutr 1991; 121:1462–1469.
211. Graham-Thiers PM, Kronfeld DS, Kline KA, et al. Dietary protein restriction and fat supplementation diminish the acidogenic effect of exercise during repeated sprints in horses. J Nutr 2001; 131:1959–1964.
212. Lawrence LM, Soderholm LV, Roberts AM, et al. Feeding status affects glucose metabolism in exercising horses. J Nutr 1993; 123:2151–2157.

213. Lawrence LM, Hintz HF, Soderholm LV, et al. Effect of time of feeding on metabolic response to exercise. Equine Vet J 1995; 18(Suppl):392–395.
214. Stull C, Rodiek A. Effects of post prandial interval and feed type on substrate availability during exercise. Equine Vet J 1995; 18(Suppl):362–366.
215. Pagan JD, Harris PA. The effects of timing and amount of forage and grain on exercise response in Thoroughbred horses. Equine Vet J 1999; 30(Suppl):451–457.
216. Rice O, Geor R, Harris P, et al. Effects of restricted hay intake on body weight and metabolic responses to high-intensity exercise in Thoroughbred horses. Proceedings of the 17th Meeting of the Equine Nutritional and Physiology Society 2001; 273–279.
217. Harris PA, Kronfeld DS. Influence of dietary energy source on health and performance. In: Robinson NE, ed. Current therapy in equine medicine, 5th ed Philadelphia, PA: Saunders; 2003; 698–704.

CHAPTER 35

Endocrine alterations in the equine athlete

Kenneth Harrington McKeever and Mary Beth Gordon

Introduction

For the most part the domestic horse spends a good part of its day either eating or seeking food.[1] In feral horses the latter can involve treks over a wide range.[1] However, most horses spend the majority of their day eating, standing and occasionally exercising.[1] Exercise can range from running up and down the fence line in anticipation of the feed truck to athletic training for a variety of competitive endeavors.[1] Under resting conditions, the horse has a relatively easy job of maintaining the internal environment. However, whatever the activity, the performance of work or exercise is a major physiological challenge, a disturbance to homeostasis, that invokes an integrative response from multiple organ systems.[1] On a gross level there is a pairing of those systems associated with convective transport and those associated with the transduction of potential energy into kinetic energy.[1] Put another way, the response to exercise requires the transport of oxygen from the atmosphere to the cells in the working muscles where it is utilized in metabolic pathways generating ATPs for fuel utilization.[1] In reality, though, the adjustments to acute exercise require the co-ordination of several systems including the respiratory, cardiovascular, muscular, integumentary, renal, hepatic and the various organs of the digestive tract.[1–5] Each tissue or organ called upon to facilitate movement must function in co-ordination with others in a variety of classic feedback loops (Fig. 35.1). Multiple layers of control exist in the body to facilitate work. The first muscle contractions associated with work will alter mechanisms of autoregulation causing changes in local control of the local environment that are sensed peripherally. Longer work causes system-wide alterations that necessitate integrated whole-body responses requiring neural and endocrine mediation.

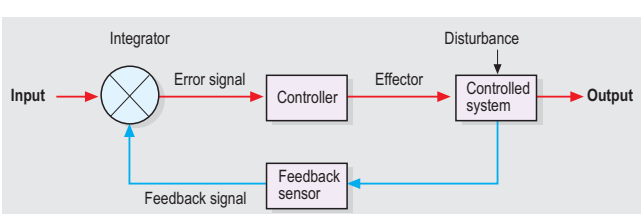

Fig. 35.1
Components of a controlled negative feedback system.

The most rapid mechanisms used to facilitate a co-ordinated response to exercise involve an integration of error signals in the periphery that are communicated via the nervous system to central command centers where adjustments are made to the respiratory and cardiovascular systems.[3–5] Some have suggested that the rapid adjustments in cardiopulmonary function at the onset of exercise can be accomplished primarily via a shift in autonomic tone with a withdrawal of parasympathetic tone and an increased sympathetic drive.[4,5] However, as exercise progresses beyond a few seconds, more sophisticated mechanisms are called upon to fine-tune the initial response to the disturbance of exercise.

Fine-tuning of the response to exercise that lasts longer than a few seconds is reliant on the regulation of several key variables governing the cardiopulmonary, vascular and metabolic response to exercise.[3–5] Regulation allows the internal environment to be maintained within relatively narrow limits so as to enhance optimal cell function. This type of classic regulation involves a multiple system response where some variables are controlled so that those most vital to the defense of the internal environment can be regulated.

This type of integrative response is slower than a neural response because it requires communication between systems that relies on the secretion of substances by one tissue or organ that are transported remotely to other tissues or organs to evoke a response to the disturbance.[3–5]

Endocrine system and hormones

By definition, a hormone is a substance that is produced and released by one organ or tissue and is transported via the blood to a remote target organ or tissue where it causes a physiological response.[2,5] Most hormones fall into two major categories: the steroid hormones and the non-steroid hormones. Steroid hormones include cortisol, aldosterone and the reproductive hormones testosterone, estrogen and progesterone.[2,5] The steroid hormones have a classic ring structure and are lipid soluble, a characteristic that allows them to diffuse across cell membranes.[2,5] Mechanistically, the steroid hormones exert their effect through direct gene activation that occurs after diffusion into the cell (Fig. 35.2).[2,5] Once across the cell membrane, they bind to receptors in either the cytoplasm or the nucleus.[2,5] This complex formed by the steroid hormone and receptor induces the DNA in the cell to produce mRNA which, when it enters the cytoplasm, is transcribed, resulting in the production of protein.[2,5] This protein results in the physiologic action of the hormone on cellular function.[2,5]

The non-steroid hormones are not lipophylic and thus, cannot pass through the cell membrane.[2,5] These hormones bind in a lock-and-key fashion to very specific receptors on the surface of the cell membrane (Fig. 35.3).[2,5] The hormone–receptor complex remains in the membrane, but is still able to activate the enzyme adenylate cyclase within the cytoplasm of the cell.[2,5] Activation starts a cascade that results in the active formation of the enzyme cAMP through the combination of adenylate cyclase and ATP.[2,5] The enzyme cAMP in turn activates specific inactive protein kinases which cause the conversion of inactive substrates into active substrates that have the capability to induce changes in cellular form or function.[2,5]

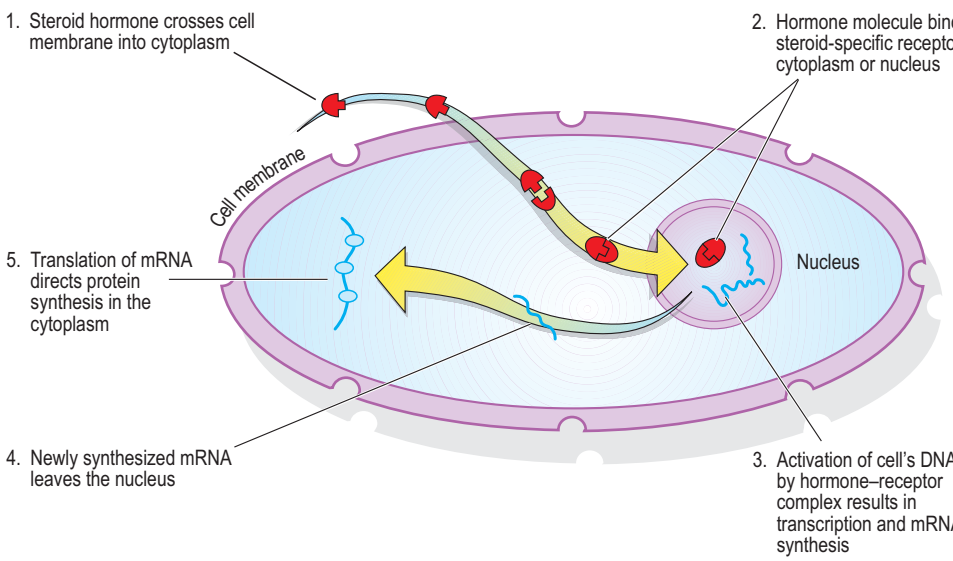

Fig. 35.2
Gene activation mechanism associated with the action of a steroid hormone.

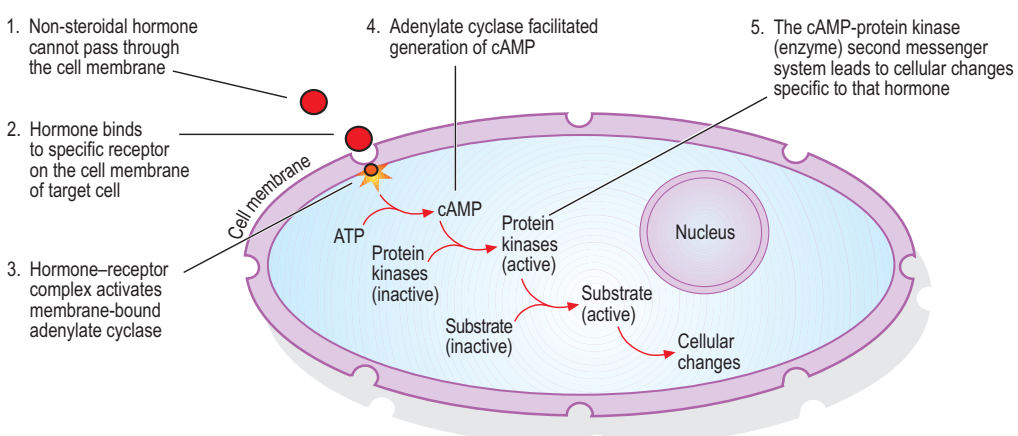

Fig. 35.3
Second messenger mechanism associated with the action of non-steroid hormones.

Release of most hormones is part of a controlled negative feedback system that keeps a specific variable within narrow limits.[2,5] The typical negative feedback system is composed of a variable that has an input or set point that is read or sensed by an integrator.[2,5] For the system to be in a state of balance or homeostasis, the input and output signals must be the same. If the input variable is changed by a disturbance, such as exercise, the integrator senses the mismatch and sends an error signal, usually via nerves, to the controller. The controller then alters the controlled system via an effector. In some cases the effector is a nervous signal; however, in some cases it is a hormone. The effector causes a change in the controlled system, inducing a change in the output that is sensed by the feedback sensor. The feedback sensor sends a signal to the integrator that then determines if the input matches the output of the system.

Physiological variables that are the most critical to normal function are regulated. *Regulation* refers to a phenomenon in which the output of a system remains relatively constant under many different disturbances. For example, mean arterial pressure, plasma osmolality, blood pH, Pco_2 and Po_2, plasma electrolyte ($Na,^+$ K^+ and Cl^-) concentrations, blood glucose concentration and body temperature are just a few of the major variables that are regulated and held within very narrow limits during exercise. Regulation of each of these variables is accomplished through a combination of neural and endocrine mechanisms affecting multiple control strategies. *Control* is a phenomenon where the output of the system constantly changes in order to manage a rate of functioning. In short, some physiological variables are controlled so that others may be regulated. The more rapid responses used to maintain homeostasis are usually mediated by neural control mechanisms with less rapid responses usually mediated by endocrine mechanisms.

For example, maintenance of systemic mean arterial pressure around a narrow set point is critical to cardiovascular performance.[4] Multiple systems are controlled to insure that MAP is sufficient to allow perfusion of all the working muscles as well as obligate tissues during exercise.[4] At the onset of exercise, there is a decrease in total peripheral vascular resistance (TPR) that results from the opening of blood vessels in the working muscles.[4] This allows for the increase in blood flow to those vascular beds.[4] However, there is an almost simultaneous increase in cardiac output which comes about through the matching of the input and output signals sensed by volume and baroreceptors placed at strategic points in the cardiovascular system.[1,4] Matching of the input and output signals (see Fig. 35.1) by the vasomotor center of the medulla (the integrator) results in an error signal via the autonomic nervous system (the controller).[1,4] A withdrawal of vagal tone and an increase in sympathetic drive results in the local release of norepinephrine (effector) which causes a rapid increase in heart rate and the force of contraction that raises cardiac output (the controlled system) enough to maintain MAP.[1,4] As exercise intensity increases the set point for MAP is increased; thus, higher intensity exercise usually requires more dramatic responses, including a decrease in blood flow to non-obligate tissues such as the splanchnic vascular beds.[1,4] The initial part of this response is mediated by neural mechanisms affecting the arteriole in those vascular beds.[1,4] However, higher intensity exercise also requires the added influence of endocrine effectors such as vasopressin and angiotensin II to cause sufficient vasoconstriction in non-obligate tissues to facilitate the rise in MAP needed for optimal cardiovascular function.[1,4] As such, one example of the role of the endocrine system during exercise can be seen in the regulation of MAP.[1,4] Longer term control of MAP can be affected by the duration of exercise which results in multiple strategies to control blood volume and defend cardiac filling pressure, cardiac output and MAP.[1,4]

Major endocrine glands and hormones

Pituitary gland

The pituitary is found at the base of the brain and is divided into three lobes: the anterior, intermediate and posterior.[2,5] Hormones of importance during exercise are produced and released by the anterior and posterior lobes.[2,5] The pituitary is vitally linked to the hypothalamus, an area of the brain with many very specific neural tracts that act as feedback sensors.[2,5] The hypothalamus also acts as the integrator in the controlled system, exerting control over the pituitary through neural and endocrine mechanisms.[2,5] The latter include various releasing hormones and inhibitory hormones and other substances.[2,5] The central location of this hypothalamic-pituitary axis makes it ideal for mediating the control of a wide variety of functions.[2,5]

Anterior pituitary hormones

Hormones produced by the anterior lobe of the pituitary include somatotrophin (growth hormone, GH, ST), thyrotrophin (thyroid-stimulating hormone or TSH), adrenocorticotrophin (ACTH), endorphins (EN), enkephalins, dynorphins, follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin.[2,5] The first three play an important role in growth and development in the young animal and metabolism in the adult animal. The endorphins, enkephalins and dynorphins are opiate-like peptide hormones that modulate pain reception and interact with the neural pathways of the hypothalamic-pituitary axis to influence releasing and inhibiting hormones.[6–8] FSH, LH and prolactin are considered hormones essential for normal reproduction and lactation.[2,5] New research in species other than horses has demonstrated that severe or prolonged exertion can alter their release and thus normal reproductive cycles.[2,5] Furthermore, prolactin appears to play an important role in the response to severe stress, interacting with many of the metabolic hormones.[2,5]

Somatotrophin (ST) Somatotrophin affects all the cells in the body, stimulating development and growth in younger animals. In mature animals it plays a vital role in muscle metabolism through its effects on protein synthesis and its role in fat and carbohydrate utilization.[2,5] The importance of somatotrophin in maintenance of normal physiologic function and its possible role in slowing or possibly even reversing the effects of aging can be seen in some younger adult humans, where somatotrophin 'deficiency' results in changes in appearance, decreased lean body mass, decreased immune function and other 'sequelae' of aging.[9,10] Amazingly, treatment of these individuals with recombinant human somatotrophin results in increased lean body mass, decreased body fat and increased muscle mass.[9,10] Chronic somatotrophin administration appears to increase strength and the ability to perform a battery of weight-lifting exercises in aged male humans.[9,10] While there have been no reported effects of ST on aerobic capacity, the increase in muscle mass and strength has been shown to benefit the quality of life in humans by increasing the ability to do daily tasks such as maintaining balance while walking and climbing stairs.[9,10] Those human experiments served as part of the justification for several recent studies of the efficacy of recombinant somatotrophin treatment in preventing or retarding functional decline in geriatric humans[9,10] and in geriatric horses.[11–14]

Researchers conducting equine studies[11–15] have asked 'quality of life' questions similar to those posed in experiments using aged humans.[9,10] While those studies demonstrated that equine ST (eST) therapy increases nitrogen retention and improves appearance in geriatric horses, they did not demonstrate any effect of chronic eST administration on bodyweight or the dimensions of several key muscles measured using ultrasonography.[13] Functionally, chronic eST administration did not alter aerobic capacity or several commonly used indices of exercise performance, at least not in unfit aged mares.[14] Furthermore, data from unfit geriatric horses indicated that eST did not alter lactate tolerance or cause an increase in maximal power that one would associate with an increase in muscular strength, a logical observation since there was no evidence of an increase in muscle mass.[14] Interestingly, studies of geriatric male humans have shown that recombinant somatotrophin therapy results in increased muscle mass and, in some cases, increased strength as measured in standardized tests performed with weight-lifting equipment.[9,10] However, while ST therapy does appear to increase strength in humans, there are no data to show that ST therapy alters maximal aerobic capacity or enhances endurance performance.[9,10]

More recent studies of younger horses have demonstrated that administration of eST prevents some of the bone demineralization that occurs in the first months of intense training.[16] Other studies found that there was minimal or no therapeutic benefit of administering eST to prevent tendon or cartilage injuries or to promote wound healing.[17–19] Another report demonstrated that eST does not alter aerobic capacity or markers of performance in young (~ 2 years) Thoroughbreds.[17,18] However, as with the studies of older horses, the experiments performed on younger animals had no way to evaluate the effects of eST administration on muscular strength; thus, data are needed to determine if eST alters strength and power.

Thyrotrophin (TSH) Release of TSH is stimulated by thyroid-stimulating hormone releasing hormone (TRH) which is produced in the hypothalamus.[2,5] Studies of humans and other species have demonstrated that acute exercise elicits mixed effects on TSH release.[20] The release of TSH appears to be linked to exercise intensity as mild and moderate exertion do not appear to have an effect on TSH release. However, there appears to be a threshold for stimulating TSH release, as plasma concentrations of this hormone increase only when exercise intensity exceeds 50% of $\dot{V}O_{2max}$ in humans.[20] This breakpoint is common to several hormonal systems including the observed increases in the catecholamines, ACTH, cortisol, PRA, etc., which may indicate that there is an interplay in the metabolic response to higher intensity exercise.[20–24] Interestingly, exercise duration beyond 40 minutes appears to cause an increase in TSH.[20] This observed increase during longer steady-state exertion is similar to the response of other metabolic hormones and may be related to substrate mobilization and attempts to prevent the onset of central fatigue mechanisms. In humans, repeated daily exercise also causes the release of TSH, suggesting the ratcheting up of metabolic function with exercise training.[5,20] Data on the effects of acute exercise and training on TSH in equine athletes are lacking.

Adrenocorticotrophin (ACTH) As with TSH, the release of ACTH is stimulated by corticotrophin-releasing hormone which is secreted by the hypothalamus.[2,5] A number of published papers have demonstrated that exercise causes an increase in ACTH in the horse; however, most of these only report postexercise values.[20,25–31] The major conclusion of most exercise studies has been that both high-intensity and endurance exercise cause an increase in ACTH and subsequent increase in cortisol.[20] Some researchers have attempted to characterize this as a stress response; however, if one looks at the role of cortisol in substrate mobilization and metabolic control during exertion, then one can see that the ACTH/cortisol response, if in the normal range, is an appropriate response to exertion.[20,25–32]

A more recent study demonstrated that ACTH increases in a curvilinear fashion with exercise intensity during controlled incremental exercise performed on a treadmill.[24] The ACTH response appeared to be highly correlated to the catecholamine and lactate responses to incremental exercise, all of which also increased in a curvilinear fashion.[24] When horses were exercised at steady-state speeds (80% or 110% $\dot{V}O_{2max}$), the ACTH response was rapid, with concentrations increasing in a linear fashion until the end of the exercise test.[24] Postexercise concentrations fell rapidly, returning to baseline within 60–120 min.[24] These responses are similar to those reported for humans and other species.[5,24]

The endorphins, enkephalins and dynorphins These peptides are released from the pituitary in response to pain or pleasure.[6–8] While some classify these substances as hormones, others classify them as neurotransmitters.[6–8] Nevertheless, these substances are naturally occurring opiate-like

pain suppressors that may allow a horse to tolerate higher intensity exercise.[6–8,31–34] The endorphins, enkephalins and dynorphins play a role in the response to physiological and psychological stress and appear to modulate pain perception.[6–8] As such, these hormones are markers of stress. However, since some sports medicine specialists have suggested that an overload of duration, intensity or resistance is needed for exercise training to elicit an adaptive response, then under controlled conditions, the endorphins may play an important role in allowing a horse to tolerate the progressive increases in exercise intensities or longer durations needed to invoke a training response. Mehl and co-workers[6–8] have demonstrated that a threshold exists for evoking an increase in plasma β-endorphin concentration. This threshold appears to correspond to ~ 60% of the speed eliciting $\dot{V}O_{2max}$. Interestingly, this is the same point at which one sees a curvilinear increase in the catecholamines, plasma renin activity, plasma lactate concentration and several other variables. This suggests a close interplay between these factors in the transition from low-intensity, primarily aerobic exercise to higher intensity exercise with an increasing anaerobic component.[21–24,35] Duration of exercise also appears to affect the magnitude of the endorphin response, with greater plasma concentrations as horses approach fatigue.[6–8] Training appears to alter the endorphin response to acute exertion with greater concentrations observed in the post-exertion peak occurring between 5 and 10 minutes post exertion.[36]

Posterior pituitary hormones

Hormones released from the posterior lobe of the pituitary include arginine vasopressin (AVP) and oxytocin. These two protein hormones are actually produced in the hypothalamus by specialized bundles of nerves.[2,5] Arginine vasopressin is synthesized in cells of supraoptic and paraventricular nuclei and stored in vesicles in the nerve endings located in the posterior pituitary. Vasopressin plays a role in blood pressure regulation and fluid and electrolyte balance. It is for this later role that some refer to AVP as antidiuretic hormone or ADH.[2,5] AVP plays a major role in the short-term and long-term control of cardiovascular function during and following exercise.[2,5] Oxytocin causes smooth muscle contraction in the epididymis of males and the uterus of females and also acts on mammary tissue, causing milk letdown in lactating mares.[2,5] Oxytocin does not appear to play a role in the response to exercise.

Arginine vasopressin (AVP) AVP is a posterior pituitary hormone associated with the acute and chronic defense of blood pressure, plasma volume and fluid and electrolyte balance.[1–3,37–39,41] The primary physiological actions of AVP include vasoconstriction and decreased free water clearance.[3,37–39,41] The mechanism for the release of AVP involves osmoreceptors in the supraoptic and paraventricular nuclei of the hypothalamus and cardiopulmonary baroreceptors in the atria of the heart.[2,3,37–39,41] Data from rats and other species have shown that a very small 1–2% decrease in cell volume in the hypothalamus or change in extracellular osmolality of 2–4 mOsm/kg will stimulate AVP secretion and drinking.[37–39] Exercise causes an increase in plasma AVP that is correlated with both duration and intensity.[21,35,37–40] Comparative data show that AVP is secreted during exercise in concentrations well above the threshold level associated with its antidiuretic effects, suggesting that its extrarenal actions are more important during acute exercise.[3,37–39,42–45] Extrarenal actions include AVP's action as a powerful vasoconstrictor and an important component in the control of blood pressure during exercise and its action on splenic blood vessels to prevent resequestration of the splenic reserve in the horse.[3,25,46] Interestingly, some studies suggest that drinking water, especially cold hypotonic water, during exercise may suppress AVP and thirst, leading to hypohydration.[38,39,41,47–49] However, sustained elevations in AVP stimulate thirst and drinking after exercise, cause a decrease in free water clearance by the kidneys and may influence the uptake of sodium and water from the colon.[3,38,39,41,49]

In exercising horses, plasma AVP concentration was recently reported to have increased from ~ 4.0 pg/mL at rest to ~ 95 pg/mL at a speed of 10 m/s.[45] It was also reported that the relation between AVP concentration and exercise intensity was curvilinear and did not plateau at speeds producing maximal heart rate.[45] Another recent paper reported that AVP increases during steady-state submaximal exercise in horses without a change in free water clearance.[42] However, the increase does not become significant until between 20–40 min of exertion.[42] Two possible explanations were given for the delay in AVP secretion in submaximally exercised horses.[42] First, a suppression of AVP secretion due to the volume overload sensed by neural pathways associated with the atrial baroreceptors and the hypothalamus.[3,42] Second, inhibition of AVP release by the increase in ANP concentrations at the beginning of exercise.[3,44] Nevertheless, an increase in AVP concentration was seen with prolonged exercise that appears to be related to sweat losses and decreases in body water that altered plasma osmolality and blood pressure.[3,44,45] Studies of humans have demonstrated that training alters the slope of the AVP response to acute exercise, suggesting a change in the sensitivity to the exercise challenge.[21,22,35,38–40,47,49] No studies have been published on the effect of training on the AVP response to acute exertion in the horse.

Thyroid

The thyroid is located in the neck in close proximity to the larynx region.[2,5] It plays a major role in the control of basal metabolic rate which has led some to refer to it as the body's 'thermostat'.[2,5] The two iodine-containing hormones produced by the thyroid, tri-iodothyronine (T3) and thyroxine (T4), act upon all cells in the body, affecting metabolic rate and subsequently energy metabolism.[2,5,20] The cells of the thyroid have three major actions when it comes to synthesis and secretion of T3 and T4: collection and transport of iodine, synthesis and secretion of the glycoprotein thyroglobulin into the intracellular colloid, and removal of T3 and T4

from thyroglobulin and secretion into the bloodstream.[2,5,20] The thyroid hormones circulate in the plasma in both a free and a protein-bound form with protein bound accounting for 99.98% of the circulating hormone and the unbound form being the active form able to act on cellular metabolism.[2,5,20] The thyroid also produces calcitonin, an important hormone in the control of calcium metabolism with potent effects on bone mineral density.[2,5,20]

Tri-iodothyronine and thyroxine

The release of these hormones is stimulated by TSH which, as previously mentioned, is released during exercise.[2,5,20] As with TSH, release of T3 and T4 is associated with both the intensity and duration of exercise in humans and horses.[5,20,50] Irvine[51] demonstrated that training increases the secretion rate of both T3 and T4 by approximately 65%. This would indirectly support the suggestion that TSH, which increases with training in humans and other species, is also increased with training in the horse. Training also increases the turnover rate of the thyroid hormones.[5,20]

Calcitonin

In addition to its control of metabolic rate, the thyroid is vital to calcium homeostasis.[2,5,20] For this function the thyroid synthesizes and produces calcitonin which plays a role in calcium homeostasis by either inhibiting osteoclast activity in bone or, through its action on the kidney tubules, causing an increase in calcium loss by actively inhibiting tubular reabsorption.[2,5,20] New bone is formed by osteoblasts and reabsorbed by osteoclasts. In young growing horses, both osteoclasts and osteoblasts are active; however, the activity of osteoblasts outpaces that of osteoclasts, allowing for bone growth and development.[2,20] To this end calcitonin appears to be more important in the young growing animal through its inhibitory action on the osteoclasts. Calcitonin is also important in the healing of fractures.[2] Chiba and co-workers[52] documented substantially elevated plasma calcitonin concentrations in racehorses with various fractures. Studies have also demonstrated that there is a period of bone demineralization in young Thoroughbreds in the first few months of training.[16] Growing and adult humans who exercise regularly have increased bone density.[5] While a great deal of work has examined markers of bone turnover, more data are needed to determine whether acute and chronic exertion affects plasma calcitonin concentrations.[9,52–56]

Parathyroid glands

The parathyroid glands, which are located in close proximity to the thyroid gland, regulate calcium homeostasis by synthesizing and secreting parathyroid hormone or parathormone (PTH) in response to a change in plasma calcium (Ca^{++}) concentration.[2,5,20] The hormone PTH has receptors in the intestinal tract, in the osteoclasts in bones and the tubules of the kidneys.[2,5,20] The action of PTH to stimulate osteoclast activity is antagonistic to calcitonin's inhibitory action. The resultant effect is a net bone reabsorption and the release of calcium and phosphate into the bloodstream.[2] Actions on the bone are relatively slower compared to PTH ability to alter both the uptake and excretion sides of the homeostatic balance equation by acting on the intestine and the kidney tubule.[2] Parathyroid hormone has a profound ability to enhance the enzymatic pathway that mediates increases in intestinal absorption of calcium and phosphate.[2,5,20] At the same time PTH can act on the kidney tubules where it enhances calcium reabsorption and phosphate excretion.[2,5] The increase in phosphate excretion counters the increased amount absorbed concurrent with the increase in calcium absorbed by the intestines.[2,5]

As with calcitonin, most equine research has focused on effects of repeated exercise on markers of bone turnover.[9,52–56] It is well recognized that nutritional influences can alter calcium and phosphate balance and bone metabolism. Thus, more work is needed to determine whether exercise intensity and/or duration are factors affecting PTH concentrations. Furthermore, data are needed to determine whether exercise alters the synthesis and secretion rate, receptor numbers and sensitivity and general interplay of PTH and calcitonin in bone metabolism.

Adrenals

The adrenal glands are multilayered organs that sit atop the kidneys.[2,5] Functionally, the primary layers are the adrenal medulla and the adrenal cortex.[2] The medullary portion of the adrenal produces epinephrine and norepinephrine which have the potential to affect most cells in the body.[2,5,20] In general, epinephrine potentiates the response to exercise, causing profound effects on central cardiovascular and respiratory function.[5,20] It can cause increases in muscle blood flow and can mobilize glycogen and free fatty acids to fuel exertion.[2,5,20] The adrenal cortex contains three specialized zones: the zona glomerulosa zona fasciculata and zona reticularis.[2] The cortex produces a multitude of steroid hormones that fall into three major categories: the mineralocorticoids (aldosterone), the glucocorticoids (cortisol) and the gonadocorticoids (androgens and estrogens).[2,5,20]

Hormones produced by the adrenal medulla (the catecholamines)

The release of the catecholamines has its origin in the fight-or-flight response.[57] This 'stress' response involves the local release of norepinephrine from the sympathetic nerve endings and a systemic release of epinephrine and norepinephrine from the adrenal medulla.[57] Receptors for the catecholamines are specialized and are divided into two primary categories, referred to as α and β-adrenergic receptors.[57] These two major categories are divided into subcategories, namely α_1 and α_2 and β_1 and β_2 receptors.[57]

Sympathetic nervous activity increases with intensity and duration of exercise; however, measurable changes in plasma

catecholamine concentrations are not apparent below 50–70% of maximal aerobic capacity.[57] Recent papers report that plasma catecholamine levels increase in a curvilinear fashion with increasing exercise intensity and are highly correlated with plasma lactate concentrations.[23,24,50] The measurable increase appears to coincide with the intensity where one would expect complete parasympathetic withdrawal.[19,20,22–24] These increases in the catecholamines enhance the increase in heart rate, force of cardiac contraction and thus cardiac output.[3,57] The catecholamines also play a role in inducing splenic contraction and the delivery of 6–12 liters of blood into the central circulation at the onset of exercise.[57,58] Even with this mobilization of reserve blood volume, the demands of exercise may exceed central cardiovascular capacity in the horse; thus, during high-intensity or long-duration exercise, the catecholamines contribute to the vasoconstriction that decreases blood flow to non-obligate tissues.[3,4,57]

The catecholamines are also vitally integrated into the respiratory response to exercise.[3,23,57,59,60,80] At the onset of exercise the β_2-adrenergic receptor action relaxes tracheal and bronchial smooth muscle, increasing airway diameter and decreasing airway resistance, and thus facilitating movement of greater amounts of air into and out of the lungs.[57] While the sympathetic system is not directly responsible for the control of ventilation during exercise, the increase in ventilatory drive associated with activation of the motor cortex can be enhanced during exercise by catecholamine secretion and augmentation of the sensitivity of chemoreceptors in the carotid bodies.[57] During high-intensity exercise ventilation may be further affected by catecholamine release; however, this is more a stress response than a 'normal' response to exercise.[57]

The catecholamines also have major effects on metabolic pathways associated with substrate utilization during exercise.[5,20,57] Increases in sympathetic activity, more specifically catecholamine concentrations, result in an increase in hormone-sensitive lipase and subsequently an increase in circulating free fatty acids.[5,20,57] Exercise-induced increases in the catecholamines also cause an increase in glycogen breakdown, resulting in elevations in blood glucose concentrations.[5,20,57] It has been suggested that one way in which warm-up exercises benefit the athlete is through activation of these metabolic pathways, allowing for elevated blood concentrations of glucose and free fatty acids prior to race-induced increases in utilization, thus facilitating delivery of substrate to tissues without a significant lag time.[5,20,57]

The above responses have been well documented during acute exercise; however, recent data suggest that exercise training alters adrenergic receptor numbers and sensitivity in selected tissues.[5,20,57] For example, β-adrenergic receptor numbers are unchanged in cardiac muscle with training, while α-adrenergic and muscarinic receptor numbers are reduced.[5,20,57] Both β-adrenergic receptor numbers and sensitivity are increased in skeletal muscle and in vascular and bronchial smooth muscle.[5,20,57] Changes in receptor number and sensitivity with training may be important with respect to adjustment of drug doses for the animal that has been trained extensively as opposed to an animal that is at the beginning of a training program or one that is being reconditioned following removal from training.[5,20,57]

Primary hormones produced by the adrenal cortex

Some sources suggest that more than 30 structurally distinct steroid hormones are secreted by the adrenal cortex.[2,5,20] Of those, the mineralocorticoid aldosterone and the glucocorticoid cortisol are the most important to the physiologic response to exercise.[2,5,20]

Aldosterone (ALDO) Aldosterone plays an important role in electrolyte homeostasis, in particular sodium and potassium balance.[2,3,5,20,61] It is well recognized that ALDO acts on the kidneys to enhance sodium (and chloride) reabsorption and potassium excretion.[3,5,20,61] It also acts on the intestines to facilitate the uptake of electrolytes and water.[3,5,20,61] Aldosterone release can be stimulated by decreases in plasma Na^+ or by increases in plasma H^+, plasma K^+, plasma ACTH and/or increased PRA.[3,38,39,61] However, the most potent of these stimuli is an increase in plasma K^+.[3,61] Studies of horses have attempted to identify factors that may stimulate the release of ALDO during exercise.[14,42,45,61–65] In one study plasma Na^+ was not significantly affected by exercise and thus, a decrease in plasma Na^+ did not appear to have been the primary stimulus for ALDO release.[42] The early mechanism for the release of ALDO appeared to have been a proportional increase in the plasma renin-angiotensin-aldosterone cascade where an increase in PRA results in the generation of angiotensin I and angiotensin II, with angiotensin II stimulating the production and release of aldosterone.[38,39,41,66–68]

The relationship between plasma aldosterone concentration and exercise intensity has been reported for horses running on a treadmill.[45] Aldosterone increased from concentrations around 20–50 pg/mL at rest to almost 200 pg/mL at a speed of 10 m/s.[45,69] A linear relation was found between exercise intensity and aldosterone concentration; however, unlike PRA, ALDO concentration did not reach a plateau at HR_{max}.[45] Another study found that during submaximal exercise, increases in plasma ALDO concentration paralleled changes in PRA; however, the magnitude of the increase in PRA (66%) was less than the relative increase (709%) in plasma ALDO concentration.[42] The authors concluded that factors other than PRA affected the release of ALDO in the horse.[42] Of all the parameters reported, a highly significant increase in plasma K^+ concentration may have served as the strongest stimulus for the release of ALDO.[3] An increase in plasma K^+ as small as 0.3 mEq/L can be sufficient to stimulate the secretion of ALDO, independent of the renin-angiotensin cascade, through the conversion of cholesterol to pregnenolone or at a later step in the biosynthetic pathway.[3] This is consistent with the acute homeostatic requirements of the horse since a major perturbation in electrolyte homeostasis observed during endurance exertion was an increase in plasma K^+ and not a drop in plasma Na^+.[45] As with humans, ALDO has a minimal role in the acute response

to exercise in horses; however, ALDO concentration remains elevated for hours after exercise and may affect the long-term reabsorption of sodium and water[40,70,72] by the kidneys and by the intestinal tract.[69,73]

Cortisol The major glucocorticoid secreted by the adrenal glands is cortisol; however, some cortisone, corticosterone and deoxycorticosterone are also produced and found in the plasma.[2,5,20] Thornton reported that deoxycorticosterone concentrations are very low in the horse.[20] Cortisol, cortisone and corticosterone can be found in a ratio of 16:8:0.5 in the plasma; thus, most exercise studies have focused on cortisol.[2,20] Cortisol undergoes diurnal variation with peak levels found in the early morning between 0600 and 1000 and lowest levels found in the late evening and night.[2,5,20] Some have characterized the glucocorticoids as 'stress' hormones.[2,5,20] However, they are released under a multitude of normal situations not characterized as stress.[2] Thus, it is the appropriateness of their release and the magnitude of their release that would indicate whether a given physiologic disturbance (or stressor) can be classified as a mere perturbation or a dangerous stress.

Release of cortisol allows an individual to tolerate and adapt to challenges to homeostasis that occur in everyday life.[5,20] To this end, the functional effects of cortisol fall into two major categories: substrate mobilization and immune modulation.[2,5,20] One such challenge is exercise where cortisol stimulates substrate mobilization by enhancing gluconeogenesis and the mobilization of free fatty acids.[5,20] At the same time cortisol release will decrease glucose utilization by some tissues, sparing it for use by the central nervous system.[5,20] One could speculate that such an action could delay the onset of central fatigue that occurs during endurance exertion when blood glucose concentrations drop.[71,72] Cortisol also causes an increase in protein catabolism with a resultant increase in the release of amino acids.[2,5,20] These building blocks of protein are thus available during exercise as a source of energy when glucose levels begin to drop.[2,5,20] They are available after exercise to repair tissues and for the synthesis of enzymes involved in many cellular pathways.[2,5,20] Cortisol also modulates immune function, acting as an anti-inflammatory agent and suppressing immune reactions.[2,5,20] Teleologically, these actions may be of benefit in the response to training. Overload through increased exercise intensity, resistance or duration is necessary for training to stimulate an adaptive response to exercise. The minor disruption of function and structure in the cells of the muscles results in protein accretion, substrate uptake and deposition, and other beneficial remodeling that increases the functional capacity of the cells. Cortisol's suppression of immune function and anti-inflammatory effects may actually provide a permissive environment for tolerating the slight amount of 'muscle damage' needed for training-induced remodeling.

Many studies have demonstrated that cortisol is increased in the horse during a wide variety of exercise activities, from racing to polo to endurance rides.[11,20,32,74–80] The release of cortisol in the horse appears to be affected by both intensity and duration of exercise.[20,79,80] However, excessive increases in cortisol concentrations following exertion can be a marker of too much exercise. Prolonged cortisol recovery times as well as either inappropriately high or low plasma concentrations of cortisol may be markers of overtraining in the horse. As mentioned above, postexertion effects of cortisol may elicit a permissive effect beneficial for training adaptation by preventing the immune system from eliciting an inflammatory and immune reaction to acute exercise.[11,81] Several studies of horses have followed cortisol levels for an extended period post exercise.[82–84] Those experiments demonstrated that exercise caused a six-fold increase in adrenal cortisol secretion and a 2–3-fold increase in plasma cortisol concentration. Urinary cortisol concentrations also increased threefold with a return to baseline levels by 10 hours post exertion.[82,83,84] The authors also noted a substantial increase in liver clearance of cortisol.

Interestingly, data are mixed as to the effects of training on the cortisol response.[20,79,80] Studies have suggested that peak postexercise cortisol concentrations are reached earlier in trained horses and that trained horses have a faster cortisol recovery time.[20,79,80] On average, peak cortisol levels were observed at about 30 minutes post exertion.[20,79,80]

Pancreas

The pancreas is a V-shaped organ that lies along the duodenum.[2,5,20] Structurally, most of the pancreas is composed of acini which function as exocrine cells, secreting digestive enzymes and bicarbonate into the small intestine via the pancreatic duct. The endocrine function of the pancreas is mediated by cells of the islets of Langerhans.[2,5,20] These specialized cells are arranged as branching cords surrounded by a large network or plexus of capillaries.[2,5,20] The cells are classified into three types: the α-cells which produce glucagon, the β-cells which produce insulin and the δ-cells which produce somatostatin.[2,5,20] Of those hormones, the most important during exercise are insulin and glucagon and their actions in the control of glucose metabolism.

Insulin

Insulin functions as part of the feedback system controlling blood glucose concentration.[2,5,20] Insulin is synthesized by the β-cells of the pancreas and is primarily a glucose 'storage' hormone because it facilitates glucose uptake by the cells, promotes glycogenesis and inhibits gluconeogenesis.[2,5,20,85,86] At rest insulin is the 'key' that opens the cellular door to allow uptake of glucose.[2,5,20] However, during exercise the working muscles take up glucose without insulin.[5,20] Thus, insulin is very important during the recovery from exercise when glycogen repletion is most active.[2,5,20,87–89]

The insulin response to acute exercise has been well documented with the horse, like humans and other species, suppressing insulin during exercise.[20,76–78,80,90–96] This suppression appears to have a threshold of 50% of $\dot{V}O_{2max}$ which coincides with the increase in catecholamines seen during exercise.[1,20] Recent more mechanistic studies have demonstrated the link between exercise-induced increases in sympa-

thetic drive and changes in insulin and glucagon secretion in the horse.[95,96] Functionally this allows the animal to increase gluconeogenesis to maintain blood glucose concentrations during exercise.[5,20,95,96] Glucose mobilized during exercise can be taken up by the muscles with insulin; however, endurance performance appears to be limited by central fatigue mechanisms more than peripheral fatigue.[5,20,95,96] Suppression of insulin and maintenance of blood glucose concentration prevent the onset of central mechanisms of fatigue.[6,71] Much of the recent work on the insulin response to exertion has centered on the composition and timing of pre-exercise feeding.[74,97–105] High-carbohydrate feeds are beneficial for optimal muscle glycogen synthesis to fuel exercise; however, the resultant increase in blood glucose seen after a horse eats a high-carbohydrate ration usually evokes an increase in insulin secretion.[102, 104–106] The goal of recent research has been to prevent this feed-induced spike in insulin that would tend to decrease blood glucose directly before or during exercise.[102,104–107] Training appears to alter the insulin response to exercise, enhancing the ability to synthesize glycogen during recovery.[20]

Glucagon

The functions of glucagon are in opposition to insulin in that it stimulates gluconeogenesis and inhibits glycogenesis.[2,5,20] Glucagon is one of many hormones needed for substrate mobilization and thus it increases during exercise in the horse.[76–78,85,108,109] As such, glucagon is important for maintaining glucose concentrations during exercise, a role that is especially important during endurance activities where a drop in blood glucose concentrations leads to the onset of central fatigue.[2,5,20] Published data from several studies have demonstrated that endurance horses have an increase in glucagon.[76–78] This increase in glucagon is also altered by exercise intensity and its release appears to be under the influence of the increases in sympathetic drive and the catecholamines.[96] Training appears to alter the glucagon response to exercise, enhancing the ability to mobilize glucose during exertion.[5,20]

Other pancreatic hormones

Other hormones produced by the pancreas and associated with both endocrine and exocrine pancreatic function may play an important role in modulating substrate disposition during and after exercise.[110] These hormones include pancreatic polypeptide, somatostatin of pancreatic origin, amylin and galanin.[110]

Pancreatic polypeptide Pancreatic polypeptide does not appear to affect insulin or glucagon concentrations. However, comparative studies have suggested that pancreatic polypeptide affects digestion.[110] Hall and co-workers[109] point out that pancreatic polypeptide (PP) inhibits pancreatic exocrine function and bile secretion, an observation that they considered appropriate for a horse during long-term exercise when food intake would tend to be minimal. Information regarding the effect of exercise on pancreatic polypeptide is minimal. However, in one study Hall et al[109] demonstrated that PP increases in the endurance horse from concentrations averaging 20 pmol/L at rest to levels as high as 102 pmol/L after an 80 km ride. Lower concentrations seen after a 42 km race would suggest a dependence on duration which may be related to the degree of hypoglycemia seen in the horses post exertion.[109] These results are similar to those seen in other species.[110] We are unaware of any published studies that have examined the effect of exercise intensity in the horse.

Somatostatin Somatostatin is produced in the hypothalamus, the gastrointestinal tract (see below) and the pancreas. It is well recognized that the somatostatin produced in the hypothalamic region of the brain inhibits somatostatin (i.e. growth hormone) as well as thyrotrophin release.[109] Somatostatin of pancreatic origin is produced by the δ-cells of the pancreas and functions locally, to alter pancreatic function, and regionally to possibly alter blood flow and also restrict nutrient absorption.[109] Hall and co-workers[109] have suggested that this fits with the well-documented reduction in splanchnic blood flow that occurs during exercise. A small but significant increase in somatotrophin concentration has been demonstrated during endurance exercise per se with no difference due to duration (42 versus 80 km).[109] This is consistent with studies of humans and other species.[110] Published studies of the horse have not examined the effect of exercise intensity on concentrations of somatostatin.

Amylin and galanin Amylin and galanin are two other substances produced by the pancreas that affect pancreatic function and influence pathways involved in insulin regulation.[110] Amylin is a 37-amino acid protein produced by the β-cells of the pancreas, whereas galanin is a 29-amino acid protein secreted by nerve cells in the pancreas.[110] These paracrine substances may be influenced by exertion; however, we are unaware of any published studies in horses or other athletic species.

Circulating gastrointestinal ('gut') hormones

Several other substances with endocrine and paracrine function are secreted by the digestive tract.[110] These substances alter digestive function and thus may influence digestion and the absorption of substrate during exercise.[110] Included in this complex array of modulatory substances are gastric inhibitory peptide (GIP), vasoactive intestinal polypeptide (VIP), gastrin, somatostatin, secretin, enteroglucagon, motilin, cholecystokinin (CCK, see also below), the enkephalins, the endorphins, substance P, gastrin-releasing peptide, neuropeptide Y, peptide YY and neurotensin.[110]

Gastric inhibitory peptide

This is a 42-amino acid peptide that has a dual action, inhibiting gastric acid production and stimulating insulin secretion.[110] Exercise does not alter GIP in humans; however, consumption of glucose during recovery appears to result in decreased concentrations of GIP in humans. Hall et al[109] reported that plasma GIP concentrations were not altered during endurance exercise (42 and 80 km). However, those

results should be looked at with caution as the authors had relatively low animal numbers. The longer endurance competition did result in a non-significant decline in plasma GIP concentration from approximately 75 pmol/L before exercise to 50 pmol/L after 80 km.[109] The decline in GIP and its insulin secretagogue action would be consistent with the substantial and significant suppression of insulin concentrations reported in those same horses.

Vasoactive intestinal polypeptide

A 28-amino acid peptide acting as a neurotransmitter that is secreted by nerve fibers in the GI tract.[110] Multiple actions of VIP include vasodilation, stimulation of glucagon secretion and enhancement of the stimulation of substrate release through lipolysis and hepatic glycogenolysis.[110] Endurance exercise has a pronounced effect on VIP secretions, with increases in plasma concentrations that appear to be affected by exercise duration.[109,110] Teleologically this fits with the energy substrate needs associated with prolonged exercise.

Gastrin

This is a 10-amino acid peptide that stimulates gastric acid secretion that is affected by prior ingestion of food.[110] Limited data are available on the effects of exercise on the plasma concentration of this hormone in the horse.[109] Human studies[110] have not reported increases in gastrin due to exercise but in a paper on horses by Hall et al,[109] while plasma concentrations of gastrin were not altered by a 42 km endurance ride, they were substantially increased following a longer 80 km ride. One would presume, though, that the horses in the longer ride went for a longer time without food intake and therefore, this increase in gastrin secretion would seem unwarranted. However, one wonders if this paradoxical increase contributes to excessive acid production and gastric ulcer formation when food is withheld from a horse for a long period of time.

Other gastrointestinal peptides with endocrine or paracrine actions

Most of these substances have not been studied in the horse; however, comparative studies have shown that they have localized action within the gastrointestinal tract. Many of these substances have been characterized as neurotransmitters that act on local tissues, altering membrane transport, stimulating motility and, in some cases, stimulating acid production.[110] For example, gastrin-releasing peptide is a 27-amino acid peptide that is also referred to as bombesin.[110] This protein stimulates gastrointestinal motility and the release of gastrin.[110] Secretin and enteroglucagon are both 29-amino acid hormones that inhibit acid secretion in the stomach.[110] Comparative studies have shown that there is an increase in peripheral blood collected after exercise in both humans and dogs.[110] Motilin has been shown to increase with exercise in humans.[110] This 22-amino acid peptide stimulates motility of the gastrointestinal tract.[110] Interestingly the enkephalins appear to have the opposite effect, decreasing motility.[110] Other peptides like substance P, neuropeptide Y and peptide YY appear to alter GI tract motility but little is known about changes during exercise.[110] Interestingly, the functional link between all the GI tract hormones appears to be their actions on motility and possibly transport.[110] These actions may make them inportant for the uptake of water, electrolytes and energy substrates during and after exercise.[110] Finally, neurotensin is a 10-amino acid GI hormone with an unknown role; however, studies have shown that it increases during exercise in humans when a glucose solution is consumed but not when water alone is consumed.[110]

Hormones related to appetite and energy balance

Maintaining energy balance is crucial for the optimal health and performance of exercising horses. The energy expended during exercise directly affects energy homeostasis, because the horse has to increase energy intake in order to compensate both for the energy lost during exercise and for the energy required for the recovery and repair of tissues. Although the neuroendocrine control of energy balance has been studied extensively in humans and rodents, it is just beginning to be examined in horses. Examples of some of the endocrine mediators measured to better understand the control of energy balance are the hormones leptin, adiponectin, ghrelin and cholecystokinin.

Leptin

Leptin is an adipocyte-derived hormone, a 16 kDa protein product of the *ob* gene, that acts as an indicator of energy balance.[111–113] Sensed levels of leptin influence neural transmission in brain pathways, affecting food intake and energy utilization.[114] Basically, high levels of leptin increase energy expenditure while decreasing food intake and vice versa.[114] Food intake is altered by leptin influencing responsive neurons in the brain that activate either a feeding or satiety system.[114] The feeding or orexigenic system contains neuropeptide Y, agouti-related protein, and other hormones and neurons that signal an animal to increase food intake while the satiety system involves neurons containing pro-opiomelanocortin and α-melanocyte stimulating hormone as well as others that decrease food intake.[115] Leptin increases energy expenditure by stimulating the sympathetic nervous system in brown adipose tissue, directly increasing the expression of uncoupling protein 1, and by possibly increasing the expression of uncoupling protein 3 in muscle.[116] Furthermore, leptin strongly stimulates triglyceride and fatty acid cycling by increasing lipolysis and fatty acid oxidation.[117] Leptin is secreted in proportion to fat mass,[117] although massively obese humans seem to be 'resistant' to leptin's slimming propensities.[111,119]

In horses, plasma leptin is positively correlated with percent fat mass and body condition score.[120,121] Leptin has also been found to have a seasonal variation in both young and old mares, with plasma leptin levels increasing in the summer and decreasing in the winter, in correlation to body-weight and percent fat mass.[122] Furthermore, 24-hour fasting decreases plasma leptin levels in young and mature mares.[123] Interestingly, one study showed serum concentrations of leptin were higher in geldings and stallions versus mares, which is incongruent with human literature in which females have higher leptin levels than males, with differences not completely explained by a greater percent fat mass in females.[121,124] In rats, recent research demonstrated that male rats had higher leptin concentrations in the blood than female rats.[125] The reason for the discrepancy between species is unclear.

With regard to exercise, there have been some interesting findings in humans on how the type and duration of exercise affect energy balance and leptin concentrations in the blood. To date, no such studies have been published in horses. In humans, however, studies involving short-term exercise (< 60 min) with varying intensities have generally shown no change in leptin concentrations due to exercise.[126,127] Studies that have reported changes in leptin concentration with short-term exercise have attributed the changes to hemoconcentration or circadian rhythm.[128,129] It is possible that short-term exercise does not cause a sufficient kilocalorie deficit to produce a disruption in long-term energy balance. Also, the interaction between other hormones (e.g. cortisol, insulin, glucose, epinephrine and norepinephrine) that fluctuate during exercise and have been found to either stimulate or inhibit leptin secretion remains to be determined.[1,129,130]

Long-term exercise (≥ 60 min) of varying intensities has been shown to decrease or cause no change in leptin concentrations.[131–133] Interestingly, studies showing reductions in leptin increased sampling times for up to 48 hours after exercise, with a reduction in the 24-hour mean and amplitude of the circadian rhythm of leptin.[130,134] It appears that long-term exercise, in well-controlled studies, provides enough of an energy deficit to decrease leptin levels, which in turn will increase food intake to help maintain energy balance.[135]

Training is another aspect of exercise that is of interest to scientists studying leptin concentrations and energy balance. Training regimens have had different effects depending on duration and intensity of exercise and subjects used. Briefly, training for less than 12 weeks generally causes no change in leptin levels, although type II diabetic individuals did show a reduction in leptin concentrations after 6 weeks of low-intensity walking and cycling, independent of body composition changes.[136,137] Training regimens for longer than 12 weeks can cause a reduction in fat mass, which lowers leptin levels, yet some studies report a reduction in leptin independent of fat mass changes.[138–140] Additionally, it appears that females are more sensitive to the training effect on leptin levels, with several studies showing female subjects, yet not their males counterparts, demonstrating lower leptin concentrations in response to training.[141]

Leptin has several potential roles in terms of the health of exercising horses. As a signal of energy homeostasis, leptin concentrations in horses can help scientists to determine if a horse is in positive or negative energy balance and can provide supportive data regarding a horse's body condition and percent fat mass. Negative energy balance is detrimental to exercise performance, reproductive status and overall health.[142] Furthermore, determining how exercise and training affect leptin concentrations in horses will allow better understanding of how horses regulate their energy balance so that training regimens and diets can be adjusted accordingly to optimize the health of the athlete.

Adiponectin

Adiponectin is another hormone secreted from adipocytes, with its role in metabolism related to the regulation of glucose, insulin and adipocyte metabolism.[143–145] In contrast with leptin, adiponectin levels are decreased in obese and insulin-resistant humans and animals.[146,147] With regard to exercise, adiponectin may have a role in the increased insulin sensitivity seen as a result of training in both humans and horses.[148–151] In a study of humans undergoing exercise training, however, plasma adiponectin concentrations did not change relative to the increased insulin sensitivity due to training.[152]

In horses, adiponectin is negatively correlated with percent fat mass in yearling fillies and mature mares.[120] The study of adiponectin in horses is of importance as it is likely related to the insulin resistance commonly seen in older horses and horses with pituitary adenomas. Studies have shown that older mares with impaired glucose tolerance were able to improve their insulin sensitivity with 12 weeks of training.[149] It would be of interest to determine if adiponectin has a role in this insulin-sensitizing phenomenon.

Ghrelin

Another hormone involved in the control of appetite and energy balance is ghrelin, a protein hormone secreted from the stomach which was first discovered as a potent growth hormone secretagogue.[153] Ghrelin has received most of its attention, however, due to its role in initiating food intake in humans and rodents.[154] In meal-fed animals, including humans, rodents and sheep, ghrelin increases before meal feeding in anticipation of the meal and will also increase during times of fasting.[155–157] In rats, ghrelin stimulates gastric acid secretion in the stomach.[158,159] Few studies to date have examined the role of ghrelin in relation to exercise, in any species. One study in humans, however, demonstrated that ghrelin levels did not change during submaximal aerobic exercise in healthy adults,[160] although the paper was focused on the relationship between ghrelin and growth hormone released during exercise and not that between exercise, ghrelin and food intake.

It would be valuable to attempt to study ghrelin in horses as it may have a significant role in helping horses to maintain

energy balance. In addition, high performing equine athletes often have problems with inappetance and gastric ulcers that may be related to abnormal ghrelin concentrations and ghrelin's stimulation of gastric acid.[161] Humans with anorexia exhibit higher ghrelin concentrations than their normal counterparts, with a presumed 'ghrelin resistance' contributing to the cachexia of this eating disorder.[162,163]

Cholecystokinin

The peptide hormone cholecystokinin (CCK), secreted from the small intestine, is involved in energy balance by signaling fullness and decreasing food intake in humans, rodents and ruminants.[164–167] To date, there has been little published data on cholecystokinin in horses but this hormone may play a role in the inappetance commonly seen in heavily exercised horses. In a study conducted in humans, exercise increased plasma CCK concentrations fourfold. Although CCK values returned to normal at the end of exercise, equine researchers have speculated that CCK concentration may increase in response to exercise in horses and remain elevated, contributing to a lack of interest in feed by some equine athletes.[168]

Finally, it must not be ignored that there is also an interaction between many of the above-mentioned hormones in relation to energy balance. For example, CCK enhances the effect of leptin administration on weight loss and the pair may directly decrease food intake.[169,170] Leptin and adiponectin, although expressed in opposite concentrations to one another, may be regulated similarly for short-term alterations, yet differently for long-term regulation.[112] Ghrelin, on the other hand, is upregulated during leptin therapy, although these increases in ghrelin are not able to overcome the food intake depression caused by leptin.[171,172] Hence, it is clear that these endocrine mediators should not just be studied in isolation but collectively to determine how they regulate various systems.

In conclusion, the regulation of energy balance in horses and how it is affected by exercise is a field that has yet to be investigated in depth. On the other hand, data published in humans and other species demonstrate the importance of such research, especially with regard to gastric ulcer syndrome and the inappetance commonly seen in heavily exercised horses and obesity and insulin resistance seen in many older horses. It is hoped that future research in this field will elucidate the characterization of energy balance in horses, how this equanimity is maintained in response to exercise and ways in which management practices can be changed to help horses remain in energy balance and achieve optimal performance and health.

Kidneys

Filtration of the blood and conservation of vital substances are the most obvious functions of the kidneys.[41,61] However, their close link with the control of cardiovascular function is more complex and multifaceted. The basic filtration unit is the kidney glomerulus.[41,61] Each of these glomeruli has a specialized group of cells referred to as the juxtaglomerular apparatus (JGA),[41,61] which has more specialized cells that act as feedback sensors in monitoring flow (and pressure), sodium and chloride concentration, and arterial P_{O_2}.[41,61] The major hormone produced by the kidney is renin, the activating substance in the renin–angiotensin–aldosterone cascade which has the potential to alter blood presssure, volume and tonicity.[41,61] The kidney also produces erythropoietin which acts on precursor cells in the bone marrow to stimulate red blood cell production. Both of these hormone systems play an important role in the defense of normal cardiovascular function.[41,61]

Plasma renin activity (PRA)

Renin is a hormone released by the JGA of the kidney. It facilitates the conversion of angiotensinogen into angiotensin I, which is converted in the lung to angiotensin II, a vasoconstrictor that also stimulates the production and release of aldosterone.[38,39,41,45,173] During exercise, PRA is a measure of the rate of angiotensin I generation.[38,39,41,45] Angiotensin I and angiotensin II are powerful vasoconstrictors involved in the control of MAP and blood flow during exercise.[38,39,41] After exercise, renin can directly affect renal function and angiotensin stimulates thirst and drinking, thus altering post-exercise fluid balance.[38–40,45,174] Three major mechanisms that may account for the increase in PRA during exercise are renal nerve stimulation via increased sympathetic drive, changes in renal blood flow and pressure associated with juxtaglomerular function, and changes in electrolyte (sodium and chloride) concentrations at the JGA in the kidney.[38–41,45,173]

Previous studies have measured PRA in horses at rest, after exercise training, during steady-state exercise or after brief maximal exercise.[42,45,61–65,68] A strong linear correlation exists between work intensity (and duration) and increases in PRA, and HR were reported up to treadmill speeds of ~ 9 m/s.[45] Above 9 m/s, HR and PRA reached a plateau and did not increase when speed was increased from 9 to 10 m/s.[45] In previously published studies of horses, PRA increased from 1.9 ± 1.0 ng/mL/h at rest to a peak of 5.2 ± 1.0 ng/mL/h at 9 m/s.[45] The observed concurrent plateau in PRA and HR rate supports the suggestion that the increase in PRA during exercise in the horse is linked to sympathetic drive. Such is the case in other species where mechanistic studies have demonstrated a correlation between renal sympathetic nerve activity and PRA.[38,39,41,173] During steady-state submaximal exercise, the major factor stimulating an increase in PRA early in exercise was an increase in sympathetic drive.[38,39,41,61] However, a secondary increase in PRA was seen in horses after 40 min of exercise and was most likely due to a decrease in plasma Cl^- concentration, which fell significantly during this period, and not plasma $Na,^+$ which remained constant.[42]

Functionally, an increase in PRA during exertion has been shown to result in an increased plasma angiotensin II concentration.[38,39,41,61] Interestingly, horses given the angiotensin converting enzyme inhibitor enalapril had significantly lower plasma angiotensin II and aldosterone

concentrations and pulmonary artery pressures during exercise compared to horses given a placebo.[68] These later observations demonstrate that the renin–angiotensin cascade plays a role in the control of blood pressure during exercise in the horse.

Erythropoietin

Erythropoietin (EPO) is a peptide hormone that is produced by the kidneys in response to hypoxia sensed by pericellular cells positioned in the vasculature of the renal matrix.[175–178] Recent papers have documented the effects of a variety of perturbations, including the effects of blood loss, acute exercise and altitude, on EPO production in humans.[175,176,179] If cardiopulmonary adjustments are insufficient to prevent hypoxemia and if the above-mentioned perturbations are large enough to cause a decrease in renal arterial partial pressure of oxygen (Pa_{O_2}), then plasma EPO concentrations increase and there is a subsequent stimulation of erythropoiesis in humans.[175,176,179] The resultant increase in red blood cell volume would be expected to couple with other compensatory mechanisms to return arterial P_{O_2} back up to normal levels.

McKeever et al[180] recently reported that acute exercise does not appear to stimulate an increase in plasma EPO concentration in normal horses. This is similar to observations made in several studies of humans which demonstrated that neither the intensity nor the duration of acute exercise alters plasma EPO concentrations in humans.[181–183] Teleologically this makes sense because one would speculate that if acute exercise caused substantial increases in EPO production and release, then repeated exercise (i.e. training) would cause a sustained increase in EPO.[184] Any such hypothetical repeated increase in circulating EPO concentration would be expected to cause a sustained stimulation of erythropoiesis. Taken a step further, this would eventually cause a red cell hypervolemia and potentially detrimental increases in blood viscosity. Mechanistically, the acidosis of exercise appears to inhibit EPO production.[185]

Altitude appears to cause a transient increase in plasma EPO production in humans and horses.[5,180,186,187] However, in horses, plasma EPO concentrations increased only during the first 3 hours of the first day at 3800 meters.[180] This is similar to studies of humans which have reported a 'temporary rise' in EPO concentrations in mountaineers at both 4900 and 7600 m.[186] One explanation for this rapid return to baseline concentrations is a rapid compensation of cardiorespiratory mechanism to the challenge of altitude that would tend to limit changes in Pa_{O_2} at the kidney.[186] Interestingly, exercise performed at altitude did not induce a secondary increase in plasma EPO concentration.[180] The authors concluded that hypobaric hypoxia positively affects EPO production in the horse rapidly upon the first day at altitude with a rapid return to prealtitude concentrations.[180] Their data suggest that horses have an innate ability to tolerate the acute challenges induced by exercise and altitude.

Interestingly, administration of recombinant human erythropoietin (rhEPO) has been shown to increase hemoglobin concentration and exercise capacity in humans with chronic renal failure.[188–190] Small doses of rhEPO have been found to increase hemoglobin concentration by 30% and increase endurance performance anywhere from 10% to 19% in healthy human subjects.[188–190] Purportedly, some human athletes and/or their trainers have decided to use higher than recommended doses of erythropoietin with the rationale that the more rhEPO injected, the greater the increase in aerobic capacity.[188–190] Injections of rhEPO have been shown to elevate resting hematocrit to levels greater than 55% in humans, which increases blood viscosity and clotting and enhances the risk for heart attack or stroke.[188,190] Rises in hematocrit increase blood viscosity and may have caused excessive increases in blood pressure and clotting problems related to the deaths of human athletes in Europe.[188,190]

Unfortunately, these practices have entered equine sports medicine, with clinicians, horse trainers and racing commission personnel reporting that this drug is being misused in race horses to improve performance through an increase in blood volume and oxygen-carrying capacity.[178,191,192] However, two major problems can develop in horses.[175,178,193] First, while the horse can tolerate hematocrits of 50–60% during exercise, no one knows what happens to a horse's cardiovascular system if the normal resting hematocrit is artificially elevated to values of 70–80%.[178,193] A large increase in resting hematocrit coupled with splenic reserve mobilization may produce dangerously viscous blood that may lead to sudden death during or after exercise.[178] If this increase in resting red blood cell volume were to be coupled with lasix-induced fluid losses the results could be devastating.[178] A second major potential problem associated with rhEPO misuse in the athletic horse is its reactivity with the horse's immune system.[178,193] Some horses have purportedly developed a life-threatening anemia associated with an immune reaction to both the exogenous rhEPO and the animal's own EPO.[178,193] Clinically, resting hematocrit has been seen to drop below 20% in horses reacting to rhEPO administration with some cases requiring blood transfusions to save the horse's life.[193]

Recently studies of splenectomized and intact horses have demonstrated that rhEPO administration in low doses causes substantial increases in resting hematocrit, red blood cell volume, maximal oxygen uptake, blood viscosity and selected hemodynamic variables during incremental exercise performed on a treadmill.[179,194] In splenectomized horses, administration of rhEPO in low doses (15 IU/kg) three times a week for 3 weeks increases resting hematocrit from 37% up to 46%.[194] The resulting 13% increase in red cell volume was associated with a 19% increase in $\dot{V}O_{2max}$ and substantial increases in blood viscosity.[194] Another study of intact horses also demonstrated that low-dose administration of rhEPO (50 IU/kg, three times/wk for 3 wks) increases red blood cell volume, $\dot{V}O_{2max}$ and the velocity at $\dot{V}O_{2max}$.[179] Viscosity was not measured in that study; however, postexercise hematocrits were in the low 70s and considered dangerously high.[179] Horses in that study also developed antibodies to the rhEPO (McKeever, unpublished data).

Heart and blood vessels

The heart and blood vessels play both a paracrine and endocrine role in the control of cardiovascular function.[3] While there are several mechanisms worthy of discussion, two hormones appear to play a major role during exercise: atrial natriuretic peptide and the endothelins.[3]

Atrial natriuretic peptide (ANP)

This is a hormone produced by the heart that is important in the regulation of blood flow and blood pressure during exercise.[3,195] Granules of ANP are stored within the walls of the atria and are released during atrial stretch.[3,196] Receptor sites for ANP have been identified in the posterior pituitary, the kidneys, vascular smooth muscle, adrenal cortex, heart and lung.[3,197] This hormone causes a rapid and profound vasodilation and a pronounced natriuresis.[3,197] ANP inhibits vasopressin, renin and aldosterone secretion and also inhibits the binding of aldosterone at the kidney tubule.[3,197]

On a practical level, ANP may be involved in accommodating the exercise-related shifts of blood volume in the horse.[3,44] Evidence for this is provided by two recent studies which demonstrated that plasma ANP increases in a linear fashion with increasing work intensity, from 5–10 pg/mL at rest to plasma concentrations exceeding 60 pg/mL at speeds eliciting $\dot{V}O_{2max}$.[3,197–199] Mean ANP concentration was strongly correlated with heart rate.[197] Furthermore, ANP increases during steady-state submaximal exercise, from ~ 10 pg/mL at rest to a peak of 40 pg/mL at 40 min, and remained elevated through 60 min of exertion.[3,42,200] Nyman and co-workers[199] presented similar peak plasma ANP concentration during steady-state exertion and reported that ANP concentrations were altered by hydration status. Horses that were hyperhydrated had the highest ANP concentrations during exercise compared to control and hypohydrated horses.[199] Another study found no differences between arterial and mixed venous ANP concentrations, suggesting that ANP is either not metabolized by the lung or is released from the left atrium at a rate matching pulmonary metabolism.[201] Even more recent work has examined the effects of exercise on ANP, with a special focus on its interaction between fluid and electrolyte status and other endocrine responses.[69,202] The authors concluded that ANP remains elevated post exercise and that this is a response to the exercise-induced increase in circulating blood volume rather than an interaction with vasopressin and the catecholamines.[69]

Endothelin

The endothelins are peptide hormones that have pronounced effects on neuroendocrine control of cardiovascular function.[203–206] The endothelins, ET-1, ET-2 and ET-3, are isoforms of a 21-amino acid polypeptide with pronounced effects on both central and peripheral control of cardiovascular function.[203–206] The three sequences of endothelin are structurally and pharmacologically distinct, arising from what has been called 'big endothelin', a 39-amino acid precursor molecule.[203–206] The half-life of ET-1 is very short, only a few minutes, which is consistent with its role in control of vascular tone.[205,206] Factors affecting the release and metabolism of endothelin include increased blood flow, vasopressin, angiotensin, shear stress and thrombin.[205–213]

Many studies have shown that ET-2 and ET-3 are limited in their vascular effects and that ET-1 has the most pronounced effect on peripheral vascular tone.[205,206,212,213] Endothelial cells produce ET-1 exclusively[205] and circulating levels of this hormone may play a role in certain forms of hypertension.[205,206,214] ET-1 and ET-2 (to a minor degree) are potent vasoconstrictors that can increase systemic arterial blood pressure and pulmonary arterial blood pressure and cause alterations in cardiac output and the distribution of blood flow in the peripheral circulation.[205,206] Thus, ET-1 may affect the redistribution of blood flow and control of blood pressure during exercise. ET-3 appears to play a role in modulating the release of vasopressin from the hypothalamus, and Rossi[205] has shown that ET-3 amplifies free water excretion independent of renal and systemic hemodynamic and osmotic clearance and/or circulating vasopressin concentrations.

Resting plasma concentrations of immunoreactive ET-1 measured in horses appear to be similar to the relatively low concentrations reported for other mammalian species such as the rat, dog, pig, cow and man[205,206,210,213,215,217] and horses.[198,204,218–221] Studies of ET-1 in horses have focused primarily on either understanding its role in horses with respiratory disease[218–221] or aging.[198,204] In some of those studies, ET-1 was found to be elevated in blood and bronchiolar alveolar lavage fluid in resting horses with respiratory disease.[219,220] Many recent experiments have only reported on samples obtained either before and after exertion[219,220] or at rest and at the speed eliciting $\dot{V}O_{2max}$.[204] However, one recent study has examined plasma ET-1 concentrations in the horse during exercise rather than just collecting blood samples before and after exercise.[204] Samples taken while the horses were running a GXT revealed that during exercise there were no changes in plasma ET-1 concentration and there were no alterations due to increases in work.[204] Interestingly, while plasma ET-1 concentration did not change with increases in exercise intensity, it did increase substantially in samples collected immediately after the exercise stimulus was withdrawn and in blood collected 2 min following cessation of running.[204] However, plasma ET-1 concentrations were back to normal by 10 min.[204] This rapid response may be physiologically significant as it coincides with the rapid recovery and transient decreases in cardiovascular function reported in other studies of horses that have involved protocols with a quick stop of the treadmill.[3,68]

Similar postexertion increases in plasma ET-1 concentration have also been reported in studies of normal humans and in studies where the subjects had various diseases affect-

ing the vasculature.[211–213,216] In one of those experiments even greater increases in plasma ET-1 concentrations were seen in dehydrated humans.[217] The greater increase in plasma ET-1 concentration due to volume depletion supports the suggestion that ET-1 plays a role in the modulation of vascular tone in the defense of mean arterial pressure.[206] Thus, the postexertion increase in plasma ET-1 concentration observed in horses[204] sampled before and after exercise is consistent with previously published reports on the hemodynamic and endocrine responses to exercise in horses.[3,62,228] An increase in plasma ET-1 concentration following rapid cessation of prolonged exercise, at a time when postexertion blood pressure would be expected to fall, fits with the neuroendocrine response to other perturbations affecting vascular fluid volume, cardiac filling pressure and mean arterial pressure. This would be an appropriate response in the regulation of cardiovascular function during the transition from exertion to recovery when heart rate, cardiac output and blood pressure are declining rapidly in the face of exercise-induced vasodilation of vascular beds supplying the muscles.[64]

A great deal of information has been published documenting elevated resting plasma ET-1 concentrations in humans and rats with diseases, in particular in humans with COPD and pulmonary hypertension.[203,206,210,211,213–223] Data reported by Benamou et al[219] demonstrated that postexercise ET-1 concentrations were substantially elevated in the bronchoalveolar lavage fluid of horses with EIPH. In another study Benamou et al[218] demonstrated that ET-1 type A receptors mediate the vasoconstrictor action of ET-1 in the pulmonary and systemic circulations of the horse. However, data from another study[221] suggest that ET-1 is not a mediator of the acute hypoxic pulmonary hypertension response to exercise, but may serve as a modulator of the acute response or slower phase of hypoxic pulmonary hypertension response to exercise. More work is needed to determine if ET-1 plays a role in the etiology of exercise-induced pulmonary hemorrhage (EIPH), especially since some feel that increases in pulmonary artery pressure during exercise may contribute to EIPH.[223,224]

Gonads and reproductive hormones

The reproductive hormones are essential for the health and well-being of a mare or stallion. However, exercise performance is not affected per se by the reproductive hormones. Nevertheless, recent human research has focused a great deal of attention on the effects of exercise on the female reproductive cycle and the interaction of prolactin, LH, FSH, estrogen and β-endorphin.[5] Human work has also examined the effects of acute exercise on the health of pregnant women. More work is needed in the horse to determine if exertion affects these hormones, especially in endurance horses and in pleasure horses that are ridden while they are in foal.

Endocrine mediation of short-term control of cardiovascular function

The cardiovascular response to exercise is dependent on a multisystem defense of blood volume, MAP and plasma tonicity.[3] These mechanisms insure adequate blood flow to the working muscles and obligate tissues along with the provision of adequate fluid volume for sweating and thermoregulation.[1,3,5,38–40] The maintenance of cardiovascular homeostasis during exercise is mediated by neuroendocrine mechanisms which insure the system can meet the increased demand for blood flow to the working muscles during exercise.[1,3,38–40]

The anticipation of exercise in humans and horses can invoke a withdrawal of parasympathetic control and an increase in sympathetic nervous activity resulting in an increase in heart rate, force of contraction, stroke volume and cardiac output. Rowell[4] suggests that the 'range of parasympathetic control of the heart by central command determines the level of exercise at which the activation of the sympathetic nervous system occurs'. In horses, resting HR averages 30–40 bpm.[3] Initial increases in heart rate up to ~120 bpm are associated with the withdrawal of parasympathetic tone.[3] However, further increases in HR during exercise, up to maximal HR between 200 and 240 bpm, are associated with increases in sympathetic activity and catecholamine release.[3] This increase in HR, coupled with increased stroke volume from 0.7 L at rest to almost 2 L, results in a rise in cardiac output from an average of 30 L/min at rest up to nearly 300 L/min during maximal exercise.[3] The cardiovascular system responds to exercise with dramatic increases in heart rate and force of cardiac contraction and subsequent increases in stroke volume and cardiac output.[4] These central cardiovascular responses are rapid and concurrent with venoconstriction and arterial vasodilation in the working muscles.[4]

Adjustments in peripheral vascular resistance that are mediated by the cardiopulmonary baroreflex cause a redistribution of blood volume from 'storage' in highly compliant venous capacitance vessels into the arterial side of the cardiovascular system, enhancing venous return.[4] In the horse there is the added component of splenic reserve mobilization which further enhances venous return and circulating red cell volume.[3,58] Splenic contraction is mediated by direct stimulation from the sympathetic nervous system, through the action of norepinephrine and epinephrine on α-adrenergic receptors.[58] From 6 to 12 liters of blood can be delivered into the central circulation at the onset of exercise, allowing the equine athlete to reach a maximal aerobic capacity (145–200 mL/kg/min in fit horses) that is almost three times greater than that of human athletes.[3,58] This extra volume is rapidly accommodated through arterial vasodilation which is mediated by increases in sympathetic

neural outflow and ANP and through local chemoreceptor mechanisms.[3,44] Resequestration of the splenic reserve is prevented by the action of vasopressin and the catecholamines on splenic arterioles.[46]

Mean arterial blood pressure increases with exercise intensity, a response essential for increasing cardiac output in the face of decreases in resistance in the vascular beds of the working muscles. Rowell[4] suggests that in addition to input from the cardiopulmonary baroreceptors, a functional arterial baroreflex and muscle chemoreflexes are essential for the regulation of heart rate, cardiac output and arterial pressure during exercise. Rowell[4] further suggests that the operating point of the arterial baroreflex is 'reset during dynamic exercise with adjustments in autonomic tone to compensate for the mismatch between cardiac output and vascular conductance'.

Modulation of the blood flow and blood pressure response to exercise involves input from both the high- and low-pressure baroreceptors. The low-pressure (cardiopulmonary) baroreceptors are volume receptors located primarily within the atria and the pulmonary circulation.[3,4] At the start of exercise, increased venous return results in atrial stretch, eliciting a neuroendocrine response by the cardiopulmonary baroreceptors. Nerves within the atria serve as stretch receptors, sensing volume overload or underload. The output from these nerves is conducted centrally via vagal afferents and integrated into the central control of peripheral vascular tone.[3,4] The endocrine component of this baroreflex involves the release of ANP, a hormone with potent vasodilatory properties and a reflex decrease in vasopressin release.[3,195]

Even with the mobilization of reserve blood volume, the demands of high-intensity or long-duration exercise may exceed central cardiovascular capacity. Baroreceptor control of arterial tone becomes vital to the maintenance of cardiac output and MAP and sympathetic-induced vasoconstriction decreases blood flow to non-obligate tissues during high-intensity exercise.[3,4] This response is even more pronounced during long-term exercise when fluid losses associated with sweating compromise vascular fluid volume and venous return. Without replacement or compensation, decreases in venous return associated with fluid losses can cause a decrease in cardiac output and decreased blood flow to the working muscles and to the vascular beds associated with thermoregulation.[3,4,40] To maintain MAP, the body compensates by increasing heart rate and contractility, a phenomenon termed cardiovascular 'drift' that is associated with an increase in sympathetic activity and circulating catecholamines.[57]

Exercise training produces chronic adaptations in the cardiovascular system that are mediated through changes in neuroendocrine control.[3,37,38,40] Work from several species has shown that exercise training produces an expansion of plasma volume.[40,65,72,225] Trained horses have significantly greater blood volumes than untrained horses[40,58,65,72] with increases in plasma volume of 30% observed after only 1 week of exercise training. Humans show significant alterations in sodium and water excretion that are attributable to repeated exercise-induced increases in plasma aldosterone concentration.[40] In the one study of the hypervolemic response in horses, the authors reported no change in resting plasma aldosterone concentration or sodium excretion; however, their measurements were taken at 1-week intervals and may have missed changes in sodium excretion that are reported to occur in the first days of training in humans.[65] A more recent study that focused on changes occurring during the first days of training demonstrates that plasma aldosterone concentration remains elevated for almost 24 hours during the first days of training.[72] It appeared that, as in humans, an aldosterone-mediated retention of sodium and water by the kidneys and digestive tract is a vital part of the hypervolemic response to training in the horse.[40,72]

Endocrine control of metabolism during acute exercise

Performance of exercise requires the transduction of potential or stored energy into kinetic energy and the endocrine system plays an integral role in the co-ordination of the mobilization and utilization of carbohydrates and free fatty acids.[226,227] The need for a rapid provision of metabolic substrates to fuel exercise and to prevent central fatigue is facilitated by a rapid increase in sympathetic drive and the rate of catecholamine release from the adrenal medulla. The degree of this response is correlated with both exercise intensity and duration.[2,5,20] At the onset of exercise the catecholamines (epinephrine and norepinephrine) act on the liver and muscles to increase the rate of glycogen breakdown (glycogenolysis).[2,5,20] This results in an increase in circulating blood glucose concentrations. The catecholamines also stimulate the release of hormone-sensitive lipase which acts on triglycerides to mobilize free fatty acids.[2,5,20] The latter are important for endurance activities where the use of fat to fuel exercise spares glycogen by offsetting the amount of glucose needed to fuel the activity.[2,5,20] However, fat cannot be used alone as a fuel source as 'fat burns in the flame of carbohydrates'. An increase in circulating catecholamines also inhibits insulin and stimulates glucagon release. As with the catecholamines, glucagon also stimulates gluconeogenesis and inhibits glycogenesis,[2,5,20] thus playing an important role in maintaining blood glucose concentrations during exercise and delaying the onset of fatigue.[2,5,20] Glucagon can also stimulate the breakdown of protein and release of amino acids which can be used as a fuel source by the liver.[2,5,20] The effects of the catecholamines and glucagon can be augmented by the release of cortisol. The latter is affected by the intensity and duration of the activity.[2,5,20] Cortisol thus is a metabolic hormone that stimulates gluconeogenesis, fatty acid mobilization and protein breakdown. In the case of the latter, amino acids not used to fuel exercise may provide resources for the synthesis of new proteins needed to repair muscle and replace enzymes used in the various metabolic pathways.[2,5,20]

References

1. McKeever KH. The endocrine system and the challenge of exercise. Vet Clin North Am Equine Pract 2002; 18:321–353.
2. Dickson WM. Endocrine glands. In: Swenson, MJ, ed. Dukes' physiology of domestic animals, Ithaca, NY: Cornell University Press; 1970; 1189–1252.
3. McKeever KH, Hinchcliff KW. Neuroendocrine control of blood volume, blood pressure, and cardiovascular function in horses. Equine Vet J 1995; 18(Suppl):77–81.
4. Rowell LB. Human cardiovascular control. New York: Oxford University Press; 1993; 441–479.
5. Willmore JH, Costill DL. Hormonal regulation of exercise. In: Willmore JH, Costill DL, eds. Physiology of sport and exercise, Champaign, IL: Human Kinetics; 1994; 122–143.
6. McLaren DPM, Gibson H, Parry-Billings M, et al. A review of metabolic and physiological factors in fatigue. In: Pandolf KB, ed. Exercise and sports science reviews. Baltimore, MD: Williams and Wilkins; 1989; 29–66.
7. Mehl ML, Schott HC, Sarkar DK, et al. Effects of exercise intensity on plasma β-endorphin concentrations in horses. Am J Vet Res 2000; 61: 969–973.
8. Mehl ML, Sarkar DK, Schott HC, et al. Equine β-endorphin concentrations are affected by exercise intensity and time of day. Equine Vet J 1999; 30(Suppl):567–569.
9. Murray RC, Vedi S, Birch HL, et al. Subchondral bone thickness, hardness and remodelling are influenced by short-term exercise in a site-specific manner. J Orthop Res 2001; 19:1035–1042.
10. Yarasheski KE. Growth hormone effects on metabolism, body composition muscle mass, and strength. In: Holloszy JO, ed. Exercise and sport sciences reviews. Philadelphia, PA: Williams and Wilkins; 1994; 285–312.
11. Horohov DW, Dimock AN, Gurinalda PD, et al. Effects of exercise on the immune response of young and old horses. Am J Vet Res 1999; 60:643–647.
12. Malinowski K, Christensen RA, Hafs HD, et al. Age and breed differences in thyroid hormones, insulin-like growth factor-I and IGF binding proteins in horses. J Anim Sci 1996; 74:1936–1942.
13. Malinowski K, Christensen RA, Konopka A, et al. Feed intake, body weight, body condition score, musculation,and immunocompetence in aged mares given equine somatotropin. J Anim Sci 1997; 75:755–760.
14. McKeever KH, Malinowski K, Christensen RA, et al. Chronic equine somatotropin administration does not affect aerobic capacity or indices of exercise performance in geriatric horses. Vet J 1997; 155:19–25.
15. Thompson DL, Rahmanian MS, DePew CL, et al. Growth hormone in mares and stallions: pulsatile secretion, response to growth hormone-releasing hormone, and effects of exercise, sexual stimulation, and pharmacological agents. J Anim Sci 1992; 70:1201–1207.
16. Day TRJ, Potter GD, Morris EL, et al. Physiologic and skeletal response to exogenous equine growth hormone in two-year-old horses in race training. Proceedings of the 15th Equine Nutritional Physiology Society Symposium, 1997; 53–58.
17. Gerard MP. The effects of equine somatotropin on the physiological responses to training in young horses. PhD dissertation. University of Sydney: 2001.
18. Gerard MP, Hodgson DR, Lambeth RR, Ray SP, Rose RJ. Effects of somatotropin and training on indices of exercise capacity in Standardbreds. Equine Vet J 2002; 34(Suppl): 496–501.
19. Smith LA, Thompson DL, French DD, et al. Effects of recombinant equine somatotropin on wound healing, carbohydrate and lipid metabolism, and endogenous somatotropin responses to secretagogues in geldings. J Anim Sci 1999; 77:1815–1822.
20. Thornton JR. Hormonal responses to exercise and training. In: Rose RJ, ed. Exercise physiology. Philadelphia, PA: Saunders; 1985; 477–496.
21. Convertino VA, Keil LC, Bernaver EM, et al. Plasma volume, osmolarity, vasopressin, and renin activity during graded exercise in man. J Appl Physiol 1981; 50:123–128.
22. Freund BJ, Shizuru EM, Hashiro GM, et al. Hormonal, electrolyte and renal responses to exercise are intensity dependent. J Appl Physiol 1991; 70:900–906.
23. Jimenez MA, Hinchcliff KW, Farris JW. Catecholamine and cortisol responses of horses to incremental exertion. Vet Res Commun 1993; 22:107–118.
24. Nagata S, Takeda F, Kurosawa M, et al. Plasma adrenocorticotropin, cortisol and catecholamines response to various exercises. Equine Vet J 1999; 30(Suppl):570–574.
25. Alexander SL, Irvine CH, Ellis MJ, et al. The effect of acute exercise on the secretion of corticotropin-releasing factor, arginine vasopressin, and adrenocorticotropin as measured in pituitary venous blood from the horse. Endocrinology 1991; 128:65–72.
26. Bruin G, Kuipers, H, Keizer, HA, et al. Adaptation and overtraining in horses subjected to increasing training loads. J Appl Physiol 1994;76:1908–1913.
27. Elsaesser F, Klobasa F, Ellendorff F. ACTH stimulation test for the determination of salivary cortisol and of cortisol responses as markers of the training status/fitness of warm-blooded sports horses. Dtsch Tierarztl Wochenschr 2001; 108:31–36.
28. Golland LC, Evans DL, Stone GM, et al. Plasma cortisol and beta-endorphin concentrations in trained and over-trained standardbred racehorses. Pflugers Arch 1999; 439:11–17.
29. Linden A, Art T, Amory H, et al. Comparison of the adrenocortical response to both pharmacological and physiological stresses in sport horses. Zentralbl Veterinarmed A 1990; 37:601–604.
30. Marc M, Parvizi N, Ellendorff F, et al. Plasma cortisol and ACTH concentrations in the warmblood horse in response to a standardized treadmill exercise test as physiological markers for evaluation of training status. J Anim Sci 2000; 78:1936–1946.
31. McCarthy RN, Jeffcott LB, Funder JW, et al. Plasma beta-endorphin and adrenocorticotrophin in young horses in training. Aust Vet J 1991; 68:359–361.
32. Caloni F, Spotti M, Villa R, et al. Hydrocortisone levels in the urine and blood of horses treated with ACTH. Equine Vet J 1999; 31:273–276.
33. Art T, Franchimont P, Lekeux P. Plasma beta-endorphin response of thoroughbred horses to maximal exercise. Vet Rec 1994; 135:499–503.
34. Li WI, Chen CL. Running and shipping elevate plasma levels of beta-endorphin-like substance (B-END-LI) in thoroughbred horses. Life Sci 1987; 40:1411–1421.
35. Convertino VA, Keil LC, Greenleaf JE. Plasma volume, renin, and vasopressin responses to graded exercise after training. J Appl Physiol 1983; 54:508–514.
36. Malinowski KE, Shock V, Roegner P, et al. Age and exercise training alter plasma β-endorphin, cortisol, and immune parameters in horses. J Anim Sci 2003 (submitted).
37. Wade CE. Response, regulation, and actions of vasopressin during exercise: a review. Med Sci Sports Exerc 1984; 16:506–511.

38. Wade CE, Freund BJ, Claybaugh JR. Fluid and electrolyte homeostasis during and following exercise: hormonal and non-hormonal factors. In: Claybaugh JR, Wade CE, eds. Hormonal regulation of fluid and electrolytes. New York: Plenum; 1989; 1–44.
39. Wade CE, Freund BJ. Hormonal control of blood volume during and following exercise. In: Gisolfi CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, volume 3: fluid homeostasis during exercise. Carmel, IN: Benchmark Press; 1990; 207–245.
40. Convertino VA. Blood volume: its adaptation to endurance training. Med Sci Sports Exerc 1991; 23:1338–1348.
41. Zambraski EJ. Renal regulation of fluid homeostasis during exercise. In: Gisolfi CV, Lamb DR, eds. Perspectives in exercise science and sports medicine volume 3: fluid homeostasis during exercise. Carmel, IN: Benchmark Press; 1990; 245–280.
42. McKeever KH, Hinchcliff KW, Schmall LM, et al. Renal tubular function in horses during submaximal exercise. Am J Physiol 1991; 261:R553–560.
43. McKeever KH, Hinchcliff KW, Cooley JL, et al. Furosemide magnifies the exercise-induced elevation of plasma vasopressin concentration in horses. Res Vet Sci 1993; 55:101–105.
44. McKeever KH, Hinchcliff KW, Cooley JL. Acute volume load during exercise in horses: atrial natriuretic peptide, vasopressin, and hemodynamics. Med Sci Sports Exerc 1991; 23:S104.
45. McKeever KH, Hinchcliff, KW, Schmall LM, et al. Changes in plasma renin activity, aldosterone, and vasopressin, during incremental exercise in horses. Am J Vet Res 1992; 53:1290–1293.
46. Davies BN, Withrington PG. The actions of drugs on the smooth muscle of the capsule and blood vessels of the spleen. Pharm Rev 1973; 25:373–413.
47. Freund BJ, Claybaugh JR, Hashiro GM, et al. Hormonal and renal responses to water drinking in moderately trained and untrained humans. Am J Physiol 1988; 254:R417–R423.
48. Geelen G, Keil LC, Kravik SE, et al. Inhibition of plasma vasopressin after drinking in dehydrated humans. Am J Physiol 1984; 249:R968–R971.
49. Thrasher TN, Nistal-Herrera JF, Keil LC, et al. Satiety and inhibition of vasopressin secretion after drinking in dehydrated dogs. Am J Physiol 1981; 240:E394–E401.
50. Gonzalez O, Gonzalez E, Sanchez C, et al. Effect of exercise on erythrocyte beta-adrenergic receptors and plasma concentrations of catecholamines and thyroid hormones in Thoroughbred horses. Equine Vet J 1998; 30:72–78.
51. Irvine CHG. Thyroxine secretion rate in the horse under various physiological states. J Endocrinol 1967; 39:313–320.
52. Chiba S, Kanematsu S, Murakami K, et al. Serum parathyroid hormone and calcitonin levels in racehorses with fracture. J Vet Med Sci 2000; 62:361–365.
53. Geor R, Hope E, Lauper L, et al. Effect of glucocorticoids on serum osteocalcin concentration in horses. Am J Vet Res 1995; 56:1201–1205.
54. Hoekstra KE, Nielsen BD, Orth MW, et al. Comparison of bone mineral content and biochemical markers of bone metabolism in stall- vs. pasture-reared horses. Equine Vet J 1999; 30(Suppl):601–604.
55. McCarthy RN, Jeffcott LB. Effects of treadmill exercise on cortical bone in the third metacarpus of young horses. Res Vet Sci 1992; 52:28–37.
56. Price JS, Jackson BF, Gray JA, et al. Biochemical markers of bone metabolism in growing thoroughbreds: a longitudinal study. Res Vet Sci 2000; 71:37–44.
57. McKeever KH. Sympatholytics and sympathomimetics. In: Hinchcliff KW, Sams RA, eds. Drug use in performance horses. Philadelphia, PA: Saunders; 1993; 1–13.
58. Persson SGB. On blood volume and working capacity. Acta Vet Scand 1967; 19(Suppl):1–189.
59. Plummer C, Knight PK, Ray SP, et al. Cardiorespiratory and metabolic effects of propranolol during maximal exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Press; 1991; 465–474.
60. Sexton WL, Erickson HH. Effect of propranolol on cardiorespiratory function in the pony during submaximal exercise. Equine Vet J 1986; 18:485–489.
61. McKeever KH. Fluid balance and renal function in exercising horses. In: Hinchcliff KW, ed. Fluids, electrolytes and thermoregulation in horses. Philadelphia, PA: Saunders; 1998; 23–44.
62. Cooley JL, Hinchcliff KW, McKeever KH, et al. Effect of furosemide on plasma atrial natriuretic peptide and aldosterone concentrations and renin activity in running horses. Am J Vet Res 1994; 55:273–277.
63. Guthrie GP, Cecil SG, Kotchen TA. Renin, aldosterone and cortisol in the Thoroughbred horse. J Endocrinol 1980; 85:49–53.
64. Guthrie GP, Cecil SG, Darden EA, et al. Dynamics of renin and aldosterone in the Thoroughbred horse. Gen Compar Endocrinol 1982; 48:296–299.
65. McKeever KH, Schurg WA, Jarrett SH, Convertino VA Exercise training-induced hypervolemia in the horse. Med Sci Sports Exerc 1987; 19:21–27.
66. Costill DL, Branum G, Fink W, et al. Exercise-induced sodium conservation changes in plasma renin and aldosterone. Med Sci Sports Exerc 1976; 8:209–213.
67. Kosunen KJ, Pakarinen AJ. Plasma renin, angiotensin II, and plasma and urinary aldosterone in running exercise. J Appl Physiol 1976; 41:26–29.
68. McKeever KH, Geiser S, Kearns CF. Role of the renin-angiotensin aldosterone cascade in the pulmonary artery pressure response to exercise in horses. Physiologist 2000; 43:356.
69. Kokkonen UM, Poso AR, Hyyppa S, Huttunen P, Leppaluoto J. Exercise-induced changes in atrial peptides in relation to neuroendocrine responses and fluid balance in the horse. J Vet Med A Physiol Pathol Clin Med 2002; 49:144–150.
70. Hyyppa S, Saastamoinen M, Poso AR. Restoration of water and electrolyte balance in horses after repeated exercise in hot and humid conditions. Equine Vet J 1996; 22(Suppl): 108–112.
71. Farris, JW, Hinchcliff KW, McKeever KH, et al. Treadmill endurance of Standardbred horses with tryptophan or glucose. J Appl Physiol 1998; 85:807–816.
72. McKeever KH, Scali R, Geiser S, Kearns CF. Plasma aldosterone concentration and renal sodium excretion are altered during the first days of training. Equine Vet J 2002; 34(Suppl):524–531.
73. Bridges RJ, Rummel W. Vasopressin-stimulated Na+ transport in rat colon descendens. In: Skadhauge E, Heintze, K, eds. Intestinal absorption and secretion. Boston, MA: MTP Press; 1984; 265–272.
74. Crandell KG, Pagan JD, Harris P, et al. A comparison of grain, oil and beet pulp as energy sources for the exercised horse. Equine Vet J 1999; 30(Suppl):485–489.
75. Hyyppa S. Effects of nandrolone treatment on recovery in horses after strenuous physical exercise. J Vet Med A Physiol Pathol Clin Med 2001; 48:343–352.
76. Lucke JN, Hall GN. Further studies on the metabolic effects of long distance riding: Golden Horseshoe Ride 1979. Equine Vet J 1980; 12:189–192.

77. Lucke JN, Hall GM. Long distance exercise in the horse: Golden Horseshoe Ride 1978. Vet Rec 1980; 106:405–407.
78. Lucke JN, Hall GM. A biochemical study of the Arab Horse Society's marathon race. Vet Rec 1980; 107:523–525.
79. Snow DH, MacKenzie G. Some metabolic effects of maximal exercise in the horse and adaptations with training. Equine Vet J 1977; 9:134–140.
80. Snow DH, Rose RJ. Hormonal changes associated with long distance exercise. Equine Vet J 1981; 13:195–197.
81. Rossdale PD, Burguez PN, Cash RS. Changes in blood neutrophil/lymphocyte ratio related to adrenocortical function in the horse. Equine Vet J 1982; 14:293–298.
82. Toutain PL, Lassourd V, Popot MA, Laroute V, Alvinerie M, Bonnaire Y. Urinary cortisol excretion in the resting and exercising horse. Equine Vet J 1995; 18(Suppl):457–462.
83. Lassourd V, Gayrard V, Laroute V, et al. Cortisol disposition and production rate in horses during rest and exercise. Am J Physiol 1996; 271:R25–33.
84. Popot MA, Houghton E, Ginn A, et al. Cortisol concentrations in post competition horse urine: a French and British survey. Equine Vet J 1997; 29:226–229.
85. Giraudet A, Hinchcliff KW, Kohn CW, McKeever KH. Early insulin response to an intravenous glucose tolerance test in horses. Am J Vet Res 1994; 55:379–381.
86. Ralston SL. Effect of soluble carbohydrate content of pelleted diets on post prandial glucose and insulin profiles in horses. Pferdeheilkunde 1992; 112–115.
87. Davie AJ, Evans DL, Hodgson, DR, et al. The effects of an oral glucose polymer on muscle glycogen resynthesis in Standardbred horses. J Nutr 1994; 124(suppl):2740S–2741S.
88. Davie AJ, Evans DL, Hodgson, DR, et al. Effects of muscle glycogen depletion on some metabolic and physiological responses to submaximal treadmill exercise. Can J Vet Res 1999; 63:241–247.
89. de la Corte FD, Valberg SJ, Mickelson JR, et al. Blood glucose clearance after feeding and exercise in polysaccharide storage myopathy. Equine Vet J 1999; 30(Suppl):324–328.
90. Duren SE, Pagan JD, Harris PA, et al. Time of feeding and fat supplementation affect plasma concentrations of insulin and metabolites during exercise. Equine Vet J 1999; 30(Suppl): 479–484.
91. Dybdal NO, Gribble D, Madigan JE, et al. Alterations in plasma corticosteroids, insulin and selected metabolites in horses used in endurance rides. Equine Vet J 1980; 12:137–140.
92. Freestone JF, Beadle R, Shoemaker K, et al. Improved insulin sensitivity in hyperinsulinaemic ponies through physical conditioning and controlled feed intake. Equine Vet J 1992; 24:187–190.
93. Freestone JF, Wolfsheimer KJ, Kamerling SG, et al. Exercise induced hormonal and metabolic changes in Thoroughbred horses: effects of conditioning and acepromazine. Equine Vet J 1991; 23:219–223.
94. Freestone JF, Shoemaker K, Bessin R, et al. Insulin and glucose response following oral glucose administration in well-conditioned ponies. Equine Vet J 1992; 11(Suppl):13–17.
95. Geor RJ, Hinchcliff KW, McCutcheon LJ, et al. Epinephrine inhibits exogenous glucose utilization in exercising horses. J Appl Physiol 2000; 88:1777–1790.
96. Geor RJ, Hinchcliff KW, Sams RA. Beta-adrenergic blockade augments glucose utilization in horses during graded exercise. J Appl Physiol 2000; 89:1086–1098.
97. Frape DL. Dietary requirements and athletic performance of horses. Equine Vet J 1988; 20:163–172.
98. Hyyppa S, Saastamoinen M, Poso AR. Effect of a post exercise fat-supplemented diet on muscle glycogen repletion. Equine Vet J 1999; 30(Suppl):493–498.
99. Pagan JD, Harris PA. The effects of timing and amount of forage and grain on exercise response in thoroughbred horses. Equine Vet J 1999; 30(Suppl):451–457.
100. Poso AR, Hyyppa S. Metabolic and hormonal changes after exercise in relation to muscle glycogen concentrations. Equine Vet J 1999; 30(Suppl):332–336.
101. Powell D, Lawrence LM, Brewster-Barnes T, et al. The effect of diet composition and feeding state on the response to exercise in feed-restricted horses. Equine Vet J 1999; 30(Suppl): 514–518.
102. Rodiek A, Bonvicin S, Stull C, et al. Glycaemic and endocrine responses to corn or alfalfa fed prior to exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Press; 1991; 368–373.
103. Sticker LS, Thompson DL, Bunting LD, et al. Feed deprivation of mares: plasma metabolite and hormonal concentrations and responses to exercise. J Anim Sci 1995; 73:3696–3704.
104. Stull CL, Rodiek AV. Responses of blood glucose, insulin and cortisol concentrations to common equine diets. J Nutr 1988; 118:206–213.
105. Stull CL, Rodiek AV. Effects of post prandial interval and feed type on substrate availability during exercise. Equine Vet J 1995; 18(Suppl):363–366.
106. Lawrence LM, Williams J, Soderholm LV, et al. Effect of feeding state on the response of horses to repeated bouts of intense exercise. Equine Vet J 1995; 27:27–30.
107. Williams CA, Kronfeld DS, Staniar WB, et al. Plasma glucose and insulin responses of Thoroughbred mares fed a meal high in starch and sugar or fat and fiber. J Anim Sci 2001; 79:2196–2201.
108. Jablonska EM, Ziolkowska SM, Gill J, et al. Changes in some haematological and metabolic indices in young horses during the first year of jump-training. Equine Vet J 1991; 23:309–311.
109. Hall GM, Adrian TE, Bloom SR, et al. Changes in circulating gut hormones in the horse during long distance exercise. Equine Vet J 1982; 14:209–212.
110. Farrell PA. Exercise effects on regulation of energy metabolism by pancreatic and gut hormones. In: Lamb DR, Gisolfi CV, eds. Perspectives in exercise science and sports medicine: energy metabolism in exercise and sport. Carmel, IN: Brown and Benchmark; 1992; 383–434.
111. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature 1994; 372:425–432.
112. Zhang Y, Matheny M, Zolotukhin S, Tumer N, Scarpace PJ. Regulation of adiponectin and leptin gene expression in white and brown adipose tissues: influence of beta3-adrenergic agonists, retinoic acid, leptin and fasting. Biochim Biophys Acta 2002; 1584(2–3):115.
113. Halaas JL, Gajiwala KS, Maffei M, et al. Weight-reducing effects of the plasma protein encoded by the obese gene. Science 1995; 269:543–546.
114. Schwartz MW, Woods SC, Porte D Jr, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000; 404:661–671.
115. Saper CB, Chou TC, Elmquist JK. The need to feed: homeostatic and hedonic control of eating. Neuron 2002; 36:199–211.
116. Giacobino JP. Uncoupling proteins, leptin, and obesity: an updated review. Ann NY Acad Sci 2002; 967:398–402.
117. Reidy SP, Weber JM. Accelerated substrate cycling: a new energy-wasting role for leptin in vivo. Am J Physiol 2002; 282:E312–317.
118. Maffei M, Halaas J, Ravussin E, et al. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in

obese and weight-reduced subjects. Nat Med 1995; 1:1155–1161
119. Hamilton BS, Paglia D, Kwan AY, Deitel M. Increased obese mRNA expression in omental fat cells from massively obese humans. Nat Med 1995; 1:953–956.
120. Kearns CF, McKeever KH, Roegner V, Brady SM, Malinowski K. Adiponectin and leptin are related to fat mass in horses. (Submitted 2002)
121. Buff PR, Dodds AC, Morrison CD, et al. Leptin in horses: tissue localization and relationship between peripheral concentrations of leptin and body condition. J Anim Sci 2002; 80:2942–2948.
122. Fitzgerald BP, McManus CJ. Photoperiodic versus metabolic signals as determinants of seasonal anestrus in the mare. Biol Reprod 2000; 63:335–340.
123. McManus CJ, Fitzgerald BP. Effects of a single day of feed restriction on changes in serum leptin, gonadotropins, prolactin, and metabolites in aged and young mares. Domest Anim Endocrinol 2000; 19:1–13.
124. Saad MF, Damani S, Gingerich RL, et al. Sexual dimorphism in plasma leptin concentration. J Clin Endocrinol Metab 1997; 82:579–584.
125. Mulet T, Pico C, Oliver P, Palou A. Blood leptin homeostasis: sex-associated differences in circulating leptin levels in rats are independent of tissue leptin expression. Int J Biochem Cell Biol 2003; 35:104–110.
126. Weltman A, Pritzlaff CJ, Wideman L, et al. Intensity of acute exercise does not affect serum leptin concentrations in young men. Med Sci Sports Exerc 2000; 32:1556–1561.
127. Dirlewanger M, di Vetta V, Giusti V, Schneiter P, Jequier E, Tappy L. Effect of moderate physical activity on plasma leptin concentration in humans. Eur J Appl Physiol Occup Physiol 1999; 79:331–335.
128. Kraemer RR, Johnson LG, Haltom R, et al. Serum leptin concentrations in response to acute exercise in postmenopausal women with and without hormone replacement therapy. Proc Soc Exp Biol Med 1999; 221:171–177.
129. Fisher JS, van Pelt RE, Zinder O, Landt M, Kohrt WM. Acute exercise effect on postabsorptive serum leptin. J Appl Physiol 2001; 91:680–686.
130. Essig DA, Alderson NL, Ferguson MA, Bartoli WP, Durstine JL. Delayed effects of exercise on the plasma leptin concentration. Metabolism 2000; 49:395–399.
131. Racette SB, Coppack SW, Landt M, Klein S. Leptin production during moderate-intensity aerobic exercise. J Clin Endocrinol Metab 1997; 82:2275–2277.
132. Torjman MC, Zafeiridis A, Paolone AM, Wilkerson C, Considine RV. Serum leptin during recovery following maximal incremental and prolonged exercise. Int J Sports Med 1999; 20:444–450.
133. Leal-Cerro A, Garcia-Luna PP, Astorga R, et al. Serum leptin levels in male marathon athletes before and after the marathon run. J Clin Endocrinol Metab 1998; 83:2376–2479.
134. Olive JL, Miller GD. Differential effects of maximal- and moderate-intensity runs on plasma leptin in healthy trained subjects. Nutrition 2001; 17:365–369.
135. Karamouzis I, Karamouzis M, Vrabas IS, et al. The effects of marathon swimming on serum leptin and plasma neuropeptide Y levels. Clin Chem Lab Med 2002; 40:132–136.
136. Houmard JA, Cox JH, MacLean PS, Barakat HA. Effect of short-term exercise training on leptin and insulin action. Metabolism 2000; 49:858–861.
137. Halle M, Berg A, Garwers U, Grathwohl D, Knisel W, Keul J. Concurrent reductions of serum leptin and lipids during weight loss in obese men with type II diabetes. Am J Physiol 1999; 277:E277–E282.
138. Okazaki T, Himeno E, Nanri H, Ogata H, Ikeda M. Effects of mild aerobic exercise and a mild hypocaloric diet on plasma leptin in sedentary women. Clin Exp Pharmacol Physiol 1999; 26:415–420.
139. Pasman WJ, Westerterp-Plantenga MS, Saris WH. The effect of exercise training on leptin levels in obese males. Am J Physiol 1998; 274:E280–E286.
140. Reseland JE, Anderssen SA, Solvoll K, et al. Effect of long-term changes in diet and exercise on plasma leptin concentrations. Am J Clin Nutr 2001; 73:240–245.
141. Hickey MS, Houmard JA, Considine RV, et al. Gender-dependent effects of exercise training on serum leptin levels in humans. Am J Physiol 1997; 272:E562–E566.
142. Saris WH. The concept of energy homeostasis for optimal health during training. Can J Appl Physiol 2001;; 26(Suppl):S167–75.
143. Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism. Trends Endocrinol Metab 2002; 13:84–89.
144. Berg AH, Combs TP, Du X, Brownlee M, Scherer PE. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. Nat Med 2001; 7:947–953.
145. Tsao TS, Lodish HF, Fruebis J. ACRP30, a new hormone controlling fat and glucose metabolism. Eur J Pharmacol 2002; 440:213–221.
146. Arita Y, Kihara S, Ouchi N, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. Biochem Biophys Res Commun 1999; 257:79–83.
147. Hotta K, Funahashi T, Arita Y, et al. Plasma concentrations of a novel, adipose-specific protein, adiponectin, in type 2 diabetic patients. Arterioscler Thromb Vasc Biol 2000; 20:1595–1599.
148. Hayashi T, Wojtaszewski JF, Goodyear LJ. Exercise regulation of glucose transport in skeletal muscle. Am J Physiol 1997; 273:E1039–E1051.
149. Malinowski K, Betros CL, Flora L, Kearns CF, McKeever KH. Effect of training on age-related changes in plasma insulin and glucose. Equine Vet J 2002; 34(Suppl):147–153.
150. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H. Effect of physical exercise on sensitivity and responsiveness to insulin in humans. Am J Physiol 1988; 254:E248–E259.
151. Powell DM, Reedy SE, Sessions DR, Fitzgerald BP. Effect of short-term exercise training on insulin sensitivity in obese and lean mares. Equine Vet J 2002; 34(Suppl):81–84.
152. Hulver MW, Zheng D, Tanner CJ, et al. Adiponectin is not altered with exercise training despite enhanced insulin action. Am J Physiol Endocrinol Metab 2002; 283:E861–E865.
153. Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo H, Kangawa K. Ghrelin is a growth-hormone-releasing acylated peptide from stomach. Nature 1999; 02:656–660.
154. Wren AM, Seal LJ, Cohen MA, et al. Ghrelin enhances appetite and increases food intake in humans. J Clin Endocrinol Metab 2001; 86:5992.
155. Cummings DE, Purnell JQ, Frayo RS, Schmidova K, Wisse BE, Weigle DS. A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. Diabetes 2001; 50:1714–1719.
156. Murakami N, Hayashida T, Kuroiwa T, et al. Role for central ghrelin in food intake and secretion profile of stomach ghrelin in rats. J Endocrinol 2002; 174:283–288.
157. Sugino T, Hasegawa Y, Kikkawa Y, et al. A transient ghrelin surge occurs just before feeding in a scheduled meal-fed sheep. Biochem Biophys Res Commun 2002; 295:255–260.

158. Masuda Y, Tanaka T, Inomata N, et al. Ghrelin stimulates gastric acid secretion and motility in rats. Biochem Biophys Res Commun 2000; 276:905–908.
159. Date Y, Nakazato M, Murakami N, Kojima M, Kangawa K, Matsukura S. Ghrelin acts in the central nervous system to stimulate gastric acid secretion. Biochem Biophys Res Commun 2001; 280:904–907.
160. Dall R, Kanaley J, Hansen TK, et al. Plasma ghrelin levels during exercise in healthy subjects and in growth hormone-deficient patients. Eur J Endocrinol 2002; 147:65–70.
161. Murray MJ, Grodinsky C, Anderson CW, Radue PF, Schmidt GR. Gastric ulcers in horses: a comparison of endoscopic findings in horses with and without clinical signs. Equine Vet J 1989; 7(Suppl):68–72.
162. Rigamonti AE, Pincelli AI, Corra B, et al. Plasma ghrelin concentrations in elderly subjects: comparison with anorexic and obese patients. J Endocrinol 2002; 175: R1–R5.
163. Otto B, Cuntz U, Fruehauf E, et al. Weight gain decreases elevated plasma ghrelin concentrations of patients with anorexia nervosa. Eur J Endocrinol 2001; 145:669–673.
164. Ballinger A, McLoughlin L, Medbak S, Clark M. Cholecystokinin is a satiety hormone in humans at physiological post-prandial plasma concentrations. Clin Sci (Lond) 1995; 89:375–381.
165. Choi BR, Palmquist DL. High fat diets increase plasma cholecystokinin and pancreatic polypeptide, and decrease plasma insulin and feed intake in lactating cows. J Nutr 1996; 126:2913–2919.
166. Gibbs J, Smith GP. Satiety: the roles of peptides from the stomach and the intestine. Fed Proc 1986; 45:1391–1395.
167. Grovum WL. Factors affecting the voluntary intake of food by sheep. 3. The effect of intravenous infusions of gastrin, cholecystokinin and secretin on motility of the reticulo-rumen and intake. Br J Nutr 1981; 45:183–201.
168. Bailey DM, Davies B, Castell LM, Newsholme EA, Calam J. Physical exercise and normobaric hypoxia: independent modulators of peripheral cholecystokinin metabolism in man. J Appl Physiol 2001; 90:105–113.
169. Matson CA, Reid DF, Ritter RC. Daily CCK injection enhances reduction of body weight by chronic intracerebroventricular leptin infusion. Am J Physiol Regul Integr Comp Physiol 2002; 282:R1368–R1373.
170. Emond M, Schwartz GJ, Ladenheim EE, Moran TH. Central leptin modulates behavioral and neural responsivity to CCK. Am J Physiol 1999; 276:R1545–R1549.
171. Bagnasco M, Dube MG, Kalra PS, Kalra SP. Evidence for the existence of distinct central appetite, energy expenditure, and ghrelin stimulation pathways as revealed by hypothalamic site-specific leptin gene therapy. Endocrinology 2002; 143:4409–4421.
172. Beretta E, Dube MG, Kalra PS, Kalra SP. Long-term suppression of weight gain, adiposity, and serum insulin by central leptin gene therapy in prepubertal rats: effects on serum ghrelin and appetite-regulating genes. Pediatr Res 2002; 52:189–198.
173. Zambraski EJ, Tucker MS, Lakas CS, et al. Mechanism of renin release in exercising dog. Am J Physiol 1984; 246:E71–E76.
174. Claybaugh JR, Pendergast DR, Davis JE, et al. Fluid conservation in athletes: responses to water intake, supine posture, and immersion. J Appl Physiol 1986; 61:7–15.
175. Geor RJ, Weiss DJ. Drugs affecting the hematologic system of the performance horse. In: Hinchcliff KW, Sams RA, eds. Drug use in performance horses. Philadelphia, PA: Saunders; 1993; 649–667.
176. Giger U. Erythropoietin and its clinical use. Compend Contin Educ Prac Vet 1992; 14:25–34.
177. Kearns CF, Lenhart JA, McKeever KH. Cross-reactivity between human erythropoietin antibody and horse erythropoietin. Electrophoresis 2000; 21:1454–1457.
178. McKeever KH. Erythropoietin: a new form of blood doping in horses. In: Wade J, ed. Proceedings of the 11th International Conference of Racing Analysts and Veterinarians, Newmarket, UK, 1996; 79–84.
179. McKeever KM, Agans JM, Geiser S. Effect of recombinant human erythropoietin administration on red cell volume, aerobic capacity, and performance in Standardbred horses. Proceedings of the 16th Equine Nutritional Physiology Society Symposium, 1999; 163–164.
180. McKeever KH, Wickler S, Smith T. Altitude not exercise increases plasma erythropoietin in horses. J Appl Physiol (Accepted with revision), 2002
181. Bodary PF, Pate RR, Wu PF, et al. Effects of acute exercise on plasma erythropoietin levels in trained runners. Med Sci Sports Exerc 1999; 31:543–546.
182. Schmidt W, Eckardt KU, Hilgendorf A, et al. Effects of maximal and submaximal exercise under normoxic and hypoxic conditions on serum erythropoietin levels. Int J Sports Med 1991; 12:457–461.
183. Schmidt W, Spielvogel H, Eckardt KU, et al. Effects of chronic hypoxia and exercise on plasma erythropoietin in high-altitude residents. J Appl Physiol 1993; 74:1874–1878.
184. Shoemaker JK, Green HJ, Coates J, et al. Failure of prolonged exercise training to increase red cell mass in humans. Am J Physiol 1999; 270:H121–H126.
185. Ekhardt KU, Kurtz A, Bauer C. Triggering of erythropoietin production by hypoxia is inhibited by respiratory and metabolic acidosis. Am J Physiol 1990; 258:R678–R683.
186. Boning D, Maassen N, Jochum F, et al. After-effects of a high altitude expedition on blood. Int J Sports Med 1997; 18:179–185.
187. Milledge JS, Cotes PM. Serum erythropoietin in humans at altitude and its relation to plasma renin. J Appl Physiol 1985; 59:360–364.
188. Adamson JW, Vapnek D. Recombinant erythropoeitin to improve athletic performance. N Engl J Med 1991; 324:698–699.
189. Berglund B, Ekblom B. Effect of recombinant human erythropoietin treatment on blood pressure and some haematological parameters in healthy men. J Intern Med 1991; 229:125–130.
190. Cowart VS. A dangerous new form of blood doping. Physician and Sportsmedicine 1989;17:115–118.
191. Jaussaud P, Audran M, Gareau RL, et al. Kinetics and haematological effects of erythropoietin in horses. Vet Res 1994; 25:1–7.
192. Souillard A, Audran M, Bressolle F, et al. Pharmacokinetics and haematological parameters of recombinant human erythropoietin after subcutaneous administrations in horses. Biopharm Drug Disposition 1996; 17:805–815.
193. Piercy RJ, Swardson CJ, Hinchcliff KW. Erythroid hypoplasia and anemia following administration of recombinant human erythropoietin to two horses. J Am Vet Med Assoc 1998; 212:244–247.
194. McKeever KH, McNally BA, Kirby KM, et al. Effect of erythropoietin on plasma and red cell volume, VO_{2MAX}, and hemodynamics in exercising horses. Med Sci Sports Exerc 1993; 25:S25.
195. Freund BJ, Wade CE, Claybaugh JR. Effects of exercise on atrial natriuretic factor: release mechanisms and implications for fluid homeostasis. Sports Med 1988; 6:364–376.

196. Richter R, Magert H, Mifune H, et al. Equine cardiodilatin/atrial natriuretic peptide. Primary structure and immunohistochemical localization in auricular cardiocytes. Acta Anat (Basel) 1998; 162:185–193.
197. McKeever KH, Hinchcliff, KW, Schmall, LM, et al. Atrial natriuretic peptide during exercise in horses. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3., Davis, CA: ICEEP Press 1991; 368–373.
198. McKeever KH, Malinowski K. Endocrine response to exercise in young and old horses. Equine Vet J 1999; 30(Suppl): 561–566.
199. Nyman S, Kokkonen UM, Dahlborn K. Changes in plasma atrial natriuretic peptide concentration in exercising horses in relation to hydration status and exercise intensity. Am J Vet Res 1998; 59:489–494.
200. Kokkonen UM, Hackzell M, Rasanen LA. Plasma atrial natriuretic peptide in standardbred and Finnhorse trotters during and after exercise. Acta Physiol Scand 1995; 154:51–58.
201. McKeever KH, Hinchcliff KW, Cooley JL, et al. Arterial-venous difference in atrial natriuretic peptide concentration during exercise in horses. Am J Vet Res 1992; 53:2174–2177.
202. Kokkonen UM, Hyyppa S, Poso AR. Plasma atrial natriuretic peptide during and after repeated exercise under heat exposure. Equine Vet J 1999; 30(Suppl): 184–189.
203. Maeda S, Miyauchi T, Waku T, et al. Plasma endothelin–1 level in athletes after exercise in a hot environment: exercise-induced dehydration contributes to increases in plasma endothelin–1. Life Sci 1996; 58:1259–1268.
204. McKeever KH, Antas LA, Kearns CF. Endothelin response during exercise in horses. Vet J 2002; 164:41–49.
205. Rossi NF. Effect of endothelin-3 on vasopressin release in vivo and water excretion in vivo in Long-Evans rats. J Physiol 1993; 461:501–511.
206. Rubanyi GM, Shepherd JT. Hypothetical role of endothelin in the control of the cardiovascular system. In: Rubanyi GM, ed. Endothelin. New York: Oxford University Press; 1992; 258–271.
207. Ahlborg G, Weitzberg E, Lundberg J. Metabolic and vascular effects of circulating endothelin-1 during moderately heavy prolonged exercise. J Appl Physiol 1995; 78:2294–2300.
208. Allevard A, Gauquelin G, Gaharib C. Endothelin and atrial natriuretic peptide after exercise performed until exhaustion in the rat. Life Sci 1991; 49:1803–1808.
209. Chou SY, Dahhan A, Porush JG. Renal actions of endothelin: interaction with prostacyclin. Am J Physiol 1990; 259:F645–F652.
210. Mann J, Farrukh IS, Michael JR. Mechanisms by which endothelin 1 induces pulmonary vasoconstriction in the rabbit. J Appl Physiol 1991; 71:410–416.
211. Miyauchi T, Yanagisawa M, Iida K, et al. Age- and sex-related variation of plasma endothelin-1 concentration in normal and hypertensive subjects. Am Heart J 1992; 123:1092–1093.
212. Ota K, Kimura T, Shoji M, et al. Interaction of ANP with endothelin on cardiovascular renal, and endocrine function. Am J Physiol 1992; 25:E135–E141.
213. Predel HG, Meyer-Lehnert H, Backer A, et al. Plasma concentrations of endothelin in patients with abnormal vascular reactivity: effects of ergometric exercise and acute saline loading. Life Sci 1990; 47:1837–1843.
214. Itoh S, van den Buuse M. Sensitization of baroreceptor reflex by central endothelin in conscious rats. Am J Physiol 1991; 260:H1106–H1112.
215. Raffestin B, Adnot S, Eddahibi S, et al. Pulmonary vascular response to endothelin in rats. J Appl Physiol 1991; 70:567–574.
216. Letizia C, Barilla F, d'Ambrosio C, et al. Dynamic exercise induces elevation of plasma levels of endothelin-1 in patients with coronary artery disease. Angiology 1995; 46:819–826.
217. Richter EA, Emmeluth C, Bie P, et al. Biphasic response of plasma endothelin-1 concentrations to exhausting submaximal exercise in man. J Clin Physiol 1994; 14:379–384.
218. Benamou AE, Marlin DJ, Lekeux P. Equine pulmonary and systemic haemodynamic responses to endothelin-1 and a selective ET(A) receptor antagonist. Equine Vet J 2001; 33:337–344.
219. Benamou AE, Art T, Marlin DJ, et al. Effect of exercise on concentrations of immunoreactive endothelin in bronchoalveolar lavage fluid of normal horses and horses with chronic obstructive pulmonary disease. Equine Vet J 1999; 30(Suppl):92–95.
220. Benamou AE, Art T, Marlin DJ, et al. Variations in systemic and pulmonary endothelin-1 in horses with recurrent airway obstruction (heaves). Pulmonary Pharmacol Ther 1998; 11:231–235
221. Benamou AE, Marlin DJ, Lekeux P. Endothelin in the equine hypoxic pulmonary vasoconstrictive response to acute hypoxia. Equine Vet J 2001; 33:345–353.
222. Filep JG, Battistini B, Sirois P. Endothelin induces thromboxane release and contraction of isolated guinea-pig airways. Life Sci 1990; 47:1845–1850.
223. Manohar M, Hutchens E, Coney E. Pulmonary haemodynamics in the exercising horse and their relationship to exercise-induced pulmonary haemorrhage. Br Vet J 1993; 149:419–428.
224. Pascoe JR. Exercise-induced pulmonary hemorrhage: a unifying concept. Proc Am Assoc Equine Prac 1996; 42:220–226.
225. McKeever KH, Schurg WA, Convertino VA. Exercise training-induced hypervolemia in greyhounds: role of water intake and renal mechanisms. Am J Physiol 1985; 248:R422–R425.
226. Rose RJ, Hodgson DR, Sampson D, et al. Changes in plasma biochemistry in horses competing in a 160 km endurance ride. Aust Vet J 1983; 60:101–105.
227. Rose RJ, Sampson D. Changes in certain metabolic parameters in horses associated with food deprivation and endurance exercise. Res Vet Sci 1982; 32:198–202.

CHAPTER 36

Nutritional management of the equine athlete

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The owners, trainers and riders of horses engaged in competitive athletic events are motivated to apply management strategies that provide a performance advantage during competition. Such strategies may include novel nutritional interventions administered before or during an event. Although there may be merit in some of these approaches, more realistically nutrition has a larger impact on performance by supporting consistent conditioning and thereby promoting the physiologic and biochemical adaptations that will ultimately result in improved athletic performance. For any athletic horse, the primary goals of nutritional management should include:

- provision of substrates for maintenance of bodyweight and replenishment of energy reserves in working muscle and other tissues
- promotion of tissue adaptation, growth and repair
- promotion of general health and well-being
- application of competition feeding strategies appropriate to the athletic task.

Although these same general principles apply to all equestrian sports, actual feeding strategies may vary widely because of the different demands of training and competition. For example, whereas the consumption of a high-fiber (roughage) diet may be of benefit to an endurance horse via promotion of a large fluid reservoir in the hindgut, this strategy is not desirable in a race horse because excess gut fill may be energetically disadvantageous during high-intensity exercise. Similarly, the rationale for nutritional intervention immediately before and/or during competition will differ between disciplines. For an endurance athlete, feed consumption before and during a race may enhance energy supply and delay the onset of fatigue. On the other hand, for a race horse the consumption of a meal within 1–2 hours of the race start is less likely to substantially impact energy use and athletic performance.

This chapter provides an overview of the nutritional needs of athletic horses with suggested feeding strategies to meet these requirements. The dietary management of horses with chronic exertional rhabdomyolysis and the putative role of ergogenic feeding strategies and nutritional supplements are also discussed.

Nutrient goals

The overall goal of diet formulation is to develop a ration that delivers optimal amounts of all essential nutrients. The 1989 edition of the National Research Council's (NRC) *Nutrient requirements of horses* provides nutritional recommendations for all classes of horses, including those undertaking regular physical activity.[1] However, it is important to realize that these recommendations are considered to be minimal rather than optimal requirements. It should also be noted that there has been considerable research in the area of athletic horse nutrition since the last NRC publication, most notably in the area of dietary energy sources. Thus, while the 1989 NRC recommendations still provide a framework for ration formulation and evaluation, many nutritionists have developed their own set of nutrient standards that, based on more recent scientific literature and practical experience, provide optimal ranges of nutrients relative to the horse's physiologic state.

Energy

Undoubtedly, the most profound nutritional effect of regular physical activity is an increase in dietary energy needs relative to non-working horses. For bodyweight to be maintained, athletic horses must consume enough energy to cover

'maintenance' energy costs together with the energy costs associated with physical activity and the building and repair of muscle tissue. There are two primary considerations with respect to dietary energy in athletic horses: provision of sufficient energy to maintain bodyweight and condition; and the sources of energy (fiber and non-fiber carbohydrates, fats and oils, proteins) in the diet. The latter impacts body substrate stores, the metabolic response to exercise and, potentially, athletic performance. These issues are discussed later in the chapter (see Feeds for attainment of nutritional goals).

Estimating energy requirements

In most parts of the world, both energy requirements and the energy content of feeds are evaluated as *digestible energy* (DE). In North America, the horse industry uses the kilocalorie (kcal) as the standard unit of energy, whereas use of the kilojoule (kJ) predominates in Europe and much of the rest of the world (4.184 kJ = 1 kcal). Digestible energy is expressed as kcal (or kJ) per gram of substance or Mcal (or MJ) per kg.

Several definitions of the energy requirements for maintenance have been used. These include: the daily food intake that maintains constant bodyweight and composition of a mature horse with zero energy retention at a defined level of activity; and the amount of DE required for zero bodyweight change plus normal activity of non-working horses. The work of Pagan & Hintz[2] indicated that maintenance energy requirements varied linearly with bodyweight and not with metabolic body size ($W^{0.75}$). Therefore, these researchers developed the following equation for prediction of maintenance energy requirements of horses weighing 100–600 kg:

$$\text{DE (Mcal/day)} = 1.4 + 0.03\ W$$

where W is the weight (kg) of the horse. This equation overestimates the energy needs of large horses (< 600 kg) and ponies and miniature horses, and this author uses $W^{0.75}$ when estimating the maintenance energy needs of these animals. Alternatively, the NRC recommends that the following equation be used for estimating the maintenance requirement of horses with mature weights of more than 600 kg:

$$\text{DE (Mcal/day)} = 1.82 + 0.0383\ W - 0.000015\ W^2$$

Several factors can influence maintenance energy requirements, including the age, breed, gender and temperament of the horse, the level of activity, ambient conditions, and diet composition. Logically, therefore, 'book values' for maintenance energy needs based on these and other equations should only be considered a guide.

Similarly, there are no practical means for precise determination of the additional energy requirements of horses in exercise training. The intensity and duration of exercise, terrain, the weight of the rider and tack, the ability of the rider, the level of training of the horse, environmental conditions and diet composition will all influence overall energy needs. Pagan & Hintz[3] developed a prediction equation for the estimation of the DE required above maintenance using oxygen consumption ($\dot{V}O_2$) data collected from horses running on a level track:

$$\text{DE (kcal per kilogram of horse, rider and tack)} = \{[e^{(3.02 + 0.0065\ Y)} - 13.92] \times 0.06\}/0.57$$

where Y is the speed (meters per minute) and 0.57 accounts for the efficiency of utilization of DE. Although this equation may be useful for horses exercising on level ground and an even surface, the wider applicability of this approach is questionable given the need to measure running speed and the variation in terrain and footing conditions in which horses train and compete. Use of the equation developed by Pagan & Hintz[3] underestimated by 30–35% the daily energy requirement of horses exercised on a treadmill for 60–75 min at 50% of maximum aerobic capacity ($\dot{V}O_{2max}$).[4,5] In the future, the availability of systems for valid field measurements of oxygen consumption in horses undertaking different exercise tasks under a variety of conditions may facilitate development of more precise prediction equations. However, it is unlikely that such equations will account for all of the factors influencing energy requirements. As such, ongoing clinical assessment of bodyweight and condition will remain the most practical means for assessment of energy balance in horses.

In 1989 the NRC recommended that daily energy intake be increased 25%, 50% and 100% above maintenance requirements for horses performing, respectively, light, moderate and intense work. These recommendations were based on data from experimental studies, feeding surveys and practical experience. Light work might include equitation and other forms of pleasure riding, while horses engaged in racing, hunting, three-day events and endurance racing would fall into the intense category (Table 36.1). Although these guidelines are clearly very general in nature, the results of field studies in working horses have provided evidence that the 1989 NRC recommendations are a useful guide for estimation of energy needs in horses in moderate and intense work.[6,7] For Standardbreds (mean bodyweight [bwt] of approximately 450 kg) and Thoroughbreds (mean bwt 500 kg) in race training, the NRC recommendations are 28.8 Mcal/day and 33 Mcal/day.[1] Consistent with these recommendations, Gallagher and co-workers estimated DE intakes of 28–31 Mcal/day for Standardbreds[8] and 31–36 Mcal/day for Thoroughbreds[6] in North American race stables. Similar DE intakes were reported for Australian

Table 36.1 Estimated digestible energy (DE) requirements for a 500 kg horse at four different levels of activity

Activity*	Examples	DE requirement (Mcal/day)+
Maintenance	Horse at pasture	16–17
Light	Pleasure riding, equitation	20–21
Moderate	Reining, showjumper or hunter	25–26
Intense	Race horse, three-day event, endurance	32–34

* According to the 1989 NRC classification of activity level
+ Mcal = megacalorie

Standardbred and Thoroughbred race horses.[7] Taylor et al[9] reported that 420 kg Arabian horses undergoing treadmill exercise 3–4 days per week maintained bodyweight when fed 19–22 Mcal DE/day, equivalent to the NRC recommendation for horses in moderate work.

The effects of body condition and composition on athletic performance

In humans, there is a strong inverse relationship between body fat content and both sprint and endurance running performance. Although data from horses are limited, there also is evidence that body composition is an important determinant of athletic performance. Kearns et al[10] used B-mode ultrasound of the rump area to calculate percentage of body fat and fat free mass (FFM) in 14 racing Standardbreds. Males had less fat mass (7.4% bwt) when compared to the females (9.9% fat). Interestingly, percentage fat mass was negatively correlated to race performance in the males but not the female horses of the study, a finding consistent with data in humans. However, for both genders, FFM was negatively correlated with race time (i.e. the higher the FFM, the shorter the race time). The authors concluded that while a low fat mass is beneficial to race performance, it is more important to possess a larger FFM.[10] A larger FFM is indicative of a greater muscle mass and, therefore, greater potential force development. Using similar methodology, this research group has demonstrated that maximum aerobic capacity ($\dot{V}O_{2max}$) is also significantly related to FFM, independent of body mass.[11]

Lawrence and colleagues[12] also used rump ultrasound to assess the relationship between body composition and endurance race performance. The average body fat content of the horses of this study (7.8%) was similar to that reported by Kearns et al[10] for Standardbred race horses. Top finishers in a 150-mile race had a lower fat mass (by approximately 20 kg) when compared to horses that could not complete the event. Taken together, the results of these studies provide evidence that excess body fat is detrimental to sprint and endurance running performance.

On a more practical level, condition scoring is a useful clinical tool for the assessment of body fatness. Although several scoring systems have been used, the version developed by Henneke and colleagues at the Texas A & M University is the most widely used (Table 36.2).[13] There are a few studies that have reported body condition score (BCS) in horses involved in different activities. In the aforementioned study by Lawrence and co-workers,[12] the mean BCS of horses in an endurance race was 4.67 (using the 1–9 scale). Gallagher et al reported that Standardbred and Thoroughbred horses in training had, respectively, mean BCS of 5.7 and 5.0.[6,8]

Recent studies of endurance horses competing in the 100-mile Tevis Cup have provided evidence of a relationship between condition score and race performance.[14] The mean BCS of horses that successfully completed the rides was 4.5, whereas horses that were eliminated for metabolic failure (e.g. colic, heat exhaustion, synchronous diaphragmatic flutter or tying up) had a mean condition score of 2.9. Horses that were eliminated for non-metabolic reasons such as lameness and overtime had a mean condition score of 4.3. The researchers were careful to point out that their results may not apply to endurance competition as a whole, given the difficult nature of the Tevis Cup course. Nonetheless, the implication from these studies is that there is an optimal level of 'fatness' for horses competing in endurance events and that training and feeding programs need to be adjusted accordingly. Endurance performance of horses with a low BCS (e.g. < 3) may be limited by the supply of energy from fat reserves. In addition, a loss of lean tissue (muscle mass) may

Table 36.2 A body condition scoring system for horses (adapted from reference[13])

Condition	Score	Description
Poor	1	Severe emaciation; bone structure is prominent, including cervical and lumbar vertebrae
Very thin	2	Emaciation; bone structure is still prominent but cervical vertebrae barely visible
Thin	3	Neck thin; junction of neck, withers and shoulder accentuated; pelvic structure remains prominent; transverse processes of lumbar vertebrae cannot be palpated
Moderately thin	4	Ribs prominent; spine still apparent but not individual vertebrae; neck, withers and shoulder normal
Moderate	5	Ribs are not visible but easily palpated; neck blends smoothly into withers and shoulder; flat back
Moderately fleshy	6	Neck, shoulder and withers appear more filled and rounded; back area may have slight depression (crease) along spine; tailhead and ribs with some flesh coverage
Fleshy	7	Fat deposited over withers and neck; crease along spine more visible; flesh over tailhead and ribs is prominent and soft
Fat	8	Thickened neck; well-defined crease along spine; ribs difficult to palpate; fat accumulation over rump
Extremely fat	9	Bulging fat in neck, withers and shoulder; prominent crease down back; patchy fat over ribs

contribute to diminished performance in horses with poor body condition.

Although further studies are needed in horses of different types, as a general recommendation the BCS of most athletic horses should fall between 4 and 6. The NRC recommendations should be used as an initial guide when making recommendations for DE intake in the face of changing work demands. Subsequently, however, frequent (e.g. weekly) assessment of bodyweight and/or BCS is necessary to determine the appropriateness of the feeding program; upward or downward adjustments in DE intake are often needed for maintenance of constant bodyweight. Trainers and/or owners should target a desired bodyweight or BCS, monitor these parameters on a weekly basis and adjust energy intake accordingly.

Protein

The dietary protein requirement of the horse is a function of the amino acid needs, the amino acid composition of the dietary protein and the digestibility of the protein. Horses have negligible ability to utilize non-protein nitrogen such that nitrogen needs must be provided in the form of protein or amino acids. Furthermore, it is thought that amino acids are not absorbed intact from the large intestine. Therefore, the horse's essential amino acid requirements must be met from protein sources that are digested in the small intestine. Whether, and to what extent, regular exercise increases the protein requirement is a controversial issue in both horse and human nutrition. Theoretically, higher turnover of muscle proteins in association with the rigors of regular exercise (oxidation of amino acids during exercise, protein synthesis to support muscle hypertrophy and tissue repair after exercise) and sweat nitrogen losses should increase protein requirements. Consistent with this hypothesis, studies in humans have demonstrated negative nitrogen balance at the onset of endurance training programs. However, within 7–10 days of the start of training the rate of leucine oxidation is attenuated and nitrogen balance approaches equilibrium, indicating adaptation in protein metabolism.[15] For the resistance-trained athlete, there also appears to be a homeostatic adaptation to the stress of exercise such that well-trained athletes require only marginally more protein than sedentary persons. For elite human endurance and strength athletes, a dietary protein intake that represents 14–15% of total energy intake (1.6–1.7 g protein/kg per day) has been recommended.[15] Protein intake above these levels has not been shown to be beneficial to human athletic performance.

Protein requirements of horses have been expressed as a function of bodyweight or in relation to DE intake. For maintenance, 1.3 g crude protein (CP) per kg bodyweight is recommended or approximately 40 g CP/Mcal DE daily. The NRC recommended that working horses receive the same dietary protein/calorie ratio, i.e. a race horse in intense training should consume twice the protein when compared to the non-trained state (2.5–2.6 g CP/kg/day or approximately 12% of dry matter intake).[1] This approach is practical with respect to ration formulation and the provision of dietary protein. However, some nutritionists have questioned the need for such high levels of dietary protein.[16,17] Specifically, it has been suggested that CP intakes greater than 2 g/kg bwt/day are detrimental to some forms of exercise because of the effects of excess dietary protein on heat production, acid–base balance, water requirements and, potentially, respiratory health. Oxidation of the phosphorus and sulfur in protein adds to the acid load on the body. In this context, Graham-Thiers and colleagues[16] evaluated the effects of a restricted protein diet (7.5% CP with added lysine and threonine) on acid–base balance in horses in moderate work. When compared to a 14.5% CP diet, protein restriction resulted in a slight increase in resting blood pH and mitigation of exercise-associated acidemia during repeated sprints. These effects may provide a performance advantage during exercise, although the actual effect of dietary protein level on exercise performance has not been determined.

There is evidence that dietary protein level alters urea metabolism in horses. In one study, horses consuming 1741 g CP per day (>3 g/kg bwt) excreted more urea in sweat and had higher plasma urea when compared to horses consuming 836 g CP per day[18] and it has been estimated that a change in dietary CP from 10% to 15% would increase water requirement by approximately 5% because of an obligate increase in urine production for clearance of endogenous urea loads.[17,19] Moreover, the higher urinary urea load could adversely affect the respiratory health of confined horses because urea is converted to ammonia, a known respiratory irritant.

Further research is needed regarding the protein requirements of athletic horses. Currently, a 10–12% CP diet is recommended for mature athletic horses. However, the recent studies by Graham-Thiers and co-workers[16] suggest that the 1989 NRC recommendations for dietary CP intake are not necessary for normal health and athletic function. Indeed, there may be advantages to a lower protein diet (8–10% CP), providing good-quality protein is fed.

Minerals and vitamins

Based on their daily requirements, minerals are usually classified as macrominerals (e.g. calcium, phosphorus, sodium, potassium and chloride) or trace elements (e.g. selenium, iron, zinc, copper). These nutrients are important in a large array of body functions. Several minerals and trace elements, such as magnesium, iron, zinc and copper, act as enzyme activators in glycolysis and oxidative phosphorylation. Minerals (electrolytes) are also critical to nerve and muscle function.

The classification of vitamins is based on their relative solubility: fat-soluble vitamins (A, D, E and K) are more soluble in organic solvents, whereas the B vitamins and vitamin C are more soluble in water. Most vitamins participate in processes related to muscle contraction and energy expenditure. Vitamins of the B complex group (e.g. thiamine, riboflavin, vitamin B_6, niacin, biotin and pantothenic acid) act as co-

factors for enzymes regulating glycolysis, the citric acid cycle, oxidative phosphorylation, β-oxidation of fatty acids and amino acid catabolism. Folic acid and vitamin B_{12} are needed for heme synthesis. The antioxidant vitamins (mainly vitamins C and E) participate in a buffer system against free radicals.

Many trainers, owners and veterinarians perceive that optimal mineral and vitamin nutrition is critical to successful athletic performance. One impression is that the rigors of training and competition promote excessive losses of these nutrients because of increased excretion or catabolism and, as a result, fortification of the diet is required to cover these losses. Moreover, there is often the opinion that increased consumption of various minerals and vitamins will improve physical performance and health. These perceptions, together with the aggressive marketing of supplements containing minerals and vitamins, appear to provide impetus for the extensive use of nutritional supplements in horses.

Macrominerals

Recommendations for macromineral (and trace mineral) intake by mature athletic horses are presented in Table 36.3. The requirements for dietary calcium (Ca) and phosphorus (P) are higher in athletic horses in comparison to their sedentary counterparts. Diets that contain inadequate levels of these nutrients or an imbalanced Ca:P ratio (i.e. Ca:P ratio < 1; high dietary P) may compromise bone integrity and predispose to injury during training and competition. Additional Ca and P are required for deposition in bone during modeling and remodeling, processes that are upregulated by the loading imposed on the bones of the limbs during exercise. It is also possible that calcium losses in sweat increase dietary requirements. However, assuming a calcium concentration in sweat of 100–120 mg per liter and daily sweat losses of 10 liters, these losses may be no more than 1–2 g per day.

Table 36.3 Estimated daily mineral needs of a 500 kg* horse at maintenance and in moderate-to-intense exercise training (adapted from references[1,40])

Mineral	Maintenance	Exercise
Sodium (g)	10	30–50¶
Potassium (g)	25	40–75¶
Chloride (g)	15	50–150¶
Calcium (g)	20	35–40
Phosphorus (g)	15	25–27
Magnesium (g)	7.5–9	10–15
Iron (mg)	320	460
Copper (mg)	80	115
Manganese (mg)	320	460
Zinc (mg)	400	575
Selenium (mg)	0.8–1.0	2.3–3.0
Iodine (mg)	0.8	1.15
Cobalt (mg)	0.8	1.15

* Assumes a dry matter intake of approximately 8 kg/day for maintenance and 11.5 kg/day for work.

¶ The sodium, potassium and chloride requirements of working horses are, in part, dependent on the extent of sweat fluid losses. The upper end of these values is recommended for horses in intense training in warm climates and during the summer months.

With respect to Ca and P requirements, the 1989 guidelines furnished by the NRC[1] assumed that if the nutrient: calorie ratio of the ration was maintained, the increase in feed intake needed to meet DE requirements for work would also supply the calcium required to replace sweat losses and support bone formation. However, the calcium needs of young horses in training (< 2 years) may be higher in comparison to mature athletic horses because of greater Ca turnover in bone.[20,21] Nolan and colleagues[21] reported that the training-associated increase in bone density in young Quarter Horses was enhanced by the consumption of diets that provided 150–170% of the NRC (1989) recommendations for Ca. In line with these findings, it has recently been suggested that diets for young horses in training should contain at least 0.4–0.45% Ca (versus the NRC recommendation of 0.34% Ca).[20] Higher levels of dietary calcium may also be beneficial in older horses. In one study, the increase in the mineral content of the metacarpus, assessed by radiographic photometry, in response to 12 weeks of treadmill training was greater in horses receiving a diet containing 0.7% Ca when compared to the current recommendation of 0.34%.[22]

Close attention should be paid to Ca:P balance in horse rations; the Ca:P ratio should be at least 1:1. It is not uncommon for athletic horses to be fed a diet with an improper Ca:P balance. This is particularly true for horses fed high cereal grain (not fortified with minerals), low roughage diets because most cereals are low in Ca and high in P. Although most grass hays contain moderate Ca content, the quantities fed may be insufficient to balance the low Ca content of the grain, resulting in an inverted Ca:P ratio (< 1). This type of ration can result in bone demineralization and pathology.[23] This problem can be averted by provision of a supplemental source of Ca or by including some legume hay in the diet. On the other hand, the Ca:P ratio of diets containing large amounts of legume hay can be greater than 3–5:1. However, such diets appear to be well tolerated by mature horses.

The NRC guidelines for Ca and P nutrition are based on the assumption that the efficiency of absorption for Ca and P is 50% and 35% respectively. However, several factors can influence the efficiency of absorption of these nutrients, including the Ca:P ratio, the form of Ca or P, the level of intake and the presence of inhibitors such as phytate and oxalate. Grains and cereal hays are high in phytates, while some tropical grasses are high in oxalates such that the efficiency of digestion and absorption of Ca and P in these feedstuffs is low. On the other hand, the efficiency of absorption of inorganic source Ca and P (e.g. calcium carbonate, dicalcium phosphate) may approach 70%. Due to the high variability in the availability of Ca and P from organic sources, most commercial horse feeds use inorganic sources of Ca and P to ensure adequate dietary levels of these nutrients. Similarly, inorganic forms of Ca and P should be added to 'homemade' rations for athletic horses (Table 36.4).

Scant data are available regarding the magnesium (Mg) requirements of athletic horses. In one study of endurance

Table 36.4 The composition of selected calcium and phosphorus supplements

Supplement	Calcium (%)	Phosphorus (%)	Magnesium (%)	Sulfur (%)
Calcium carbonate	39	–	0.05	–
Limestone	34	0.02	2.1	0.04
Oyster shells, ground	38	–	0.3	–
Dicalcium phosphate	22	19	–	–
Monosodium phosphate	–	22	–	–
Magnesium oxide	0–3	–	51–59	–

horses, serum magnesium concentrations were unchanged after an 80 km race.[24] Muscle (intracellular) magnesium content was unchanged in horses after intense trotting over 2600 m.[25] However, athletic horses may have slightly increased requirements for dietary magnesium to cover sweat losses (equine sweat contains 100–120 mg magnesium per liter). The NRC[1] recommends 0.1% dietary magnesium for maintenance or approximately 7.5–9 g/day based on a daily DM intake of 7.5–9.0 kg. As the magnesium content of feeds commonly consumed by horses is 0.1–0.3%, typical daily intake by athletic horses will be much greater than 7.5–9 g/day and should cover daily losses associated with sweating.

The dietary requirements for sodium, potassium and chloride are increased by physical activity because of the substantial sweat loss of these ions. The extent of these losses will depend on the intensity and duration of exercise, the training and heat acclimation status of the horse and the ambient conditions. A more detailed discussion on the effects of exercise on fluid and ion balance, strategies for electrolyte replacement and daily electrolyte requirements can be found elsewhere in this book.

Trace minerals

Few data exist regarding the effects of regular physical activity in horses on trace mineral requirements. With the exception of selenium, clinical signs consistent with a trace mineral deficiency are rare in horses fed typical diets. Nonetheless, several of the trace minerals are routinely supplemented to working horses. Most notably, iron, often in combination with copper, zinc and some of the vitamins, is widely given to athletic horses because of the perception that the provision of these nutrients will enhance erythropoiesis and oxygen-carrying capacity. In reality, there is no evidence that this practice results in altered red cell number or hemoglobin concentration, and iron deficiency anemia is a rare diagnosis in horses. Daily Fe losses of horses in training have not been reported. However, sweat contains a small amount of iron and other trace minerals such as zinc. Therefore, there is some rationale for increased provision of dietary Fe in working horses. Practically, however, common horse feedstuffs provide iron well in excess of requirements. The NRC maintenance requirement for iron is 40 mg/kg of diet (DM basis) or approximately 0.65 mg/kg bwt/day (320 mg/day for a 500 kg horse).[1] Forages usually contain 100 mg Fe per kg DM and most grains more than 50 mg per kg DM. Thus, a diet of 6 kg of hay and 5 kg of grain concentrate for a 500 kg working horse would provide approximately 850 mg Fe.

Selenium is a functional component of the intracellular enzyme glutathione peroxidase and, in concert with vitamin E, is important in the defense of cells against oxidant stress. Selenium deficiency is associated with development of nutritional myodegeneration. Selenium is also essential for the development of acquired immunity. Whether regular physical activity increases the Se requirements of horses is not known. However, single bouts of exercise[26] have been reported to increase erythrocyte glutathione peroxidase activity. This increase in enzyme activity may be a reflection of an increase in demand on this antioxidant system and, perhaps, an indication that working horses have higher Se needs relative to idle horses. The 1989 NRC[1] concluded that the Se requirement for mature idle horses was 0.1 ppm on a dry matter basis (0.1 mg/kg diet). Yet, many nutritionists now favor higher dietary Se for idle and working horses, in the range of 0.2–0.3 ppm, to account for variation in the efficiency of selenium digestibility and utilization and increased work demands (Table 36.3).

Vitamins

There is very limited information regarding the vitamin requirements of horses and even fewer data concerning the effects of habitual exercise on these requirements. Microbes in the large intestine synthesize the B vitamins and absorption from the large intestine has been demonstrated for several of the B vitamins.[27] In addition, an ample supply of the B-complex vitamins, with the exception of vitamin B_{12}, is provided by good-quality forage. Therefore, a combination of dietary intake and microbial synthesis in the hindgut should meet the B vitamin requirements of horses.

In recent years, there has been considerable interest regarding the role of vitamins C and E (and other antioxidant nutrients such as β-carotene and lipoic acid) in the mitigation of oxidative stress and lipid peroxidation in horses during exertion. Vitamins E (α-tocopherol) and C, along with glutathione, are important non-enzymatic antioxidants. Vitamin E is a lipid-soluble scavenger of reactive oxygen species (ROS) that is located in cell membranes, while vitamin C is located in the aqueous phase of cells where it scavenges free radicals and recycles vitamin E to its active form.[28]

Exercise causes a dramatic increase in oxidative metabolism and, therefore, the production of ROS. During prolonged

and/or strenuous exercise, the extent of ROS production may overwhelm antioxidant systems such that the susceptibility of cells and tissues to damage by ROS (lipid peroxidation) is enhanced, particularly in animals with inadequate endogenous stores of the antioxidant nutrients. Several research groups have investigated the relationship between exercise and plasma markers of oxidative stress in horses. For example, Hargreaves et al[26] reported an association between muscle cell 'leakage' (exercise-associated increases in the activities of creatine kinase [CK] and aspartate aminotransferase [AST]) and indices of antioxidant status in horses during 80 and 160 km endurance races. Specifically, plasma vitamin C and erythrocyte glutathione concentrations decreased during the races, while erythrocyte glutathione peroxidase was increased. On the other hand, Marlin and colleagues[29] reported no change in plasma vitamin C after a 140 km race, but significant decreases after 16 h of recovery. In both studies, no changes in plasma α-tocopherol concentrations were detected. However, Marlin et al[29] demonstrated a negative correlation between pre-race plasma α-tocopherol and total red cell glutathione and end competition total barbituric acid reactive substances (TBARS), and suggested that horses with low antioxidant reserves may be more prone to lipid peroxidation from ROS during endurance exercise.

The NRC[1] recommended a dietary vitamin E concentration of 80–100 IU/kg DM for all classes of horses. Whether or not higher amounts of dietary vitamin E are beneficial in athletic horses is unresolved. Siciliano et al[30] demonstrated a decrease in plasma and muscle α-tocopherol concentrations in working horses fed a diet supplemented with 80 IU α-tocopherol per kg DM, whereas plasma concentrations were maintained when horses were supplemented with 300 IU/kg DM. Similarly, plasma concentrations of α-tocopherol were significantly higher in hard-working polo ponies fed a diet providing 300% of the current NRC recommendation for vitamin E (240 IU/kg versus 80 IU/kg diet).[31] In both studies, however, there was no association between dietary vitamin E and the serum activities of CK and AST in response to exercise. Further research is needed to better define the vitamin E requirements for different classes of athletic horse. In the meanwhile, it is recommended that athletic horses be fed a diet providing at least 100 IU vitamin E per kg DM. Intensely working horses (e.g. race and endurance horses) may benefit from higher levels of vitamin E (200–250 IU/kg diet). Most equine feedstuffs contain less than 50 IU/kg DM. Therefore, supplemental vitamin E must be added to horse rations to meet requirements.

As horses have L-gluconolactone oxidase, the enzyme required for the synthesis of vitamin C (ascorbic acid) from glucose, there is no dietary requirement for this nutrient. However, the demand for ascorbic acid may be increased by regular exercise because it is thought to spare tissue vitamin E by reducing the tocopheroxyl radical and restoring the radical scavenging activity of vitamin E.[32] Although there have been several studies on the effects of ascorbic acid metabolism and supplementation in athletic horses,[29,31,33–35] no consensus has emerged regarding a dietary requirement for horses under performance stress. Dietary supplementation with ascorbic acid (5–10 g/day) does result in higher serum ascorbate concentrations relative to non-supplemented horses.[29,31] However, the effects of these higher ascorbate concentrations remain unclear. In two equine studies, there was no effect of ascorbic acid supplementation on exercise-induced increases in serum CK activity.[31,33] One concern with high-level ascorbic acid supplementation is the potential for suppression of endogenous synthesis.

Water

The NRC guidelines recommend 2–4 liters of water per kg of DM intake.[1] However, diet, ambient conditions and level of activity will modify these needs. Horses maintained on an all-forage diet will consume approximately 3.6 liters of water per kg of DM intake, whereas the water-to-feed ratio for horses fed a typical hay and grain diet is about 3:1.[1] Water intake by horses living in warm climates (> 25–30°C daytime temperature) may be increased by 15–30%, whereas heavy work in warm to hot ambient conditions may increase the need for water by as much as 200–300% due to large sweat fluid losses.

Feeds for attainment of nutritional goals

For horses in training, a combination of forage and energy concentrate is generally required to achieve nutritional goals. In some situations, a vitamin-mineral supplement is added to the ration. Several guiding nutritional principles should be used in the development of a feeding program for an athletic horse. In general, the main considerations in ration formulation are:

- provision of adequate fiber (roughage) to maintain normal gut and digestive function (and perhaps limit the development of behavioral disturbances)
- targeting an overall energy density that will allow energy requirements to be met at typical fed intakes
- supplying sufficient hydrolyzable carbohydrate to maintain muscle glycogen concentrations
- provision of the optimal amounts and balance of the other essential nutrients (i.e. protein, minerals, vitamins)
- the inclusion of only the highest quality feedstuffs.

The four main sources of energy in horse rations are:

1. fermentable carbohydrates (components of dietary fiber or roughage, including hemicellulose, that cannot be digested by mammalian enzymes but can be fermented by micro-organisms, primarily in the hindgut, i.e. cecum and large colon)
2. hydrolyzable carbohydrates (simple sugars and starch) that are digested by mammalian enzymes in the small intestine, yielding hexoses
3. oils and fats

4. protein (not primarily fed as an energy source because metabolism of amino acids to useable energy is inefficient).

Knowledge of the horse's digestive physiology and the impact of diet composition and meal size on the efficiency of digestive processes are important in the selection of an appropriate ration and feeding strategy. The horse evolved as a grazing animal and its gastrointestinal tract, with a well-developed cecum and large colon, is highly adapted to the utilization of fiber-rich feeds that are consumed on an almost continuous basis.[36] The hindgut (cecum and colon) comprises approximately 64% of the total (empty) volume of the gastrointestinal tract, whereas the stomach (7%) and small intestine (25%) have a relatively small capacity. Similar to other mammalian species, the small intestine is the major site of digestion of protein, fat and hydrolyzable carbohydrates. However, as further discussed below, the horse has a limited ability to digest and absorb hydrolyzable carbohydrates (particularly starch) in the small intestine. Large concentrate meals may overwhelm the digestive capacity of the small intestine and promote the flow of undigested hydrolyzable carbohydrate to the large intestine. This not only reduces the efficiency of feed utilization but also increases the risk for digestive disturbances associated with excessive and uncontrolled fermentation of the undigested hydrolyzable carbohydrate in the large intestine.

Roughage/dietary fiber

From the preceding discussion, it is clear that forage (roughage) should always be the foundation of an equine ration. Although a requirement for dietary fiber has not been established in horses, some long stem roughage is important for maintenance of normal hindgut function and thus for normal digestion. There also is evidence that diets low in long stem fiber favor development of certain stereotypies.[37–39] Therefore, adequate dietary roughage may be important for prevention of some undesirable behavioral traits, particularly in horses kept in confinement. Some trainers prefer to feed low-roughage diets because such rations may reduce the weight of ingesta in the intestinal tract ('dead weight'), thereby providing an energetic advantage during some forms of exercise. The possible benefits of this practice should be weighed against the increased risks of gastrointestinal dysfunction (e.g. colic, gastric ulcers) and behavioral abnormalities when horses are fed low-roughage diets.

Meyer has suggested that performance horses be fed at least 0.5 kg of roughage per 100 kg bwt (0.5% of bwt).[40] However, this author recommends *at least* 1.0 kg forage per 100 kg (i.e. 5.0 kg for a 500 kg horse). One survey of Australian race horses indicated that forage intake is often less than this minimum recommendation. In that study, mean daily forage intake was 3.3 kg and 4.1 kg for Thoroughbreds and Standardbreds, respectively.[7]

Pastures and different forms of conserved forages (i.e. hay, chaff, hay cubes, haylage) are the primary source of roughage in horse rations. Although several factors can affect the nutrient value of conserved forages, the most important is the stage of maturity at the time of harvest (Fig. 36.1). The energy content, digestibility and palatability of forage all decrease with increasing maturity. Therefore, forages harvested at an early stage of plant maturity should be fed to working horses to maximize nutritional value and intake of the offered quantities (Table 36.5). An exception to this recommendation is the feeding of a very high-quality alfalfa, which may not contain adequate fiber (specifically, acid detergent fiber [ADF]) for normal hindgut function. Figure 36.2 illustrates how the energy content of the forage affects the relative proportions of forage and energy concentrates required to meet the energy needs of an athletic horse.

The relative use of grass, legume or cereal (usually oaten) hays and the different forms of preserved forages made from these species often depends on availability and personal preference. Legume hays such as alfalfa usually have higher energy, protein and mineral (particularly calcium) content when compared to the grass species. These differences will influence the type and quantity of energy concentrate to be fed with hay. For example, as discussed above, the total diet should provide 10–12% crude protein. Therefore, when feeding alfalfa the protein content of the concentrate can be

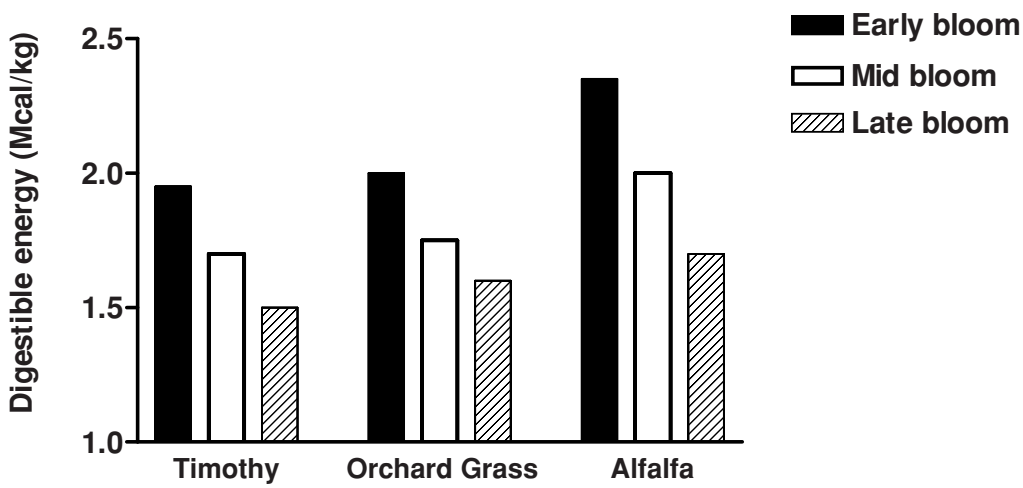

Fig. 36.1 The effects of maturity at the time of harvest on estimated digestible energy content of timothy, orchard grass and alfalfa hay.

lower than when grass hay is fed. In addition, a higher roughage-to-concentrate ratio is possible when high-quality (energy) forage is fed. However, even within a plant species the nutrient composition of preserved forage can vary greatly depending on growing conditions, plant maturity and harvesting methods. Thus, proximate analysis (including crude protein, neutral detergent fiber and macrominerals) should be performed when practical to best guide ration balancing and the selection of an appropriate energy concentrate.

Preserved forages should also be free of contaminants such as molds. Hay that is baled at high moisture content is likely to heat and become heavily contaminated with molds that can exacerbate chronic airway diseases such as recurrent airway obstruction and inflammatory airway disease. In areas with high rainfall during the growing and hay-making season (e.g. the UK), the feeding of ensiled hay or 'haylage' (50–60% DM) is sometimes practiced. Haylage is a suitable alternative to hay providing that it is stored correctly and fed in sufficient quantity to ensure adequate fiber intake. One concern with haylage is the potential for clostridial growth and production of botulinum toxin.[41] Haylage should be examined carefully for the presence of mold and other contaminants before feeding and sealed haylage bales should be fed within a few days of opening. Hay cubes and pellets, 'complete feeds', or the feeding of forage that has been thoroughly soaked in water can also aid in minimizing exposure to dusts and molds when managing chronic airway disease.

Daily feed intakes in mature horses (on an as-fed basis) range between 1.5% and 3.0% of bodyweight, although a more typical intake for a performance horse is between 1.8% and 2.2% (i.e. 9–11 kg for a 500 kg horse). Accordingly, the energy requirements of horses performing light athletic activities (e.g. pleasure riding 2–3 times per week) can, in most instances, be met by forage alone. Other essential nutrients may be provided in the form of a vitamin-mineral or vitamin-mineral-protein supplement. On the other hand, horses in moderate and intense training are unable to meet energy needs if forage is the only energy source. Therefore, energy concentrates must be fed to increase the caloric density of the diet and ensure that energy requirements are met within the confines of a realistic daily dry matter intake.

Energy concentrates

Cereal grains

Traditionally, cereal grains such as oats, corn and barley (alone or in combination) have been a source of energy in rations for athletic horses. Starch, a hydrolyzable carbohydrate, is the primary component of cereal grains. Oats are approximately 47–50% starch while the starch content of corn and barley is between 60% and 66% (Table 36.5). Digestion of starch in the small intestine yields glucose, the substrate for liver and muscle glycogen synthesis. As muscle glycogen is a primary fuel during exercise, the provision of some hydrolyzable carbohydrate (starch and/or sugar) in the diet of an athletic horse is important for replenishment of glycogen reserves. However, there is evidence that the horse has a limited capacity to digest and absorb starch (and perhaps other simple carbohydrates) from the small intestine. Low production and secretion of pancreatic amylase[42,43] and a limited capacity for mucosal monosaccharide transport[44] are factors that may contribute to this apparent constraint in small intestinal carbohydrate digestion. Regardless of the

Table 36.5 Nutrient composition of some feedstuffs used in horse rations

Feed	Dry matter %	DE (Mcal/kg DM)	CP %	Acid detergent fiber %	NSC %	Fat %	Ca %	P %
Alfalfa hay, early bloom	90	2.5	20	32	22	–	1.4	0.3
Alfalfa hay, full bloom	91	2.2	17	39	21	–	1.2	0.25
Timothy hay, early bloom	90	1.9	10	35	17	–	0.45	0.26
Timothy hay, full bloom	90	1.7	7.5	40	17	–	0.3	0.2
Rice hulls	92	0.5	3	72	7	–	0.12	0.07
Rice bran	91	2.9	14	20	14–15	20–22	0.1	1.5–1.7
Oats	90	3.2	10–13	16	49.5	4.5	0.1	0.35
Barley grain	89	3.7	13	8	62	1.7	0.05	0.34
Corn grain	88	3.85	8–10	4	66	3.7	0.05	0.3
Beet pulp	91	2.6	10	27.5	38	–	0.7	0.1
Soy hulls	92	2.0	11–13	46–54	–	–	0.4–0.7	0.15–0.2
Molasses	78	3.4	2–6	0	77	–	0.15	0.03
Wheat bran	89	3.3	16–17	13–15	15–17	–	0.14	1.27

DE = digestible energy; CP = crude protein; NSC = non-structural carbohydrate; Ca = calcium; P = phosphorus
All nutrients expressed as a percentage in feed dry matter.
Primary source of data is 1989 NRC.

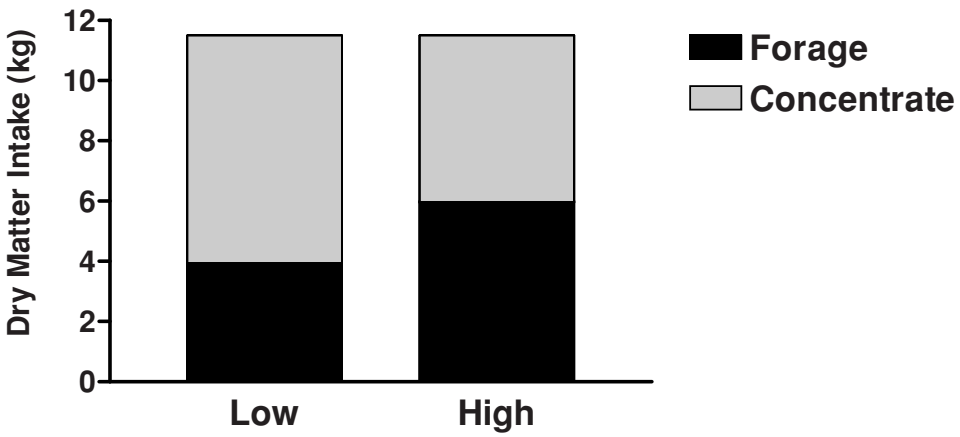

Fig. 36.2 The effects of forage energy content on the proportions of hay and energy concentrate required to meet the energy requirements of a 500 kg horse with daily digestible energy (DE) needs of approximately 30 Mcal/day. This example assumes a daily dry matter (DM) intake of 11.5 kg or approximately 2.2% of bodyweight. **Low** = hay with DE content of 1.5 Mcal/kg DM; **High** = hay with DE 2.0 Mcal/kg. The DE content of the energy concentrate is 3.3 Mcal/kg. The diet proportions in these two scenarios are: Low (4 kg hay and 7.5 kg concentrate or a ratio of 35:65); High (6 kg of hay and 5.5 kg of concentrate or a ratio of 52:48).

mechanism, with the ingestion of large grain meals a substantial proportion of the ingested starch may escape hydrolysis in the small intestine with a resultant delivery of this substrate to the hindgut. Rapid fermentation of starch in the hindgut by lactate-producing bacteria can result in lactate accumulation, excess gas production, cecal and colonic acidosis and increased risk of intestinal disturbances.[45,46] Epidemiological studies have identified the level of grain feeding as a risk factor for colic. Tinker et al[47] reported odds ratios of 4.8 and 6.3 (relative to no episode of colic) for horses fed, respectively, 2.5 kg/day and more than 5.0 kg/day of concentrate. Similarly, Hudson and colleagues[48] reported that recent (within the previous 2 weeks) changes in the type of grain or concentrate fed or feeding more than 2.7 kg of oats per day was associated with increased risk for an episode of colic. High-starch (grain) diets have also been implicated in the pathogenesis of some forms of chronic exertional rhabdomyolysis.[49]

While it is necessary to feed some hydrolyzable carbohydrate to athletic horses to ensure an adequate supply of substrate for glycogen replenishment, several strategies can be employed to mitigate the risk of digestive disturbances attributable to heavy grain (starch) feeding. First, it is advisable to limit the size of individual grain-based meals to avoid 'starch bypass' to the large intestine. Second, only cereal grains with high pre-cecal starch digestibility should be included in energy concentrates for horses. Third, energy concentrates for athletic horses should make more use of non-starch carbohydrates (e.g. sugar beet pulp) and vegetable fats. Inclusion of these alternative energy sources facilitates a reduction in the level of starch feeding without compromising the caloric density of the ration.

A suggested upper limit of starch intake in a single meal is between 2 and 4 g starch per kg bodyweight (0.2–0.4% of bwt per feeding),[43,50] although one nutritionist has suggested that 2 g/kg per meal is the safe upper limit.[46] Thus, if a concentrate feed contains 50% starch (e.g. plain oats) the maximum recommended amount of concentrate per feeding is approximately 2 kg for a 500 kg horse. Pre-cecal starch digestibility varies with the type of grain and the nature of any mechanical or thermal processing. For example, whereas oat starch (at up to 3 g/kg per meal) has a pre-cecal digestibility of greater than 90%, approximately 35% of an equivalent dose of cornstarch reaches the cecum undigested.[46] Similarly, the pre-cecal digestibility of unprocessed barley is substantially lower when compared to oats. However, heat treatments such as micronization, extrusion and steam flaking significantly improve the pre-cecal starch digestibility of barley and corn. Overall, oats appear to be the safest source of starch for horses, although barley and corn are acceptable if they are subjected to some form of heat treatment.

Fats and oils

The addition of fat to horse rations is now commonplace. Although animal fat (tallow or lard) has been fed to horses, palatability and digestibility[51,52] are inferior when compared to vegetable oils. Therefore, most commercial fat-supplemented concentrates for horses contain a vegetable oil such as soy, corn or canola. Other oils that may be used in equine rations include peanut, safflower, coconut, linseed or flaxseed. Vegetable oils are highly unsaturated and contain approximately three times as much DE as oats and 2.5 times as much as corn. Other sources of fat used in horse rations include stabilized rice bran (18–22% fat), flaxseed meal (40% fat) and copra meal (8–9% fat). Vegetable oils are both highly digestible (90–100%)[53] and palatable,[52] although there can be slight variation in the acceptance of the different oils. For example, Holland et al[52] demonstrated that corn oil is preferred over soy, peanut and cottonseed oils. Rice bran (as a powder or an extruded pellet) is also well accepted by horses and is commonly fed at a rate of 0.5–2.5 kg per day to

mature horses, providing 90–500 g fat per day. Rice bran is rich in phosphorus and has an inverted Ca:P ratio, but many commercial rice bran products contain added calcium (e.g. calcium carbonate) to correct this imbalance. Alternatively, a mineral supplement can be added to the ration to ensure an appropriate Ca:P ratio (at least 1:1) in rations containing rice bran.

Fat is often added to the diet to increase the energy density of the ration, which can offer an advantage when dry matter intake limits provision of adequate energy to maintain condition ('hard keeper' horses). Alternatively, substitution of fat for a portion of the grain in an energy concentrate allows for a decrease in hydrolyzable carbohydrate intake. This strategy is advocated for horses with some forms of chronic exertional rhabdomyolysis (see below).

Fat is also added to the diet of athletic horses because of the reputed benefits of fat-supplemented diets on exercise performance, specifically that performance is improved by *fat adaptation*, a set of physiologic responses to the consumption of a high-fat diet during training that confer advantages to the horse during exercise.[54] As discussed in Chapter 34, there is evidence that a fat-supplemented diet is associated with an increased capacity for fat oxidation during exertion, as shown by a lower respiratory exchange ratio during low and moderate intensity exercise.[55,56] However, this effect of fat supplementation on fuel selection is not evident at higher workloads, reflecting the high dependence of horses on carbohydrate metabolism during moderate and high intensity exercise.[55] Nonetheless, the increase in fat oxidation and decrease in carbohydrate oxidation (carbohydrate sparing) evident during low intensity exercise in fat-supplemented horses should be beneficial during endurance exercise, although the actual effect of fat supplementation on endurance performance has not been reported.

It should also be noted that the level of fat supplementation used in the aforementioned research studies (approximately 20–25% of DE from fat)[55,56] is considerably higher than that commonly practiced by horse owners and trainers (4–15% of DE from fat). Whether these lower levels of fat supplementation confer similar metabolic advantages during exercise is unknown.

The ideal amount of dietary fat for horses has not been determined, nor is there much information regarding the effects of fatty acid chain length or degree of saturation on metabolism and health in horses. Kronfeld[53] has stated that horses can safely consume diets containing up to 15–20% vegetable oil by weight (on a total diet basis), providing the horse is adapted to this level of fat inclusion over a 2–3-week period. However, one study demonstrated a decrease in total tract fiber digestibility in horses fed a 14% soy oil diet.[57] Commercially, the level of fat or oil added to a concentrate is often limited by manufacturing constraints (e.g. poor pellet quality when large amounts of oil are included in pelleted feeds; greasy appearance of concentrate mixes). Therefore, fat-supplemented concentrates designed for performance horses usually contain between 5% and 14% fat (as fed), providing between 8% and 30% of the DE. However, as these concentrates are fed with forage, the amount of fat on a total diet basis is much lower (approximately 3–8% fat or 4–15% of the DE from fat assuming a 50% concentrate, 50% forage diet). These levels of fat supplementation carry minimal risk of negative associative effects such as a decrease in fiber digestibility.

Many horse owners and trainers add vegetable oil to existing rations. A suggested upper limit of oil supplementation is 100 g per 100 kg bwt per day. For reference, one standard measuring cup contains 250 ml (8 fluid ounces) of oil (~200 g) and provides approximately 1.67 Mcal (6.7 MJ) of DE. For a 500 kg horse in moderate work (daily DE needs of 26 Mcal), the inclusion of 500 g of oil per day will provide about 16% of the DE requirements. There should be a gradual introduction to oil feeding to avoid digestive disturbances (loose and oily feces). Initially, 1/4–1/2 cup of oil/day can be added to the ration. Over a 2–3-week period, the amount of added oil can be increased to 2–2$\frac{1}{2}$ cups/day, divided into at least 2–3 feedings.

One concern with the addition of vegetable oils (or rice bran) to an existing diet is the potential for nutrient imbalances. Commercial energy concentrates with added fat are fortified to maintain appropriate nutrient-to-calorie ratios and are designed to complement the forage source. On the other hand, the on-farm addition of a substantial amount of oil (e.g. 400–500 g per day) to an existing ration may result in an unbalanced diet. Consultation with a nutritionist is recommended in these situations. Supplementation with vitamin E (100–200 IU per 100 g of added oil) is recommended for prophylaxis against oxidant stress when oil is directly added to the ration. This practice may not be necessary when rice bran is the source of added fat as it contains substantial quantities of vitamin E and other natural antioxidants.

Non-starch carbohydrates

There are two main types of non-starch polysaccharides used in equine rations: simple sugars; and highly digestible sources of fiber (so-called 'fermentable fibers'), particularly sugar beet pulp (SBP) and soya hulls and, to a lesser extent, citrus pulp. Simple sugars in the form of molasses (a mixture of glucose, sucrose and fructose) are often added to grain mixes at 6–8% by weight. In general, these sugars are well utilized by the horse, as shown by pronounced glycemic responses following the administration of glucose, sucrose or fructose at dosages of 1.0–2.0 g/kg bwt.[58]

SBP contains major fractions of highly digestible fiber fractions, including pectins, arabinans and galactans, which are readily fermented by equine hindgut microflora[59] Digestibility studies have demonstrated that, in contrast to the fibers in traditional roughage sources, the fibers in SBP and soya hulls are extensively degraded within the time that such a feedstuff would be resident in the gut.[60] This high digestibility accounts for the higher energy value of these feedstuffs when compared to hay. It has also been demonstrated that the addition of 30% SBP to the ration increases the digestibility of the hay portion of the diet.[60] SBP

is available in two forms, molassed (i.e. molasses is added to the beet shreds, generally at the 5% level) or non-molassed, and can be fed alone or as a component of a concentrate mix. When fed alone, it is recommended to soak the beet shreds in water for 3–4 hours before feeding. Soya hulls are generally included in pelleted feeds.

SBP or soya hulls can be included as a substitute for cereals (starch) in energy concentrates. Studies in horses have demonstrated that up to 3.0 g SBP per kg bwt per day (i.e. 1.5 kg for a 500 kg horse) may be fed to adult horses without any adverse effects on overall nutrient utilization or performance.[61–63] Indeed, as discussed in Chapter 34, there may be metabolic advantages of diets that include non-starch polysaccharides such as SBP, including a muscle glycogen-sparing effect during moderate and heavy exercise.

Although the feeding of straight grains or sweet feed mixes to athletic horses remains a popular practice, there is increasing emphasis on use of energy concentrates in which some starch and sugar has been substituted by fat and/or a fermentable fiber such as SBP and soya hulls (so-called 'fat and fiber' feeds). Such diets may reduce the risk of gastrointestinal disturbances and, as discussed below, are useful in the nutritional management of horses with chronic exertional rhabdomyolysis. Figure 36.3 compares the sources of digestible energy in a traditional race horse diet (forage plus grain) and a diet in which a fat and fiber energy concentrate is fed.

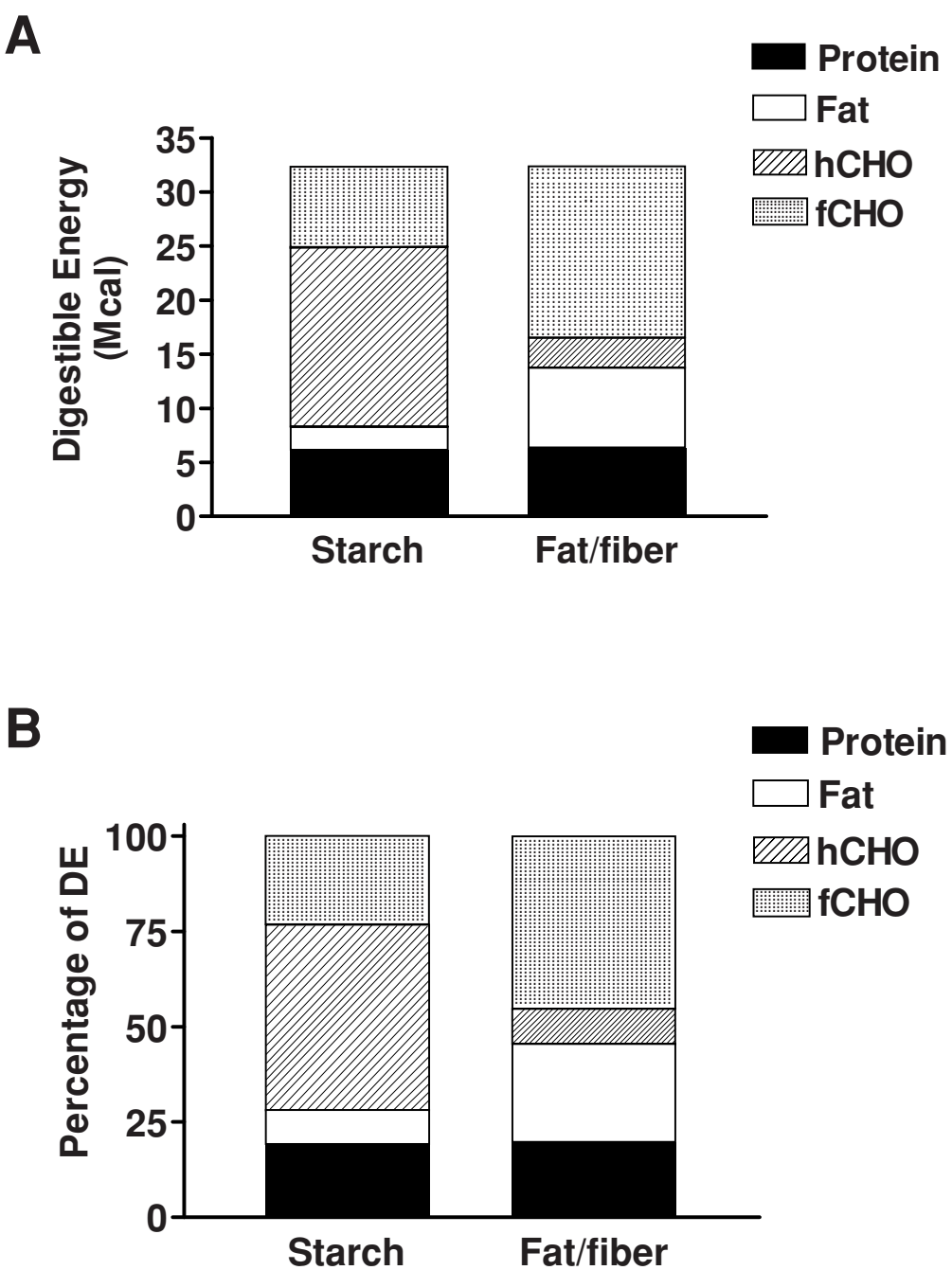

Fig. 36.3 Graphical representation of the sources of energy in a traditional grain and hay diet (**Starch**) and a contemporary fat and fiber energy concentrate and hay diet (**Fat/fiber**) fed to a 500 kg racehorse requiring approximately 32 Mcal of digestible energy (DE) per day. Both diets include 6 kg of mid-bloom timothy hay and, on a total diet basis, provide 12% crude protein. For Starch, the horse is fed ~ 7 kg of an energy concentrate composed of oats (57%), cracked corn (37%) and sugar cane molasses (6%). The same quantity of energy concentrate is fed in Fat/fiber (~ 13% fat), the primary ingredients of which are beet pulp, rice bran, soy hulls and vegetable oil. Graph A depicts estimates of the absolute DE provided by protein, fat, hydrolyzable carbohydrate (hCHO; starch and sugar) and fiber carbohydrates (fCHO) in the respective diets. Graph B shows the percentage contribution of the four energy sources to the total DE intake. Note the dramatic reduction in hCHO intake in the Fat/fiber when compared to the Starch diet.

Special considerations: horses with chronic exertional rhabdomyolysis

Special considerations are needed in the selection of energy concentrates for horses with two forms of chronic exertional rhabdomyolysis (ER): polysaccharide storage myopathy (PSSM) and recurrent exertional rhabdomyolysis (RER). Although the pathogenesis of PSSM and RER is distinctive[64] (see Chapter 27), there is increasing evidence that diets low in starch and higher in fat are beneficial in the management of both conditions.[49,65–68]

Quarter horses and related breeds with PSSM have enhanced insulin sensitivity, as demonstrated by a more rapid clearance of blood glucose after intravenous glucose loading[69] or the feeding of grain meal,[70] and this increase in insulin sensitivity is probably a contributing factor in the development of excessive muscle glycogen storage. Thus, diets high in starch and/or sugar may promote clinical expression of the disease by providing substrate for glycogen synthesis, and the cornerstone of dietary management for horses with PSSM is a severe restriction of hydrolyzable carbohydrate (starch and sugar) intake. There is also emerging evidence that beyond the simple removal of hydrolyzable carbohydrate from the diet, additional clinical improvement occurs when fat is added to the ration. It has been hypothesized that an increase in dietary fat alters intracellular glucose metabolism and glycogen synthesis in horses with PSSM,[49] although as yet there is no direct evidence in support of this hypothesis. Whether similar metabolic mechanisms contribute to the glycogen storage syndrome recognized in draft breeds (equine polysaccharide storage myopathy, EPSM) is not known. However, there is evidence that an increase in dietary fat is also beneficial in the management of horses with EPSM.[65,66]

The role of diet in the pathogenesis of RER is less clear. As with PSSM, there is evidence that a reduction in starch intake and increase in fat supplementation can be beneficial.[49,67,68,71] However, experimental studies in a small group of RER-affected Thoroughbreds have demonstrated that dietary energy source (i.e. the relative amounts of starch and sugar versus fat) is only important when total caloric intake is high (> 28–30 Mcal DE per day for a 500 kg horse).[67,68,71] Specifically, when daily calorie intake was moderate (~21–22 Mcal/day) diet composition had little influence on exercise-associated increases in plasma creatine kinase (CK) activity.[67,68] However, postexercise CK activity was significantly higher in horses consuming a hay and grain (starch) diet that provided 28.8 Mcal of DE per day when compared to an isocaloric diet low in starch with 20% of DE supplied by fat.[71] It has been suggested that high-calorie, high-starch diets are associated with a more nervous disposition in horses. This association may explain the relationship between dietary starch level and subclinical or clinical tying up in RER-susceptible horses given that stress and excitement are apparent trigger factors for the condition.[64] In support of this hypothesis, RER-affected horses fed the low-starch, high-fat diet had lower resting heart rates and, subjectively, a less excitable temperament when compared to observations made in the same horses while consuming the high-starch diet.[67,68,71]

In general, there should be a reduction in hydrolyzable carbohydrate intake and increased reliance on fat and fermentable fibers as energy sources. With respect to PSSM, the diet should be devoid of grain (starch) and sugar such that on a total diet basis, less than 15% of DE is supplied by hydrolyzable carbohydrate. There is some controversy with respect to the amount of supplemental fat required for management of PSSM.[49] A suggested target is 20% of DE as fat; however, in some horses this can be difficult to achieve at very high daily DE intakes (> 30 Mcal/day). 'Easy keeper' horses with PSSM that are only in light work will maintain condition on a diet that is predominantly medium-quality hay (supplied at approximately 1.5% of bwt), with a small quantity of fat (e.g. 0.5–1 kg rice bran per day or 1/2–1 cup of oil), and a vitamin–mineral supplement. Lush pasture and legume hays (alfalfa) should be avoided because these forages can supply a substantial quantity of sugar. Possible options for meeting the energy needs of affected horses in harder training include the provision of larger quantities of rice bran (e.g. 1–2 kg/day), a combination of hay pellets and vegetable oil (up to 100 g per 100 kg bwt/day), or a 'fat and fiber' energy concentrate. As mentioned, the latter utilizes a combination of vegetable fats (oils and/or rice bran) and fermentable fiber (SBP and/or soya hulls). Some of these feeds provide less than 10% of DE from hydrolyzable carbohydrate and 20% of DE as fat.

A typical race horse with RER is consuming greater than 30 Mcal of DE per day, with much of the energy supplied by starch. Indeed, it is not uncommon for race horses to consume 5–8 kg/day of a grain concentrate and this level of starch intake appears to contribute to an increased frequency of tying-up episodes.[49,71] Therefore, as with PSSM, a lower starch, higher fat and fermentable fiber diet is indicated in the management of horses with RER. One recommendation for race horses in intense work is a diet that provides no more than 20% of DE from hydrolyzable carbohydrate, with a minimum of 20% DE from fat (Fig. 36.3).

These dietary interventions are not a panacea for the prevention of PSSM and RER. As discussed in Chapter 27, a number of other management changes are needed for the successful management of horses with chronic ER. For example, along with strict dietary control, daily exercise is critical to the successful management of horses with PSSM, while strategies for reduction of stress and excitability are important in the management of RER-susceptible horses.

Putative ergogenic feeding strategies and supplements

Beyond provision of a diet that meets the energy and nutrient requirements of an athletic horse, horse owners often apply different feeding strategies or administer a variety of nutritional supplements in an attempt to enhance a horse's

performance during competition. The term *ergogenic* means 'work generating';[72] thus, an ergogenic nutritional supplement or feeding manipulation is one that enhances work performance (e.g. an increase in speed, endurance or strength). A plethora of nutritional supplements are marketed for use in horses, often on the basis of performance enhancement. However, with rare exceptions, there is little or no scientific basis for these claims because there are no data available regarding the efficacy of a given supplement in horses. Instead, the rationale for use is most often based on data from studies in humans or other species.[73]

This section provides a brief overview of the effects of selected feeding strategies or nutritional supplements that have been purported to enhance athletic performance of horses. The reader is also referred to Chapter 34 for discussion on the effects of fat supplementation, dietary protein content and pre-exercise feeding on exercise metabolism and performance.

Manipulation of carbohydrate supply

In humans, it is universally accepted that carbohydrate availability to skeletal muscle is an important determinant of exercise performance, particularly during moderate intensity exercise lasting 1 hour or more.[74,75] Low muscle glycogen concentration before exercise is associated with decreased performance, whereas high muscle glycogen content enhances endurance performance.[74,76] Similarly, an increase in blood glucose availability by ingestion of glucose or glucose polymers before and/or during exercise enhances the performance during prolonged moderate intensity exercise.[75,76] Therefore, feeding strategies that increase pre-exercise muscle glycogen content and enhance blood glucose supply to skeletal muscle during exercise are ergogenic in human athletes. This is especially true for events lasting more than 60–90 min.

The effect of carbohydrate supply on exercise performance in horses is less well studied but, similar to humans, there is evidence that glucose availability and muscle glycogen content are important determinants of performance during moderate and intense exercise. Time to exhaustion in horses running at 6–7 mph was decreased by 35% when pre-exercise muscle glycogen content was 70% lower than normal.[77] Anaerobic work capacity in horses, as assessed by the run time until fatigue during a 'supramaximal' treadmill exercise test, was decreased by approximately 28% when muscle glycogen content was 60–70% lower relative to a control treatment.[78] Thus, similar to humans, low pre-exercise muscle glycogen content is associated with decreased exercise performance in horses. On the other hand, an increase in blood glucose availability has been demonstrated to enhance performance in horses undertaking moderate intensity exercise. In two studies of horses running on a treadmill at 50–60% of $\dot{V}O_{2max}$, the time to fatigue was increased by 14–20% when glucose availability was increased by intravenous administration of glucose (2–3 g/min).[79] These data have generated interest in the development of nutritional strategies for horses that optimize pre-exercise muscle glycogen content or glucose availability during exercise.

Muscle glycogen storage

In humans, the term 'glycogen loading' refers to maximization of muscle glycogen stores prior to a competitive event in which performance is limited by the depletion of muscle glycogen stores. The original CHO loading protocols, pioneered by Bergström & Hultman,[74] involved a 3–4-day depletion phase of hard training and a low carbohydrate diet, followed by a 3–4-day loading phase of high carbohydrate intake and exercise taper. This protocol resulted in a more than 50% increase in glycogen content, hence the term 'muscle glycogen supercompensation'. More recent studies have shown that well-trained athletes are able to achieve similar muscle glycogen supercompensation without the need to undertake a glycogen-depletion phase.[80] Accordingly, the more practiced method for glycogen loading in human athletes involves 3 days of exercise taper and high carbohydrate intake (7–10 g/kg bwt per day).[81]

Research in horses has indicated that only modest (~10%) increases in muscle glycogen content can be achieved through dietary manipulation.[77,82,83] For example, Essén-Gustavsson et al[83] reported a 12% increase in the resting muscle glycogen content of Standardbred horses fed a diet that provided approximately 2 kg/day of starch and sugar when compared to an isocaloric diet that provided about 1.3 kg/day of hydrolyzable carbohydrate. An increase in muscle glycogen content of this magnitude was not associated with improved performance during moderate intensity exercise.[82,83] These observations notwithstanding, a number of glycogen or 'carbo' loader products are marketed for use in athletic horses.

One possible reason for the apparent disparity in capacity for glycogen supercompensation between humans and horses is a difference in hydrolyzable carbohydrate intake. In humans, a daily carbohydrate intake of 7–10 g/kg bwt is required for a substantial increase in muscle glycogen content.[81] For a 500 kg horse, an equivalent carbohydrate dose would require the consumption of 7–10 kg of oats (~50% starch) per day. Such a high grain (starch) intake is not realistic for most horses, nor recommended given the risks of gastrointestinal dysfunction associated with high starch intake.

Although an increase in muscle glycogen content is perhaps not achievable in horses, it is still desirable to apply dietary and management practices that optimize glycogen resynthesis after exercise such that low glycogen does not prevail at the start of the next exercise session. Following exercise in horses that depletes muscle glycogen content (middle gluteal m.) by greater than 50–60%, complete glycogen replenishment is achieved by 24 hours when glucose (6 g/kg) is administered intravenously.[78,84] In contrast, oral administration of a glucose polymer (3 g/kg bwt) within 60 min of the completion of glycogen-depleting exercise does not accelerate glycogen replenishment.[85,86] Similarly, when horses are fed meals with high hydrolyzable carbohydrate

content (grain), the rate of muscle glycogen replenishment is not different[87] or only slightly faster[88] when compared to horses fed a hay diet. Studies in humans, on the other hand, have shown that carbohydrate ingestion during the postexercise period substantially enhances the rate of muscle glycogen resynthesis.[75] Over a 6–12-hour period following exercise, the ingestion of carbohydrate at a rate of 0.7–1.0 g/kg bwt every 2 hours results in muscle glycogen synthetic rates of 5–8 mmol/kg/hr and complete glycogen replenishment is achieved within 24 hours. By comparison, the maximum rate of muscle glycogen synthesis in horses after exercise that results in a 40–70% decrease in glycogen content is approximately 1.5 mmol/kg/h,[87–89] and as much as 48–72 hours is required for complete replenishment.[88,89] As discussed, the horse appears to have a limited capacity for the digestion of hydrolyzable carbohydrates and this may limit systemic glucose availability, thereby restraining the rate of muscle glycogen resynthesis.

The performance implications of the slow rate of glycogen replenishment in horses are likely dependent on the type of athletic activity. In a study of Thoroughbreds fed a hay and grain concentrate diet, the muscle glycogen loss sustained during training gallops (19–25% decrease) was fully restored within 2–3 days.[90] Thus, in situations where intense exercise bouts occur at 3-day intervals, as is typical in the conventional training of Thoroughbred race horses, muscle glycogen content can be well maintained. However, for horses competing in multi-day events (e.g. three-day event) or multiple heats on a single day (e.g. Standardbred race horses), inadequate glycogen replenishment may adversely affect subsequent exercise performance. For these horses, small grain meals (e.g. 1–1.5 kg for a 500 kg horse) should be provided at frequent intervals (e.g. every 3 h) during the first 12 hours of recovery. Limiting the size of the grain meals and increasing the frequency of feeding should minimize the risks of digestive disturbance.

Enhancement of blood glucose supply during exercise

The only practical means for enhancement of blood glucose availability during exercise is the pre-exercise feeding of a meal high in starch and/or sugar or the intragastric administration of a glucose or glucose polymer solution. For endurance horses, similar strategies could be applied at rest stops during races. However, there is some controversy regarding the merits of these pre-exercise dietary interventions. It has been argued that the suppression in lipid oxidation associated with pre-exercise carbohydrate ingestion may be detrimental to performance because an accelerated rate of carbohydrate oxidation will result in premature depletion of endogenous carbohydrate stores (see Chapter 34). Certainly, there is evidence that the hyperglycemia and hyperinsulinemia consequent upon grain ingestion or intragastric glucose administration alter substrate selection during moderate intensity exercise. The consumption of a grain meal (~2 kg corn) 2 hours before exercise[5] or the oral administration of glucose (2 g/kg bwt) 1 hour pre-exercise[91] increases the rate of blood-borne glucose utilization and the rate of whole-body carbohydrate oxidation in horses during treadmill exercise at 50–55% $\dot{V}O_{2max}$. Conversely, the rate of whole-body lipid oxidation is suppressed under these conditions,[5,91] most probably as a result of an insulin-induced suppression in lipolysis.

It must be emphasized that the effects of pre-exercise carbohydrate ingestion (grain meals or glucose solutions) on exercise performance have not been determined in horses. Although speculative, it is possible that the pre-exercise ingestion of hydrolyzable carbohydrate is beneficial for events requiring moderate and intense exercise. However, for more prolonged, lower intensity exercise, such as that required of the endurance horse, the suppression in lipid oxidation associated with pre-exercise carbohydrate ingestion may be detrimental to performance (see Chapter 34). Therefore, for endurance events it is recommended that no grain be fed in the 3-hour period before competition exercise. Further research is required to determine the metabolic and performance effects of various pre-event (and mid-event) feeding strategies.

Alterations in dietary fiber intake

The horse's large intestine contains a fluid volume equivalent to 8–10% of bodyweight, with 10–20% of total body sodium, potassium and chloride.[92,93] There is limited evidence that a portion of this fluid can be absorbed during prolonged exercise, thereby partially offsetting sweat fluid losses.[92] Accordingly, some nutritionists advocate a high-fiber diet for endurance horses because such diets should increase the size of the hindgut fluid reservoir. Indeed, Meyer et al[92] demonstrated that feeding a high-fiber diet (hay only) when compared to a low-fiber diet (a complete feed composed of grain, bran and beet pulp) to ponies resulted in greater water content of the large intestine (183 and 101 mL/kg bwt for the high- and low-fiber diets, respectively). Warren and co-workers[93] also reported an approximately 15% increase in estimated gastrointestinal tract fluid volume when horses were fed a high-fiber (54% neutral detergent fiber [NDF], 31% ADF) when compared to a low-fiber diet (31% NDF, 19% ADF). Whether such an increase in gut fluid volume is beneficial to thermoregulatory function and performance is unclear. In the study by Warren and co-workers,[93] neither the loss of bodyweight nor the decrease in plasma volume differed between dietary treatments during 45 min of low intensity exercise. Furthermore, as discussed by Kronfeld,[17] the putative benefits of a high-fiber diet in terms of improved water balance and thermoregulatory function must be weighed against energetic disadvantages associated with an increase in hindgut weight (bowel ballast). For example, in a 500 kg horse, an extra 4 kg in hay intake can be estimated to increase bowel ballast by between 10 and 24 kg. On balance, there is little justification for very high-fiber diets in endurance horses and as for other equine athletes, a diet that provides roughage at about 1.5% of bodyweight is recommended.

Anecdotally, many race horse trainers limit hay intake in the day leading up to races or, alternatively, eliminate hay

from the diet and instead feed a 'complete' beet pulp-based diet. There is some evidence that a short-term reduction in forage intake is beneficial in horses undertaking high-intensity exercise. When compared to ad libitum hay consumption, restricting hay intake to ~1% of bodyweight for a 3-day period before a treadmill exercise test (2 min at 115% $\dot{V}o_{2max}$) resulted in a 2% decrease in bodyweight and a reduction in anaerobic energy expenditure during exercise, as evidenced by reduced oxygen deficit and plasma lactate concentrations. The reduction in bodyweight was attributed to a decrease in bowel ballast (gut fill).[94] The practical implications of these findings are uncertain given that many race horses do not consume more than 1% of bwt as roughage. Furthermore, a more drastic reduction in roughage intake (e.g. less than 0.75% bwt) is not recommended because, as previously discussed, low-fiber diets may predispose horses to gastrointestinal dysfunction (e.g. gastric ulcers, colic).

Nutritional ergogenic supplements

Although electrolyte, vitamin and mineral (especially iron) supplements are the most widely used in horses, the use of supplements touted to enhance performance is also common.[73] Yet, very few of these substances have been the subject of scientific studies designed to evaluate their metabolic and performance effects. The following discussion is restricted to some supplements that have been evaluated in the horse. The effect of sodium bicarbonate administration on exercise performance is discussed elsewhere in this book.

Creatine

Creatine (methylguanidine-acetic acid) is a compound derived from amino acids that is stored primarily in skeletal muscle at typical concentrations of 100–150 mmol/kg dry weight (dw) of muscle. About 60–65% of this creatine is phosphorylated. Creatine phosphate (CP) provides a rapid but brief source of phosphate for the resynthesis of adenosine triphosphate (ATP) during intense exercise and therefore helps to maintain normal ATP/ADP homeostasis. Other functions of CP metabolism include the buffering of hydrogen ions produced during anaerobic glycolysis.[72] As both ADP and hydrogen ion accumulation are factors that may contribute to development of fatigue during sprint exercise, the size of the skeletal muscle CP store may be an important determinant of performance during high-intensity exercise. Therefore, nutritional manipulations leading to increases in total muscle creatine and CP might be expected to have an ergogenic effect during intense exercise.

The use of creatine supplements by human athletes is widespread; according to one estimate, 80% of the athletes competing in the 1996 Olympic Games were using a creatine supplement.[95] There is support for an ergogenic effect of creatine supplementation in human athletes engaged in repeated sprints, probably related to an increase in the rate of CP resynthesis during recovery between bouts of exercise. However, oral creatine supplementation is not considered ergogenic for single-bout or first-bout sprints or for prolonged, submaximal exercise. The evidence is inconclusive for effects on muscle strength although creatine supplements are widely used by body builders and weight lifters.[96]

Studies in humans have demonstrated that a daily creatine dose of 20–25 g (~250 mg/kg bwt/day), divided into four doses, results in increased muscle creatine concentrations, with an apparent upper limit in creatine storage of 150–160 mmol/kg dw. About 20% of the increased muscle creatine content is stored as CP and saturation occurs 2–3 days after the start of supplementation.[96] The increase in muscle creatine content is greatest in those subjects with a low initial concentration. Lower daily doses of 3 g/day (~40–44 mg/kg bwt) will achieve a slower loading over 14–28 days and elevated muscle creatine stores can be maintained by continued daily supplementation of 2–3 g creatine.[97] Creatine is transported into muscle against a high concentration gradient, via saturable transport processes that are stimulated by exercise[98] and by insulin.[99]

There are two published reports of oral creatine supplementation in horses.[100,101] Sewell & Harris[101] demonstrated that, in contrast to humans and dogs, creatine is poorly absorbed in the horse. The intragastric administration of 50 mg Cr per kg bwt resulted in an increase in plasma creatine concentration from 40 to 100 fmol/L after 4–6 h. By comparison, the same dose in humans results in plasma concentrations of 800–1000 fmol/L.[73] Furthermore, the administration of creatine at 150 mg/kg per day (divided into three doses) for 13 days had no effect on muscle creatine content.[101] In a randomized, crossover design, Schuback et al[100] fed Standardbred trotters 25 g creatine monohydrate twice daily (total daily dose of ~100–120 mg/kg bwt) for 14 days. Before and after the period of supplementation, horses completed an incremental treadmill exercise test until exhaustion. There was no significant effect of supplementation on plasma or muscle creatine concentrations, nor an effect on treadmill run time and the muscle metabolic response to exercise.[100] Thus, creatine supplementation in the horse at dosages shown to be effective in humans has failed to result in an increase in muscle creatine content. Without a change in muscle creatine content, creatine supplementation is unlikely to exert an ergogenic effect in horses. The reason for the apparent low bioavailability of orally administered creatine in horses has not been determined. It is possible that, as an herbivorous animal, the horse's gastrointestinal tract is not adapted to the absorption of creatine.

L-Carnitine

L-Carnitine is a component of the enzymes carnitine-palmityltransferase I, carnitine-palmityltransferase II and carnitine-acylcarnitine translocase that are involved in the transport of long-chain fatty acids across the inner mitochondrial membrane.[102] As such, long-chain fatty acid oxidation is carnitine dependent and, therefore, it has been proposed that increased availability of L-carnitine by supplementary ingestion might up-regulate the capacity to transport fatty acids into the mitochondria and increase fatty acid oxidation.[72] This augmentation in fat oxidation could be of

benefit during endurance exercise. Another role of carnitine is to act as a 'sink' for acetyl-CoA units produced during high-intensity exercise. The conversion of acetyl-CoA to acetylcarnitine maintains CoA availability and decreases the ratio of acetyl-CoA:CoA. As such, an increase in carnitine availability could enhance substrate flux through the citric acid cycle and increase the activity of pyruvate dehydrogenase, which is otherwise inhibited by high levels of acetyl-CoA. These mechanisms would serve to increase oxidative metabolism of glucose, decrease lactate production and perhaps enhance performance during exercise tasks that might be limited by excess hydrogen ion and lactate accumulation.[72]

However, the weight of evidence from human studies indicates that oral carnitine supplementation has no effect on muscle carnitine concentration. In addition, there is no evidence that muscle carnitine content limits fat oxidation other than in patients with inborn errors in metabolism that result in inadequate muscle carnitine. This is also likely to be the case in horses as the carnitine content of equine skeletal muscle is 2–3-fold higher when compared to human muscle.[103] Supplementation studies in humans have failed to demonstrate an effect of carnitine on measures of fat oxidation or muscle metabolism during exercise.[72,102]

Studies in humans[104] and in horses[105,106] have demonstrated that the oral bioavailability of L-carnitine is poor. In horses, large oral doses of L-carnitine (10–60 g) are required to effect an approximate doubling in plasma carnitine concentration.[105] Importantly, supplementation at these levels for 58 days had no effect on muscle carnitine content. In a subsequent study, intravenous doses of 10 g L-carnitine were administered daily for 26 days.[106] These infusions resulted in peak plasma carnitine concentrations 30-fold higher when compared to pre-injection values and concentrations remained three-fold higher after 6 h. Yet, there was no change in muscle carnitine content. Thus, from the available data there is no evidence that muscle carnitine content in horses is enhanced as a result of oral or intravenous L-carnitine supplementation.

Although the weight of evidence suggests that L-carnitine is unlikely to be ergogenic in horses, a recent study has provided evidence that supplementation during conditioning may augment training-associated skeletal muscle adaptations.[107] In a small group of 2-year-old Standardbred horses subjected to a 10-week conditioning program, supplementation with L-carnitine (10 g/day per os) was associated with significant increases in the percentage of type IIA muscle fibers and the intensity of periodic acid-Schiff staining (an indicator of intrafiber glycogen content) when compared to untreated control horses.[107] The mechanism of these effects is unclear and somewhat perplexing, given that previous studies have failed to demonstrate a change in muscle carnitine content in horses receiving an identical carnitine dosage. Further studies are required to determine the performance implications of these apparent carnitine-induced muscular adaptations.

Amino acids

Amino acid or 'refined' protein supplements are often touted for their ability to 'build' muscle mass or, in the case of the branched-chain amino acids (BCAA) (leucine, isoleucine, valine), enhance endurance performance by modifying factors that contribute to central fatigue.[108,109] In addition, it has been proposed that BCAA supplementation during exercise may provide carbon intermediates for the citric acid cycle at a time when endogenous carbohydrate reserves are depleted, thereby delaying the onset of fatigue.[72]

The 'central fatigue' hypothesis proposes that increased brain serotonin contributes to fatigue development during prolonged moderate-intensity exercise.[109] The increase in brain serotonin synthesis occurs as a result of increased transport of free (unbound) tryptophan across the blood–brain barrier. Key to this increase in tryptophan uptake is an increase in the plasma ratio of free tryptophan to BCAA,[109] which may increase for two reasons. First, as blood free fatty acid (FFA) concentration rises during exercise, the FFA compete with tryptophan for binding sites on albumin and the FFA displace some of the tryptophan molecules from albumin; therefore, free tryptophan concentration increases. Second, an increase in the oxidation of BCAA in muscle results in a decrease in blood BCAA concentration. As BCAA and tryptophan compete for carrier-mediated entry into the central nervous system, an increase in the free tryptophan-to-BCAA ratio leads to increased tryptophan transport. Therefore, it has been theorized that BCAA supplementation could reduce the exercise-induced increase in brain tryptophan uptake and thus delay fatigue.[109] Interestingly, when horses were infused with tryptophan (100 mg/kg, i.v.) during submaximal exercise, run time to fatigue was decreased by ~15% relative to the placebo treatment, providing evidence that an increase in circulating tryptophan adversely affects endurance performance in horses.[79] However, the oral ingestion of a tryptophan solution that markedly increased plasma free tryptophan concentration and estimated brain tryptophan uptake had no effect on time to exhaustion in exercising humans.[110] Furthermore, in this and other studies, the ingestion of large quantities of BCAA also had no effect on endurance performance.[72,110] These data cast some doubt on the 'central fatigue' hypothesis and suggest that BCAA supplementation is not ergogenic during dynamic exercise in humans.

BCAA supplements are marketed for use in horses, but there are no published data regarding their effects on exercise performance per se. Glade[111] reported that BCAA supplementation mitigated the increase in blood lactate during exercise. However, the exercise test involved treadmill walking and the applicability of these results to equine athletic activities is questionable. More recent studies have failed to demonstrate a beneficial effect of BCAA supplementation in horses. The administration of a mixture of L-leucine (9 g), isoleucine (4.5 g) and L-valine (9 g) to Standardbreds 1 h before training had no measurable effect on energy metabolism during intense exercise.[112] Similarly, there were no changes in plasma biochemical variables during and after exercise in horses fed BCAA three times per week for 5 weeks.[113]

Several studies in humans have demonstrated that increased amino acid availability early in the postexercise period modifies protein metabolism in skeletal muscle.[114–117]

Specifically, hyperaminoacidemia resulting from ingestion or intravenous infusion of amino acids increases postexercise muscle protein synthetic rate and prevents the exercise-induced increase in protein degradation. Thus, postexercise amino acid or protein supplementation may promote anabolism in skeletal muscle during conditioning. Neither the effects of exercise in muscle protein metabolism nor the effect of postexercise amino acid or protein supplementation on these processes have been investigated in horses.

Antioxidants

As discussed, exercise has been linked with an increase in free oxygen radical species that may cause cellular damage. Thus, it has been postulated that supplementation of athletes with antioxidants such as vitamin E or vitamin C will increase antioxidant status and confer protection against free radical-associated damage. Although there is evidence in humans that antioxidant supplementation provides some degree of protection during periods of increased stress, such as a sudden increase in training load (see Packer 1997 for review),[32] overall the literature on the effects of antioxidant supplementation is confusing and no clear recommendations have emerged for supplementation strategies in human athletes. Similarly, the performance effects of large-dose antioxidant supplementation in horses are unclear. On the other hand, there is evidence that antioxidant supplementation of horses with recurrent airway obstruction improves antioxidant status and moderates airway inflammation.[118]

References

1. National Research Council, Nutrient requirements of horses. Washington, DC: National Academy of Science; 1989.
2. Pagan JD, Hintz HF. Equine energetics: relationship between body weight and energy requirements in horses. J Anim Sci 1986; 63:815–821.
3. Pagan JD, Hintz HF. Equine energetics. II. Energy expenditure in horses during submaximal exercise. J Anim Sci 1986; 63:822–830.
4. Rose R, Knight PK, Bryden WL. Energy use and cardiorespiratory responses to prolonged submaximal exercise. In: Persson S, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 281–287.
5. Jose-Cunilleras E, Hinchcliff KW, Sams RA, et al. Glycemic index of a meal fed before exercise alters substrate use and glucose flux in exercising horses. J Appl Physiol 2002; 92:117–128.
6. Gallagher K, Leech J, Stowe H. Protein, energy and dry matter consumption by racing Thoroughbreds: a field survey. J Equine Vet Sci 1992; 12:43–48.
7. Southwood L, Evans DL, Bryden WL, et al. Nutrient intake of horses in Thoroughbred and Standardbred stables. Australian Vet J 1993; 70:164–168.
8. Gallagher K, Leech J, Stowe H. Protein, energy and dry matter consumption by racing Standardbreds: a field survey. J Equine Vet Sci 1992; 12:382–386.
9. Taylor L, Ferrante P, Kronfeld D, et al. Acid-base variables during incremental exercise in sprint-trained horses fed a high-fat diet. J Anim Sci 1995; 73:2009.
10. Kearns C, McKeever KH, Kumagai K, et al. Fat-free mass is related to one-mile race performance in elite standardbred horses. Vet J 2002; 163:260–266.
11. Kearns C, McKeever KH, John-Alder H, et al. Relationship between body composition, blood volume and maximal oxygen uptake. Equine Vet J 2002; 34(Suppl):485–490.
12. Lawrence L, Jackson SJ, Kline K, et al. Observations on body weight and condition of horses in a 150-mile endurance ride. J Equine Vet Sci 1992; 12:320–324.
13. Henneke D. A condition score system for horses. Equine Pract 1985; 7:13–15.
14. Garlinghouse S, Burrill MJ. Relationship of body condition score to completion rate during 160 km endurance races. Equine Vet J 1999; 30(Suppl):591–595.
15. Tarnopolsky M. Protein and amino acid needs for training and bulking up. In: Burke L, Deakin V, eds. Clinical sports nutrition. Roseville, NSW, Australia: McGraw-Hill; 2000; 90–123.
16. Graham-Thiers P, Kronfeld DS, Kline KA, et al. Dietary protein restriction and fat supplementation diminish the acidogenic effect of exercise during repeated sprints in horses. J Nutrition 2001; 131:1959–1964.
17. Kronfeld D. Body fluids and exercise: influences of nutrition and feeding management. J Equine Vet Sci 2001; 21:417–428.
18. Miller-Graber P, Lawrence LM, Foreman J, et al. Effect of dietary protein level on nitrogen metabolites in exercised Quarter horses. In: Persson S, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 305–314.
19. Kronfeld D. Dietary fat affects heat production and other variables of equine performance, under hot and humid conditions. Equine Vet J 1996; 22(Suppl):24–34.
20. Nielsen B, Potter GD, Greene LW. An increased need for calcium in young racehorses beginning training. 15th Conference of the Equine Nutrition and Physiology Society, 1997; 153–158.
21. Nolan M, Potter GD, Mathiason KJ, et al. Bone density in the juvenile racehorse fed differing levels of minerals. 17th Conference of the Equine Nutrition and Physiology Society, 2001; 33–36.
22. Porr C, Kronfeld DS, Lawrence LA, et al. Diet and conditioning influence bone development. Equine Pract 2002; 22:18–21.
23. Hintz H, Schryver HF. Nutrition and bone development in horses. J Am Vet Med Assoc 1976; 168:39–44.
24. Aguilera-Tejero E, Estpa JC, Lopez I, et al. M. Plasma ionized calcium and parathyroid hormone concentrations in horses after endurance rides. J Am Vet Med Assoc 2001; 219:488–490.
25. Gottlieb-Vedi M, Dahlborn K, Jansson A, et al. Elemental composition of muscle at rest and potassium levels in muscle, plasma and sweat of horses exercising at 20 degrees C and 35 degrees C. Equine Vet J 1996; 22(Suppl):35–41.
26. Hargreaves B, Kronfeld DS, Waldron JN, et al. Antioxidant status and muscle cell leakage during endurance exercise. Equine Vet J 2002; 34(Suppl):116–121.
27. Stillions M, Teeter SM, Nelson WE. Utilization of dietary B12 and cobalt by mature horses. J Anim Sci 1971; 32:252–256.
28. Ji L. Exercise and oxidative stress: role of the cellular antioxidant systems. Exercise Sports Sci Rev 1995; 23:135–141.

29. Deaton C, Marlin DJ, Roberts CA, et al. Antioxidant supplementation and pulmonary function at rest and exercise. Equine Vet J 2002; 34(Suppl):58–65.
30. Siciliano P, Aparker AL, Lawrence LM. Effect of dietary vitamin E supplementation on the integrity of skeletal muscle in exercised horses. J Anim Sci 1997; 75:1553–1560.
31. Hoffman R, Morgan KL, Phillips A, et al. Dietary vitamin E and ascorbic acid influence nutritional status of exercising polo ponies. 17th Conference of the Equine Nutrition and Physiology Society, 2001; 129–130.
32. Packer L. Oxidants, antioxidant nutrients and the athlete. J Sports Sci 1997; 15:353–363.
33. White A, Estrada M, Walker K, et al. Role of exercise and ascorbate on plasma antioxidant capacity in Thoroughbred racehorses. Comp Biochem Physiol A 2001;128:99–104.
34. Snow D, Gash SP, Cornelius J. Oral administration of ascorbic acid to horses. Equine Vet J 1987; 19:520–523.
35. Loscher W, Jaeschke G, Handel J, et al. Pharmacokinetics of ascorbic acid in horses. Equine Vet J 1984; 16:59–65.
36. Stevens C. Comparative physiology of the vertebrate digestive system. In: Blaxter K, MacDonald, I, eds. Comparative Nutrition. Britol, UK: John Libbey; 1988; 21–36.
37. Goodwin D, Davidson HPB, Harris P. Foraging enrichment for stabled horses: effects on behaviour and selection. Equine Vet J 2002; 34:686–691.
38. McGreevy P, Cripps PJ, Nicol CJ. The prevalence of abnormal behaviours in Dressage, Eventing and Endurance horses in relation to stabling. Vet Rec 1995; 137:36–37.
39. McGreevy P, Cripps PJ, French NP, et al. Management factors associated with stereotypic and redirected behaviour in the Thoroughbred horse. Equine Vet J 1995; 27:86–91.
40. Meyer H. Nutrition of the equine athlete. In: Robinson N, ed. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 644–673.
41. Whitlock R. Feed additives and contaminants. Vet Clin North Am Equine Pract 1990; 6:467–478.
42. Kienzle E, Radicke S, Landes E, et al. Activity of amylase in the gastrointestinal tract of the horse. J Anim Physiol Nutrit 1994; 72:234–241.
43. Potter G, Arnold FF, Householder DD, et al. Digestion of starch in the small or large intestine of the equine. Pferdeheilkunde 1992; 1:107–111.
44. Dyer J, Fernandez-Castano ME, Salmon KS, et al. Molecular characterization of carbohydrate digestion and absorption in equine small intestine. Equine Vet J 2002; 34:349–358.
45. Clarke L, Roberts MC, Argenzio RA. Feeding and digestive problems in horses: physiologic responses to a concentrated meal. Vet Clin North Am Equine Pract 1990;6:433–450.
46. Cuddeford D. Starch digestion in the horse. In: Pagan J, Geor RJ, eds. Advances in equine nutrition II. Nottingham: Nottingham Press; 2001; 95–104.
47. Tinker M, White NA, Lessard P, et al. Prospective study of equine colic risk factors. Equine Vet J 1997; 29:454–458.
48. Hudson J, Cohen ND, Gibbs PG, et al. Feeding practices associated with colic in horses. J Am Vet Med Assoc 2001; 219:1419–1425.
49. McKenzie E, Valberg SJ, Pagan JD. Nutritional management of exertional rhabdomyolysis. In: Robinson N, ed. Current therapy in equine medicine 5. Philadelphia, PA: Saunders; 2003; 727–734.
50. Meyer H, Radicke S, Kienzle E, et al. Investigations on preileal digestion of starch from grain, potato and manioc in horses. Zentralbl Veterinarmed A 1995; 42:371–381.
51. Bowman V, Fontenot JP, Meacham TN, et al. Acceptability and digestibility of animal, vegetable and blended fats by equine. 6th Conference of the Equine Nutrition and Physiology Symposium, 1979; 74.
52. Holland J, Kronfeld DS, Rich GA, et al. Acceptance of fat and lecithin containing diets by horses. Appl Anim Behav Sci 1998; 56:91–96.
53. Kronfeld D, Holland JL, Rich GA, et al. Digestibility of fat. 17th Conference of the Equine Nutrition and Physiology Symposium, 2001; 156–158.
54. Harris PA, Kronfeld DK. Influence of dietary energy sources on health and performance. In: Robinson N, ed. Current therapy in equine medicine 5. Philadelphia, PA: Saunders; 2003; 698–704.
55. Dunnett C, Marlin DJ, Harris RC. Effect of dietary lipid on response to exercise: relationship to metabolic adaptation. Equine Vet J 2002; 34(Suppl):75–80.
56. Pagan J, Geor RJ, Harris PA, et al. Effects of fat supplementation on glucose kinetics and substrate oxidation during low intensity exercise. Equine Vet J 2002; 34(Suppl):33–38.
57. Jansen W, van der Kuilen J, Geelen SN, et al. The apparent digestibility of fiber in trotters when dietary soybean oil is substituted for an isoenergetic amount of glucose. Arch Tierernahr 2001; 54:297–304.
58. Roberts M. Carbohydrate digestion and absorption studies in the horse. Res Vet Sci 1975; 18:64–69.
59. Sunvold G, Hussein HS, Fahey Jr GC, et al. In vitro fermentation of cellulose, beet pulp, citrus pulp and citrus pectin using fecal innoculum from cats, dogs, horses, humans and pigs and ruminal fluid from cattle. J Anim Sci 1995; 73:3639–3648.
60. Moore-Colyer M, Longland AC. The effect of plain sugar beet pulp on in vitro gas production and the in vivo apparent digestibility of hay when offered to ponies. 17th Conference of the 17th Equine Nutrition and Physiology Society, 2001; 145–147.
61. Lindberg J, Palmgren-Karlsson C. Effect of replacing oats with sugar beet pulp and maize oil on nutrient utilisation in horses. Equine Vet J 2001; 33:585–590.
62. Lindberg J, Jacobsson KG. Effects of barley and sugar beet pulp on digestibility, purine excretion and blood parameters in horses. Pferdeheilkunde 1992; 1:116–118.
63. Palmgren-Karlsson C, Jansson A, Essen-Gustavsson B, et al. Effect of molassed sugar beet pulp on nutrient utilisation and metabolic parameters during exercise. Equine Vet J 2002; 34(Suppl):44–49.
64. Valberg S, Mickelson JR, Gallant EM, et al. Exertional rhabdomyolysis in quarter horses and thoroughbreds: one syndrome, multiple aetiologies. Equine Vet J 1999; 30(Suppl): 533–538.
65. Valentine B, Hintz HF, Freels KM, et al. Dietary control of exertional rhabdomyolysis in horses. J Am Vet Med Assoc 1998; 212:1588–1593.
66. Valentine B, Van Saun RJ, Thompson KN, et al. Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. J Am Vet Med Assoc 2001; 219:1537–1544.
67. MacLeay J, Valberg S, Pagan JD, et al. Effect of diet on Thoroughbred horses with recurrent exertional rhabdomyolysis. Equine Vet J 1999; 30(Suppl):458–462.
68. MacLeay J, Valberg S, Pagan JD, et al. Effect of ration and exercise on plasma creatine kinase activity and lactate concentration in Thoroughbred horses with recurrent exertional rhabdomyolysis. Am J Vet Res 2000; 61:1390–1395.
69. de la Corte F, Valberg SJ, MacLeay JM, et al. Glucose uptake in horses with polysaccharide storage myopathy. Am J Vet Res 1999; 60:458–462.

70. de la Corte F, Valberg SJ, Mickelson JR, et al. Blood glucose clearance after feeding and exercise in polysaccharide storage myopathy. Equine Vet J 1999; 30(Suppl):324–328.
71. McKenzie E, Valberg SJ, Godden SM, et al. Effects of dietary starch, fat, and bicarbonate on exercise responses and serum creatine kinase activity in equine recurrent exertional rhabdomyolysis. J Vet Int Med 2003; 17:693–701.
72. Wagenmakers A. Nutritional supplements: effects on exercise performance and metabolism. In: Lamb D, Murray, R, eds. Perspectives in exercise science and sports medicine. The metabolic basis of performance in exercise and sport. Carmel, IN: Cooper Publishing; 1999; 207–260.
73. Harris P, Harris RC. Nutritional ergogenic aids in the horse: uses and abuses. In: Pagan J, Geor RJ, eds. Advances in equine nutrition II. Nottingham: Nottingham Press 2001; 491–507.
74. Bergstrom J, Hermansen L, Hultman E, et al. Diet, muscle glycogen and physical performance. Acta Physiol Scand 1967; 71:140–150.
75. Hargreaves M. Metabolic responses to carbohydrate ingestion: effects on exercise performance. In: Lamb D, Murray, R, eds. Perspectives in exercise science and sports medicine. The metabolic basis of performance in exercise and sport. Carmel, IN: Cooper Publishing; 1999; 93–124.
76. Hawley J, Schabort EJ, Noakes TD, et al. Carbohydrate-loading and exercise performance. An update. Sports Med 1997; 24:73–81.
77. Topliff D, Potter GD, Dutson TR, et al. Diet manipulation and muscle glycogen in the equine. Proceedings of the 8th Equine Nutrition and Physiology Symposium, 1983; 224–229.
78. Lacombe V, Hinchcliff KW, Geor RJ, et al. Muscle glycogen depletion and subsequent replenishment affect anaerobic capacity of horses. J Appl Physiol 2001; 91:1782–1790.
79. Farris J, Hinchcliff KW, McKeever KH, et al. Effect of tryptophan and of glucose on exercise capacity of horses. J Appl Physiol 1998; 85:807–816.
80. Sherman W, Costill DL, Fink WJ, et al. Effects of exercise-diet manipulation on muscle glycogen and its subsequent utilization during performance. Int J Sports Med 1981; 2:114–118.
81. Burke L. Preparation for competition. In: Burke L, Deakin V, eds. Clinical sports nutrition. Roseville, NSW: McGraw-Hill; 2000; 341–368.
82. Pagan J, Essen-Gustavsson B, Lindholm A, et al. The effect of dietary energy source on exercise performance in Standardbred horses. In: Robinson N, ed. Equine exercise physiology 2. Davis, CA: ICEEP Publishing; 1987; 686–700.
83. Essen-Gustavsson B, Blomstrand E, Karlstrom K, et al. Influence of diet on substrate metabolism during exercise. In: Persson S, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 288–298.
84. Davie A, Evans DL, Hodgson DR, et al. Effects of intravenous dextrose infusion on muscle glycogen resynthesis after intense exercise. Equine Vet J 1995; 18(Suppl):195–198.
85. Davie A, Evans DL, Hodgson DR, et al. The effects of an oral glucose polymer on muscle glycogen resynthesis in Standardbred horses. J Nutrition 1994; 124:2740S–2741S.
86. Davie A. The energy supply for exercise in horses and factors influencing glycogen resynthesis in equine skeletal muscle. PhD dissertation, University of Sydney; 1996.
87. Snow D, Harris RC, Harman JC, et al. Glycogen repletion following different diets. In: Robinson N, ed. Equine exercise physiology 2. Davis, CA: ICEEP Publishing; 1987; 701–706.
88. Lacombe V, Hinchcliff KW, Kohn CW, et al. Post-exercise feeding of meals of varying glycemic index affects muscle glycogen resynthesis in horses. J Vet Int Med 2002; 16:336 (abstract).
89. Hyyppa S, Rasanen LA, Poso AR. Resynthesis of glycogen in skeletal muscle from Standardbred trotters after repeated bouts of exercise. Am J Vet Res 1997; 58:162–166.
90. Snow D, Harris RC. Effects of daily exercise on muscle glycogen in the Thoroughbred racehorse. In: Persson S, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 299–304.
91. Geor RJ, Hinchcliff KW, McCutcheon LJ, et al. Epinephrine inhibits exogenous glucose utilization in exercising horses. J Appl Physiol 2000; 88:1777–1790.
92. Meyer H, Coenen M. Influence of exercise on the water and electrolyte content of the alimentary tract. 11th Conference of the Equine Nutrition and Physiology Symposium, 1989; 3–7.
93. Warren L, Lawrence LM, Roberts A, et al. The effect of dietary fiber on gastrointestinal fluid volume and the response to dehydration and exercise. 17th Conference of the Equine Nutrition and Physiology Symposium, 2001; 148–149.
94. Rice O, Geor R, Harris P, et al. Effects of restricted hay intake on body weight and metabolic responses to high-intensity exercise in Thoroughbred horses. 17th Conference of the Equine Nutrition and Physiology Society, 2001; 273–279.
95. Maughan R. The athlete's diet: nutritional goals and dietary strategies. Proc Nutrition Soc 2002; 61:87–96.
96. Greenhaff P. Creatine. In: Maughan R, ed. Nutrition in sport. Oxford, UK: Blackwell Science; 2000; 367–378.
97. Hultman E, Soderlund K, Timmons JA, et al. Muscle creatine loading in men. J Appl Physiol 1996; 81:232–237.
98. Harris R, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle in normal subjects by creatine supplementation. Clin Sci 1992; 83:367–374.
99. Green A, Simpson EJ, Littlewood JJ, et al. Carbohydrate ingestion augments creatine retention during creatine feeding in man. Acta Physiol Scand 1996; 158:195–202.
100. Schuback K, Essen-Gustavsson B, Persson SGB. Effect of creatine supplementation on muscle metabolic response to a maximal treadmill exercise test in Standardbred horses. Equine Vet J 2000; 32:533–540.
101. Sewell D, Harris RC. Effect of creatine supplementation in the Thoroughbred horse. Equine Vet J 1995; 18(Suppl): 239–242.
102. Brass E. Supplemental carnitine and exercise. Am J Clin Nutrition 2000; 77(Suppl):618S–623S.
103. Forster C, Harris RC, Snow DH. Total carnitine content of the middle gluteal muscle of Thoroughbred horses: normal values, variability and effect of acute exercise. Equine Vet J 1992; 24:52–57.
104. Ceretelli P, Marconi C. L-carnitine supplementation in humans: the effects on physical performance. Int J Sports Med 1990; 11:1–14.
105. Forster C, Harris RC, Snow DH. The effect of oral L-carnitine supplementation on the muscle and plasma concentration in the Thoroughbred horse. Comp Biochem Physiol A 1988; 91:827–835.
106. Harris R, Forster CV, Snow DH. Plasma carnitine concentration and uptake into muscle with oral and intravenous administration. Equine Vet J 1995; 18(Suppl): 382–387.
107. Rivero J, Sporleder HP, Quiroz-Rothe E, et al. Oral L-carnitine combined with training promote changes in skeletal muscle. Equine Vet J 2002; 34(Suppl):269–274.
108. Blomstrand E, Hasseman P, Ek S, et al. Influence of ingesting a solution of branched-chain amino acids on perceived exertion during exercise. Acta Physiol Scand 1997; 159:41–49.

109. Davis J. Carbohydrates, branched-chain amino acids and endurance: the central fatigue hypothesis. Int J Sports Med 1995; 5(Suppl):S29–S38.
110. Van Hall G, Raaymakers JSH, Saris WHM, et al. Ingestion of branched-chain amino acids and tryptophan during sustained exertion: failure to affect performance. J Physiol 1995; 486:789–794.
111. Glade M. Effects of specific amino acid supplementation on lactic acid production by horses exercised on a treadmill. 11th Conference of the Equine Nutrition and Physiology Symposium, 1989; 244–248.
112. Stefanon B, Bettini P, Guggia P. Administration of branched-chain amino acids to Standardbred horses in training. J Equine Vet Sci 2000; 20:115–119.
113. Casini L, Gatta L, Magni B, et al. Effect of prolonged branched-chain amino acid supplementation on metabolic response to anaerobic exercise in Standardbreds. J Equine Vet Sci 2000; 20:120–123.
114. Rennie M, Tipton KD. Protein and amino acid metabolism during and after exercise and the effects of nutrition. Ann Rev Nutrition 2000; 20:457–483.
115. Tipton K, Ferrando AA, Phillips SM, et al. Postexercise net protein synthesis in human muscle from orally administered amino acids. Am J Physiol 1999; 276:E628–E634.
116. Tipton K, Rasmussen BB, Miller SL, et al. Timing of amino acid-carbohydrate ingestion alters anabolic response of muscle to resistance exercise. Am J Physiol 2001; 281:E197–E206.
117. Volpi E, Ferrando AA, Yeckel CW, et al. Exogenous amino acids stimulate net muscle protein synthesis in the elderly. J Clin Invest 1998; 101:2000–2007.
118. Kirschvink N, Fievez L, Bougnet V, et al. Effect of nutritional antioxidant supplementation on systemic and pulmonary antioxidant status, airway inflammation and lung function in heaves-affected horses. Equine Vet J 2002; 34:705–712.

CHAPTER 37

Metabolic diseases of athletic horses

Seppo Hyyppä and A. Reeta Pösö

Exhausted horse syndrome

- Occurs in events that require sustained (endurance) exercise.
- Clinical signs include depression, hyperthermia, delayed recovery of heart rate, muscle fasciculations and soreness, shortened stride and increased capillary refill time.
- Treatment focuses on correction of fluid and electrolyte deficits and aggressive cooling of the overheated horse.
- Despite extensive supportive care, severely affected horses may die.

Recognition

In events that require sustained exercise, horses are sometimes pushed past their performance limit and show signs of what has been termed the exhausted horse syndrome.

History and presenting complaint

The syndrome begins with subtle signs of distress: changes in the sensory state and attitude of the horse, mild muscle soreness and small inconsistencies in gait. If exercise is continued, signs will become more and more pronounced. Muscles start to show localized hardening and pain on palpation, the gait becomes stiff and stilted, muscle spasms and cramps may occur, as may synchronous diaphragmatic flutter. Severely affected horses are often unwilling to continue to exercise and are depressed. They may even show inco-ordination (ataxia) or become recumbent.

Physical examination

Temperature, heart and respiratory rates are elevated and after cessation of exercise show a delayed return to resting values. Although the heart and respiratory rates of an exhausted and a non-exhausted horse may be similar immediately following exercise, these rates return to normal (heart rate under 60 bpm, respiratory rate under 25 breaths/min) within 10–20 minutes of recovery in the non-exhausted horse but not in the exhausted one. Rectal temperature may be 42°C or higher. However, measured rectal temperature may be lower than true body temperature if the horse has diminished anal sphincter tone. Respiratory rate is elevated in an attempt to increase respiratory heat loss; heart rate is elevated to maintain cardiac output. Auscultation of the heart may reveal cardiac irregularities, capillary refill time is increased and both pulse pressure and jugular distensibility are decreased. Dehydration is expressed clinically as decreased skin turgor, sunken eyes, dry mucous membranes, firm, dry feces and decreased urine output. Mild signs of dehydration usually become apparent at a body water deficit of 4–5%. Subjectively, the sweating response may appear inappropriate relative to the level of hyperthermia (e.g. a patchy appearance or, in severe cases, a hot and dry coat). Despite significant dehydration, affected horses often are not interested in water or feed. Intestinal stasis commonly occurs with decreased or absent boborygmi, poor anal tone and, occasionally, colic.

In severely affected horses, a number of serious complications may develop immediately or over the following 1–4 days. These include exertional rhabdomyolysis, renal failure secondary to muscle necrosis and myoglobinuria, hepatic dysfunction, gastrointestinal dysfunction, laminitis and central nervous system disorders. Despite intensive supportive care, the horse may die.

Laboratory examination

In an exhausted horse, routine hematology reveals increased packed cell volume and plasma protein concentration due to dehydration. Serum or plasma biochemical analysis may

show normo- or slight hyponatremia, hypokalemia, hypocalcemia (ionized), hypochloremia and associated metabolic alkalosis.[1] Three-day event and combined driving horses have metabolic acidosis until excess lactate is oxidized. As a result of muscle exertion or damage, increases in muscle enzyme activity and plasma phosphorus concentration may be evident. Plasma creatinine values may be elevated, suggesting a reduction in glomerular filtration rate because of dehydration. Urine samples appear dark due to myoglobin, hematuria, proteinuria and glycosuria.[2,3]

Necropsy examination

Necropsy findings include skeletal and myocardial muscle damage, gastrointestinal ulceration, renal necrosis and sometimes renal infarction as well as laminitis.[4]

Treatment and prognosis

Therapeutic aims

Cooling the overheated horse and fluid therapy to replace fluid losses and to assist in restoration of circulating blood volume are essential components of therapy.

Therapy

Exercise must cease to minimize further damage and a horse with marked elevation in rectal temperature (41°C or greater) should be cooled down as quickly as possible. Repeated application of cool or cold water by sponges or by hosing down and ventilation via a natural breeze or a fan will enhance heat loss via convection and evaporation. Ice-water enemas can be effective in a severely compromised patient. Cooling should continue until the body temperature is reduced to nearly normal (< 39°C).

For mildly affected horses, rest together with cooling out and access to water, salt and feed may be sufficient, but if no improvement occurs within 30 minutes, fluid therapy is required. In severe cases, fluid therapy should be started immediately. Under most circumstances, it is better to treat a horse in the field and not to attempt a trailer ride until it has been rehydrated. The severely dehydrated horse will need 30–80 L of fluid. In many cases, however, after the first 15–20 L the horse will start to drink and eat and be able to restore the remaining deficit itself.

Oral administration offers the advantages of speed and convenience and can be used if the horse has normal gut sounds. Via nasogastric tube, 5–8 L of fluid can be given every 30–60 min until the horse shows signs of improvement. Oral administration can be started immediately after exercise, because consumption of 10–15 L of cool (~ 16°C) water within 3–5 min of completing exercise is not harmful.[5] Isotonic solutions containing sodium, potassium, calcium, chloride and glucose are often well tolerated and fairly rapidly absorbed. Commercial electrolyte powders should be those formulated for horses. For example, electrolyte formulations designed for use in calves with diarrhea usually contain bicarbonate, lactate or citrate. Therefore, these preparations are not the best choice for the treatment of horses with exercise-induced dehydration because of their alkalinizing effects. Hypertonic solutions should also be avoided, because they may cause a transient reduction in plasma volume due to movement of water into the bowel lumen.[6] Oral administration should be halted if any discomfort or gastric reflux becomes apparent.

If the horse is severely compromised, gut sounds are absent or gastric reflux is evident, intravenous (i.v.) fluids are indicated. An i.v. catheter should be placed in a jugular vein. The rate of fluid administration will depend on the extent of hypovolemia and dehydration. In severely affected horses, a second catheter may be inserted to facilitate a rapid rate of fluid administration (~ 20 L/h) during the first hour. In less compromised patients, 8–10 L/h is a suitable initial rate of fluid administration. Preferred fluids are isotonic or only slightly hypertonic solutions containing sodium, potassium, chloride, calcium and glucose (e.g. Ringer's solution with 5% glucose). An alternative is 0.9% saline with glucose and potassium added: 1–3 g of potassium chloride/L and 5–10 g of glucose/L.[4] The added glucose will also assist in the replacement of energy deficits. Because these horses often have metabolic alkalosis, lactated Ringer's solution or sodium bicarbonate solution is not the best choice, especially in a severely compromised patient. In hypoproteinemic horses (e.g. secondary to diarrhea or renal disease), colloids and/or plasma may be necessary to limit development of pulmonary or peripheral edema.[7]

Sometimes non-steroidal anti-inflammatory agents (NSAIDs) and phenothiazine derivatives such as

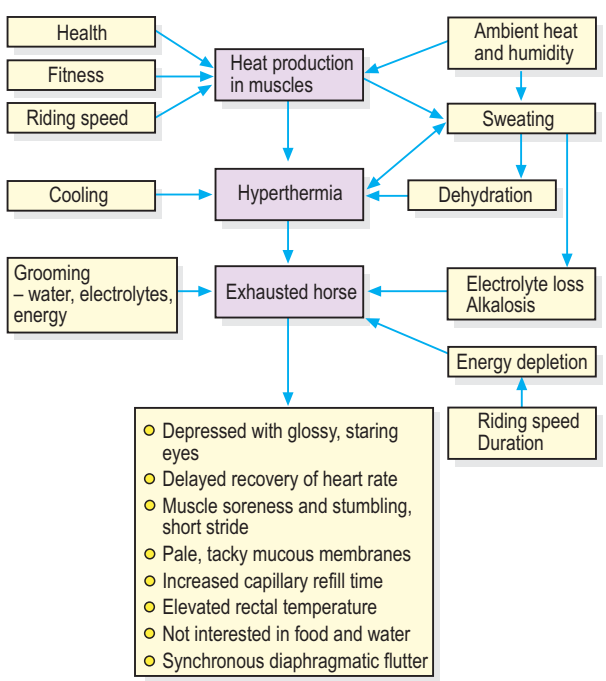

Fig. 37.1
Both internal and external factors contribute to dehydration, electrolyte loss and overloading which, if untreated, may lead to the exhausted horse syndrome.

acepromazine are required to control muscle pain and anxiety. As dehydration and hypovolemia increase the risk for NSAID toxicity, these agents should be administered only in conjunction with fluid therapy. Flunixin meglumine (0.5–1.0 mg/kg), phenylbutazone (2.2–4.4 mg/kg) or ketoprofen (0.5–1.0 mg/kg) can be used. Parenteral dimethylsulfoxide (DMSO) may be administered for its anti-inflammatory effects.[7] Corticosteroids may be indicated in severe cases with shock and possible pulmonary edema. Heparin (30 000 IU three times daily s.c.) may be useful to prevent or treat the effects of hypercoagulability.[7]

About 50 g of a non-iodized salt (NaCl) and 25 g of potassium chloride should be added to the grain/concentrate and fed twice a day for several days. During treatment the horse should be moved as little as possible and severely affected horses should be rested for several weeks afterwards.

Prognosis

Prognosis is good for mildly and moderately affected horses, but severely affected horses may die.

Etiology and pathophysiology

The main underlying causes of the syndrome are dehydration, electrolyte loss and overheating. Depletion of energy stores in endurance horses, especially during 100 km or longer rides,[8] and high lactate production in event and driving horses may contribute to the onset of exhaustion.

Dehydration occurs as a result of heat dissipation. Physical exercise leads to considerable heat production, because only 20–25% of the energy utilized in muscles is converted to mechanical energy. Evaporation of sweat is the most efficient means of heat loss during exercise and may be the only means of heat dissipation in a hot environment. The amount of sweat produced depends on the horse's size and fitness, on work intensity and the environmental conditions. Under cool climatic conditions, horses may sweat 5–8 L/h but in hot weather sweat production may amount to 10–15 L/h when activity levels are maintained at a high rate (e.g. 15 km/h). During endurance competitions, horses routinely lose 4–7% of their bodyweight but in hot conditions, net water loss may be about 40 L or close to 10% of bodyweight.[9] Respective values during the endurance phase of three-day eventing range from 2% to 4% of bodyweight under normal conditions[10] and in hot conditions deficits greater than 9% of bodyweight have been reported.[11] During sweating, water is mainly lost from the extracellular fluid and the consequent decreases in blood and plasma volumes[12] can reduce perfusion in skeletal muscle and in other vital organs. Inadequate tissue perfusion leads to inefficient oxygen and substrate transport, and hampers thermoregulation. If severe, this cardiovascular compromise may contribute to impaired renal function and partial renal shutdown.

Sweating-induced dehydration is always accompanied by electrolyte loss. Equine sweat is isotonic or slightly hypertonic relative to plasma and contains high concentrations of sodium, potassium and chloride and also some calcium and magnesium.[9] Abundant sweating will incur significant ion deficits; these will lead to alterations in skeletal muscle ion content, increasing the potential for muscular dysfunction and contributing directly to fatigue.[13]

Because of sweating, the most consistent acid–base alteration associated with endurance horses in a hot environment is metabolic alkalosis. These horses exercise at moderate work intensities at a fairly constant speed between 10 and 20 km/h and rely almost totally on aerobic energy metabolism, producing very little or no lactate. Typical plasma lactate concentrations during such exercise are 1.0–3.3 mmol/L.[14] The degree of metabolic alkalosis is dependent on the severity of hypochloremia and hypokalemia.[4] Hypochloremia is associated with an increase in plasma bicarbonate because in the kidney when chloride concentration is low, bicarbonate (HCO_3^-) is resorbed. As plasma sodium concentration tends to decrease due to loss in sweat, the kidney conserves sodium at the expense of potassium and hydrogen ions, which also contributes to the alkalosis.[4] Potassium, magnesium, and calcium depletion associated with metabolic alkalosis may alter membrane potential and neuromuscular transmission, contributing to gastrointestinal stasis, cardiac arrhythmias and muscle cramps and spasms including synchronous diaphragmatic flutter.[9]

The situation differs during the endurance phase in three-day eventing and the marathon phase in combined driving, during which anaerobic metabolism significantly contributes to energy transduction, plasma lactate concentrations are very high (up to 38.5–40.2 mmol/L)[15,16] and horses develop metabolic acidosis. After exercise, the acidosis is resolved through oxidation of lactate during a 30-min to 2-h period. Thereafter, metabolic alkalosis prevails.[10]

In an effort to maintain blood volume, significant dehydration and electrolyte loss result in impairment in the efficiency of sweating and evaporative cooling. Heat dissipation is markedly compromised when dehydration is severe (> 10% of bodyweight).[17] If exercise is continued, the thermoregulatory system will be overwhelmed and this will lead to an excessive elevation of body temperature (hyperthermia). Ultimately this may cause life-threatening heat stroke, with damage to the central nervous system. Heat stroke is more often observed in three-day horses and combined driving horses that do fast anaerobic work at a high rate of heat production, but it may also occur in endurance horses.

Epidemiology

Exhausted horse syndrome is most often seen in association with long-distance riding, but may also be seen in horses competing in the endurance phase of three-day eventing or in the marathon phase of combined driving, in which horses perform moderate- and high-intensity exercise for a period of 1–2 hours, depending on the level of competition. As ambient temperature and humidity and the duration of exercise increase, the incidence of exhausted horse syndrome rises. For example, in 160 km endurance rides, about half the

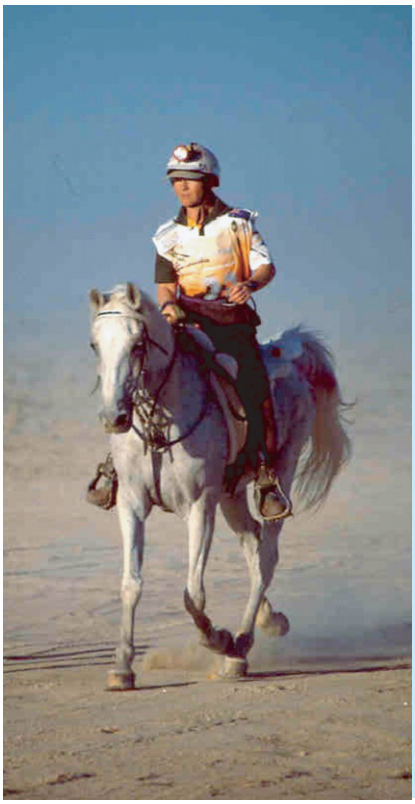

Fig. 37.2 Endurance ride is a competition to test the speed and endurance ability of a horse. But equally important is the horsemanship of the rider so that he understands the physiology of the horse and can take care of him during a competition. Horse and rider approaching the first veterinary check point in good condition during the World Endurance Championship 1998 in the United Arab Emirates. (Photo by S. Hyyppä.)

horses may retire from the competition or be eliminated at veterinary checks.[18]

Prevention

The first prerequisite for a successful endurance competition is that the horse is truly fit and healthy. Mild, undetected lameness may cause a horse to compensate and overuse some muscle groups. Pain also may lead to peripheral vasoconstriction and poor blood flow. These factors may contribute to the onset of exhaustion. But even fit and healthy horses may be over-ridden. Therefore, in the heat of competition riders have to keep a cool head and be alert to any changes in the condition of their horse.

During transport, a horse typically experiences substantial loss of weight (approximately 3 kg/h of transport) and will become dehydrated.[5] The horse therefore requires sufficient time to recover from a long trailer ride such that hydration state and electrolyte balance are normal at the start of the event.

Hyperhydration prior to exercise has been shown to be beneficial in human athletes who exercise for prolonged periods, but it is difficult to achieve in horses because they refuse to drink excess amounts of water and electrolyte solutions voluntarily. Such fluids can therefore be supplied only by nasogastric intubation or intravenously. This may, however, be forbidden by doping regulations.

Athletic horses do not regulate their salt intake according to need, at least not when offered salt from salt blocks.[19] It is therefore wise to include salt and other electrolyte supplements in their diet. Electrolyte loading by feeding supplemental electrolytes for several days prior to competition is not effective because the kidneys readily excrete excess electrolytes within a few hours of administration. Nevertheless, electrolytes administered in the few hours immediately before a prolonged exercise competition may be of benefit if adequate water is also ingested.[6]

During the endurance ride, it is critical to give the horse a chance to drink as often as possible. Horses should be taught to drink electrolyte solutions because plain water, although better than nothing at all, is inadequate. Water intake without electrolyte replacement exacerbates dilution of sodium in the extracellular fluid such that the osmotic thirst stimulus is mitigated. An isotonic, polyionic electrolyte solution that replaces some of the electrolyte deficit is therefore more beneficial. Frequent sponging of the horse with cool water will assist in evaporative heat loss and cool the horse. However, riders should keep in mind that especially during warm and hot climatic conditions, even when a horse is a good drinker, it is impossible to compensate for all the losses during the ride. It is therefore important to monitor the horse very carefully and adjust the speed accordingly or retire from the ride if necessary.

In the endurance phase of three-day eventing and in the marathon phase of combined driving, the sequence of the competitions does not allow for proper rehydration because the 10-minute rest occurs towards the end of the ride. It is unlikely that fluid consumed at this point will be absorbed in time to significantly assist rehydration and thus improve performance. On the contrary, if a large volume of fluid is given, the extra weight that the horse must carry could limit performance during the last part of the competition. Therefore, in hot weather, the best strategy is to use the rest periods to effectively cool the horse.

During the recovery period, the fullest restoration of fluid losses can be achieved by the inclusion of salts in the ration and by allowing free access to both isotonic electrolyte solution and water. Achieving complete replenishment of fluid and electrolytes is important because in the case of multiday rides, horses may fail to replenish bodyweight losses overnight and may enter the next day's competition with some degree of dehydration. Our own studies have shown that a persistent bodyweight deficit of 2% or more impairs performance on the following day.[12]

Good veterinary supervision is vital to prevent horses from being over-ridden by excessively ambitious riders. At vet gates, horses must be carefully monitored when deciding whether they are 'fit to continue'. Attending veterinarians should also be well prepared to handle any metabolic disorders and other problems that may occur.

Synchronous diaphragmatic flutter (thumps)

- Occurs in events that require sustained exercise.
- Clinical signs include a rhythmic convulsive motion in one or both flanks that is synchronous with each heart beat.

- Treatment consists of fluid therapy to replace loss by sweating.
- It is not a life-threatening condition, but may lead to more dangerous metabolic problems if exercise is continued.

Recognition

History and presenting complaint

Synchronous diaphragmatic flutter (SDF) is evident as a rhythmic movement, twitching or convulsive motion in one or both flanks of the horse that is synchronous with each heart beat. Signs of dehydration and exhaustion often accompany SDF.

Laboratory examination

Typical laboratory findings include hypocalcemia (ionized), slight hyponatremia, hypokalemia, hypochloremia, hypomagnesemia and hyperphosphatemia. Hemoconcentration and metabolic alkalosis are also commonly observed.

Treatment and prognosis

Therapy

Synchronous diaphragmatic flutter may resolve on its own and no treatment is required provided the animal is eating and drinking voluntarily. If treatment is required, calcium administered by slow intravenous injection will frequently result in rapid recovery. Normally 100–300 mL of 20% calcium borogluconate is sufficient.[20] The heart must be continuously auscultated during this procedure for assessment of heart rate and rhythm: if irregularities develop, calcium administration should be discontinued.

When SDF occurs in association with sustained athletic stress, many horses will also respond to treatment with isotonic or slightly hypertonic polyionic fluids (Ringer's with 5% glucose; regular saline with some glucose and potassium added: 1–3 g of potassium chloride/L and 10 g of glucose/L) administered intravenously.[4] This treatment offers less chance of cardiac problems than with the i.v. 20% calcium borogluconate infusion.

Prognosis

Synchronous diaphragmatic flutter is not a life-threatening condition but does indicate an electrolyte imbalance which, if allowed to progress, may lead to more dangerous metabolic problems.

Etiology and pathophysiology

Alterations in acid–base and electrolyte balance may alter the membrane potential of the phrenic nerve, allowing it to discharge in response to an electrical impulse associated with atrial depolarization. Such stimulation is possible because the phrenic nerve, which originates in the cervical spine, courses over the atria before terminating in the diaphragm.

After prolonged exercise, particularly in the heat, large quantities of sodium, potassium and chloride and also some calcium and magnesium are lost in sweat[9] and horses develop metabolic alkalosis. Alkalosis increases binding of calcium to albumin and thus less calcium is present in ionized form. In addition, stress and subsequent increases in cortisol may lower calcium levels. The resultant hypocalcemia, especially that of ionized calcium, affects sodium channels in neurons and results in a lowered threshold potential of the phrenic nerve, thus allowing depolarization.[9]

Synchronous diaphragmatic flutter often occurs following a rest stop because if the horse is rehydrated without electrolyte intake, the water replenishment further dilutes Ca^{++} and K^{+} and exacerbates metabolic alkalosis.

Epidemiology

Synchronous diaphragmatic flutter is most often associated with sustained athletic stress but may also be seen in colic, lactation tetany, shipping, blister beetle toxicosis and urethral obstruction.[21] It may occur following administration of furosemide and sodium bicarbonate.[22]

Prevention

Dietary supplementation with calcium and other electrolytes is recommended in horses used for prolonged exercise tasks. However, excessive calcium feeding (e.g. alfalfa hay diets) is generally not recommended because high calcium intake may reduce the activity of calcium homeostatic mechanisms. During prolonged exercise, frequent consumption of balanced ion solutions to avoid extreme electrolyte depletion will reduce the incidence of SDF as well as that of other metabolic problems.

Synchronous diaphragmatic flutter is a sign of metabolic problems and exercise should be discontinued to prevent development of more serious disorders. In endurance competitions, SDF is a sufficient reason for elimination of the horse from the competition.

Hormonal disturbances

Endocrine dysfunction as a cause of reduced performance in horses is poorly documented. Much has been made of hypothyroidism and adrenal exhaustion, but few data support their existence.

Thyroid gland

Hypothyroidism

- Controversy exists over its true incidence in sport horses.
- Clinical signs attributed to hypothyroidism include weight gain, poor performance and myopathies.

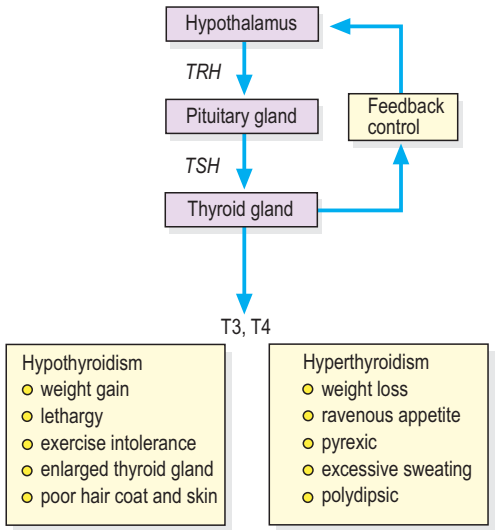

Fig. 37.3
Release of thyroid hormones is under the control of hypothalamic and pituitary hormones, with the release of those being under negative feedback regulation by thyroid hormones. Both low and high concentrations of thyroid hormones may be harmful as indicated by the signs of hypo- and hyperthyroidism.

- Diagnosis should never be based on a single low thyroid hormone value.
- Treatment consists of ascertaining adequate dietary intake of iodine and supplementation with thyroid hormones.

Recognition

Hypothyroidism is defined as a deficiency in thyroid activity. It has been identified as a cause of poor performance and myopathies in racing horses.[23]

History and presenting complaint

Clinical signs frequently attributed to hypothyroidism include weight gain, lethargy, poor coat and skin, cresty neck, exercise intolerance, exertional rhabdomyolysis, laminitis, fertility problems, agalactia, retarded growth and enlarged thyroid glands (goiter).[24,25] In most adult horses the thyroid glands, which are located at the dorsal aspect of the trachea just distal to the pharynx and made of two discrete firm lobes connected by a narrow isthmus, are barely detectable by palpation.

Signs similar to those attributed to hypothyroidism are seen in adult horses after thyroidectomy. These include reduced resting heart and respiratory rates, resting body temperature and cardiac output, but increased blood and plasma volumes.[26] Thyroidectomized horses develop edema of the rear limbs, a dull and coarse coat and lethargy.[27] After thyroidectomy, changes occur also in blood lipid concentrations: triglycerides and total cholesterol increase and non-esterified fatty acids decrease.[28]

Laboratory examination

Diagnostic testing is often limited to measurement of total and free tri-iodothyronine (T3) and thyroxin (T4) concentrations. In the circulation, the thyroid hormones are bound to plasma proteins, with free thyroid hormones constituting only about 1% of the total. Reported reference ranges for normal horses are 0.32–1.23 nmol/L for total T3 and 15–74 nmol/L for total T4 concentrations.[29] However, hypothyroidism should never be diagnosed on the basis of a single low value, because several factors influence the concentrations of T3 and T4. Circulating levels show some diurnal variation, because thyroid-stimulating hormone (TSH) is released in a pulsed manner and mainly in the afternoons.[30] Thyroid activity increases as horses acclimatize to colder climates and decreases as horses acclimatize to warmer climates. After a high carbohydrate diet, serum T3 increases and serum T4 decreases[24] and prolonged food restriction results in decreases in total and free T3 concentrations.[31] González and co-workers[32] reported a sudden increase in T3 in response to an acute race stress and Irvine[33] reported T4 to increase with training. In mares, stage of estrus cycle also affects T4 concentrations.[24] Most importantly, any concurrent disease condition may lead to a decrease in circulating serum T3 and T4. Furthermore, certain medications, including phenylbutazone and corticosteroids, will lower thyroid hormone concentrations.[30,34]

Diagnostic confirmation

Hypothyroidism may be confirmed by a thyroid-releasing hormone (TRH) stimulation test, e.g. 1 mg of synthetic TRH injected intravenously.[29] Four hours after TRH injection in healthy horses, serum total T3 and T4 concentrations are more than double that before injection.[29] Similarly, T3 concentration increases fivefold (peak at 2 h) and T4 more than twofold (peak at 4 h) after administration of TSH, (5 IU intravenously).[29,36,37] Primary thyroid deficiency may be confirmed by minimal response to stimulation.[26] Unfortunately, in practice situations the use of these function tests is limited by the availability and cost of TSH and TRH.

Treatment and prognosis

Therapeutic aims

The first step in formulation of a treatment plan is to ascertain that dietary intake of iodine is adequate. The NRC

Table 37.1 Serum T4 and T3 concentrations in a population of clinically healthy horses by age group[35]

Age	T4 (μg/100 mL)		T3 (ng/100 mL)	
	Mean	Min–max	Mean	Min–max
1.5–4 months	4.0	2.9–5.3	193	135–270
2–5 years	1.9	1.2–2.9	120	72–180
6–10 years	1.7	1.3–2.2	86	48–118
11–25 years	1.6	0.9–2.2	84	47–145

recommends a minimum daily intake of 0.1 mg/kg of feed.[38] If correction of dietary deficiency does not solve the problem, replacement hormone supplementation is indicated.

Therapy

Because T3 is formed from T4 by deiodination, supplementation with T4 should be effective unless there is a deiodination defect. An oral dose of 5–20 μg T4 per kg bodyweight once daily has been recommended[26,30] and if T3 is to be used, a recommended oral dose is 0.6 μg/kg twice daily.[26] Clinical response to therapy will take at least 2 weeks. Hormone levels should be monitored periodically and thyroid function and dosages reassessed. Overdosage should be avoided because it may lead to loss of muscle mass, poor performance, muscle strain and hyperexcitability.[39]

Prognosis

Thyroid hormones have a wide array of functions but are not essential for life in adults. Supplementation therapy will usually alleviate clinical signs of hypothyroidism and improve performance.

Etiology and pathophysiology

Hypothyroidism can result from abnormalities in the formation, secretion, transport or metabolism of thyroid hormones. Primary hypothyroidism results in inadequate production of T3 and T4 by the thyroid gland. This can result from a deficiency (< 1 mg/day) but also from excess (> 35 mg/day) iodine intake. Some supplements, particularly those containing kelp, are extremely high in iodine.[24] Additionally, malnutrition (hypoproteinemia), ingestion of goitrogenic feeds (e.g. raw soybeans, cabbage, turnip, rapeseed, white clover) and a catabolic state due to excessive training or chronic disease may cause hypothyroidism.[24,38,40] In secondary hypothyroidism, there is a deficiency of TSH from the pituitary gland and in tertiary hypothyroidism an inadequate quantity of TRH is released from the hypothalamus.

Epidemiology

Congenital hypothyroidism of foals is a well-established entity,[41,42] but controversy exists over its true incidence in adult horses.[43] Although no controlled studies have confirmed an association between serum thyroid concentrations and poor performance, on the basis of an apparent response to exogenous thyroid hormone treatment many practitioners consider hypothyroidism to be a real clinical syndrome.

Prevention

Ascertain that dietary intake of iodine is adequate.

Hyperthyroidism

- Occurs due to high iodine intake or thyroid tumors.
- Clinical signs include weight loss despite ravenous appetite, elevated body temperature, excessive sweating and polydipsia.
- Blood samples show increased thyroid hormone concentrations.
- Treatment consists of ascertaining appropriate dietary iodine intake, antithyroid treatment or unilateral thyroidectomy.

Recognition

Hyperthyroidism is defined as an excess in thyroid activity.

History and presenting complaint

One or both thyroid glands may be enlarged. The horse may be emaciated, tachycardic, pyrexic, polydipsic, enophthalmic and alopecic, and sweat excessively. The horse may also be hyperexcitable and have a ravenous appetite.[42]

Laboratory examination

Blood samples show increased thyroid hormone concentrations.[44]

Diagnostic confirmation

A tri-iodothyronine suppression test may be effective to confirm the diagnosis.[44] In mares, high thyroid hormone levels without clinical signs may be evident during pregnancy.[30]

Treatment and prognosis

When hyperthyroidism is suspected, the first step is to ascertain that dietary intake of iodine is acceptable. In mature horses daily iodine intake should not exceed 35 mg per day. In addition to feeds, other products such as leg paints and shampoos containing iodine can be the source of excess iodine. If the problem is not solved after dietary correction, antithyroid treatment such as 1 g potassium iodide orally per day can be tried.[30] If this treatment is ineffective, a unilateral thyroidectomy may be considered.[44] If severe distress from thyrotoxicosis occurs, glucocorticoids may alleviate the signs.[30]

Etiology and pathophysiology

Horses may develop accelerated thyroid hormone production due to high iodine intake,[30] and hyperthyroidism has also been reported in elderly horses with thyroid adenoma or adenocarcinoma.[44,45]

Epidemiology

Hyperthyroidism is rare; it may be associated with thyroid tumors, which are moderately common in aged horses.[45] In race horses, cases of hyperexcitability associated with hyperthyroidism have been reported.[46]

Prevention

Ascertain that dietary intake of iodine is not excessive.

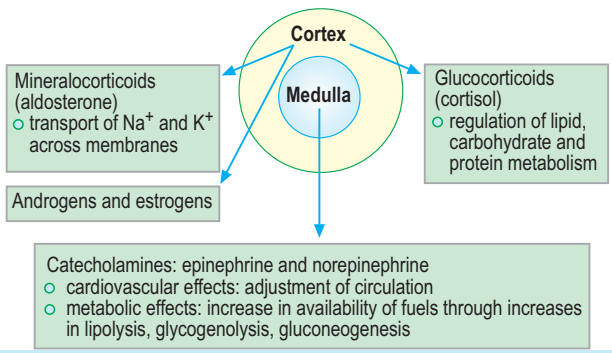

Fig. 37.4
The hormones produced by the adrenal cortex and medulla and their primary effects on metabolism, electrolyte balance and cardiovascular system.

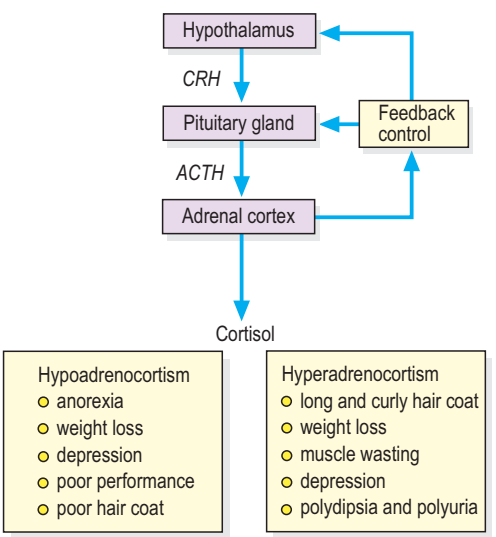

Fig. 37.5
Hypothalamic and pituitary hormones that are under feedback regulation by circulating cortisol control the release of cortisol from the adrenal cortex. Hypoadrenocorticism may be due to colic, endotoxemia or intensive training and also may be caused by cessation of exogenous glucocorticoid or anabolic steroid administration. Pituitary adenoma (equine Cushing's disease) is the most common cause of hyperadrenocorticism in horses. These tumors secrete ACTH, thereby resulting in hypercortisolemia.

Adrenal glands

Adrenal exhaustion (hypoadrenocortism, adrenal insufficiency, steroid letdown syndrome, Addison's disease)

- May develop after discontinuation of prolonged administration of glucocorticoids or anabolic steroids, colic and endotoxemia, or hard training.
- Clinical signs include depression, anorexia, weight loss and poor performance.
- Diagnostic confirmation requires an ACTH stimulation test.
- Treatment consists of avoidance of stress and supplementation with small quantities of corticosteroids.

Recognition

History and presenting complaint

Clinical signs attributed to adrenal exhaustion include depression, anorexia, weight loss, mild abdominal discomfort, poor coat and lameness. In adrenalectomized rats, exercise induces a less pronounced increase in muscle lactate concentrations, a less pronounced decrease in liver and muscle glycogen concentrations, much lower blood glucose concentrations and decreased exercise time to fatigue when compared to intact rats.[47]

Laboratory examination

Serum chemistry may be normal or hyponatremia, hypochloremia, hyperkalemia or hypoglycemia may be found. Measurement of cortisol levels is complicated by a number of factors that affect cortisol release in response to emotional and particularly physical stress, and is further complicated by circadian and ultradian fluctuations in total and free plasma cortisol concentration.

Diagnostic confirmation

Confirmation of the diagnosis requires an adrenocorticotrophin (ACTH) stimulation test, e.g. 25 IU synthetic ACTH intravenously.[48] In healthy horses 2–4 hours after an ACTH injection, plasma cortisol concentration is more than twice that before injection but in adrenal exhaustion, plasma cortisol concentration will be diminished.[49–51]

Treatment and prognosis

Treatment consists of strict avoidance of any stress. Small daily quantities of corticosteroids may be helpful.

Etiology and pathophysiology

Most cases involve sudden cessation of exogenous glucocorticoid or anabolic steroid administration following prolonged treatment regimens.[49,52] Naturally occurring adrenal exhaustion may be secondary to adrenal atrophy following conditions such as colic and endotoxemia, as the gland is a shock organ.[53] In normal Thoroughbred horses, hard training and racing at a high level may cause a decline in basal and ACTH-stimulated cortisol concentrations.[50] Moreover, poorly performing red cell hypervolemic Standardbred horses have lower cortisol concentrations than do untrained or normally performing horses.[51] Furthermore, in red cell hypervolemic horses, ACTH injection results in a smaller increase in plasma cortisol concentration than in trained normovolemic horses, which suggests that adrenal exhaustion may be a component of this syndrome.[51]

Cortisol deficiency reduces exercise capacity by depressing energy mobilization. Lipolysis is reduced, which in turn reduces the amount of free fatty acid available for aerobic energy metabolism. Gluconeogenesis decreases, which reduces carbohydrate availability. Cortisol deficiency also causes diminution of the important permissive effect of glucocorticoids on catecholamine action and causes apathy via direct neural effect.[46]

Epidemiology

Adrenal exhaustion is poorly documented in horses.

Hyperadrenocorticism (Cushing's disease)

- Primarily due to pituitary (pars intermedia) tumors.
- Clinical signs include long curly-hair coat, weight loss, muscle wasting, polydipsia, polyuria and poor performance.
- The most consistent clinicopathologic finding is hyperglycemia.
- Treatment with a serotonin antagonist or a dopamine agonist may ameliorate clinical signs.

Recognition

History and presenting complaint

The condition most often occurs in horses older than 12 years. They usually present with a history of weight loss, muscle wasting, lethargy and an abnormally long curly-hair coat that fails to shed at the appropriate time. Horses are often polydipsic and polyuric. Mares may show abnormal estrus cycles. Recurrent infections due to immune suppression and chronic laminitis have also been associated with the disease.

Laboratory examination

The most consistent finding is hyperglycemia, which in many cases also results in glucosuria and osmotic diuresis. A blood sample may also reveal neutrophilia and hyperlipemia. Blood cortisol concentration may be elevated, but this is not a consistent finding. Couetil et al[54] have suggested that plasma ACTH concentration determined with a commercial human radio-immunoassay can serve as a sensitive indicator of Cushing's disease in horses and ponies.

Necropsy examination

Post-mortem examination reveals a variably sized tumor of the intermediate lobe of the pituitary and hypertrophy of the adrenal cortex.

Diagnostic confirmation

Diagnosis should be confirmed by laboratory tests because neglect, poor dental care, parasites and other underlying systemic illnesses may lead to many of the same clinical signs. Confirmation may be achieved through detection of a poor response to a dexamethasone suppression test (DST) and an exaggerated response to an ACTH stimulation test.[55] A TRH response test and glucose tolerance test may also be used.[56]

Treatment and prognosis

Treatment is usually attempted with the serotonin antagonist cyproheptadine or the dopamine agonist pergolide mesylate. Clinical experience has indicated that pergolide is the treatment of choice. An initial dose of 0.001 mg/kg per day (0.5 mg/day for a 500 kg horse) is recommended. The horse should be re-evaluated (e.g. with a DST) after 4–8 weeks of treatment. If there has been no clinical improvement, the dose may be increased by 0.25 mg per day until improvement in clinical signs or results of a DST. When an effective dose is established, the horse is maintained on that dose for life. The results of cyproheptadine treatment have been less consistent. The recommended dose for initial treatment is 0.25 mg/kg once daily. If no improvement occurs, the dose may be increased to 0.5 mg/kg once daily or 0.25 mg/kg twice daily.[55,56]

These drug treatments do not affect tumor size, but may reduce the secretion of ACTH and other peptides. Signs caused by excess ACTH will usually be ameliorated in 6–8 weeks. Horses with long thick hair coats that do not shed should be body clipped.

Etiology and pathophysiology

Chronically elevated blood cortisol has a number of potential effects. It may lead to hyperglycemia via stimulation of gluconeogenesis. Muscles become more prone to fatigue and often exhibit marked weakness and wasting. A high cortisol concentration may contribute to polyuria and polydipsia by antagonizing antidiuretic hormone activity, and promote immunosuppression and mediate the development of lamini-

tis. Hypercortisolemia may also cause polycythemia with inappropriately increased blood viscosity, which places an increased load on the cardiovascular system.[46] In addition, the tumor mass of the pituitary adenoma can impinge upon surrounding structures, resulting in a variety of neurologic abnormalities.

Epidemiology

Adrenal tumors are almost unknown in horses as a cause of hyperadrenocorticism. However, pituitary adenomas, which are commonly reported in older horses, are associated with increased ACTH production, resulting in hyperadrenocorticism accompanied by an increase in circulating cortisol.

Problems associated with training programs

Surveys indicate that the most common reason why young race horses are withheld from training and racing is some form of lameness, with respiratory disease the next most common cause. However, when no apparent abnormality can account for the alleged poor or reduced performance, an evaluation of the management and training program is indicated. Critical assessment of training programs can be difficult because even within a given equine sport, there is wide variation in successful training programs.

Over-reaching (overloading, short-term overtraining)

- Occurs due to short-term maladaptation to training.
- Clinical signs include decreased appetite, irritability, muscle soreness and reluctance to exercise.
- Treatment consists of rest for up to 2 weeks.
- Training program needs to be evaluated to prevent recurrence.

Recognition

History and presenting complaint

Short-term maladaptation to training that causes fatigue and poor performance due to insufficient metabolic recovery is called over-reaching. As for true overtraining, the condition is characterized by immediate or delayed onset of muscle soreness, stiffness and performance decrement, and by decreased appetite, as well as behavioral changes (irritability), including a reluctance to exercise.

Laboratory examination

Blood samples may show increased activity of muscle enzymes (aspartate aminotransferase (ASAT), creatine kinase (CK) and lactate dehydrogenase (LDH)).

Treatment and prognosis

The problem is solved with up to 2 weeks of rest and proper nutrition. In horses, recovery of glycogen stores is slower

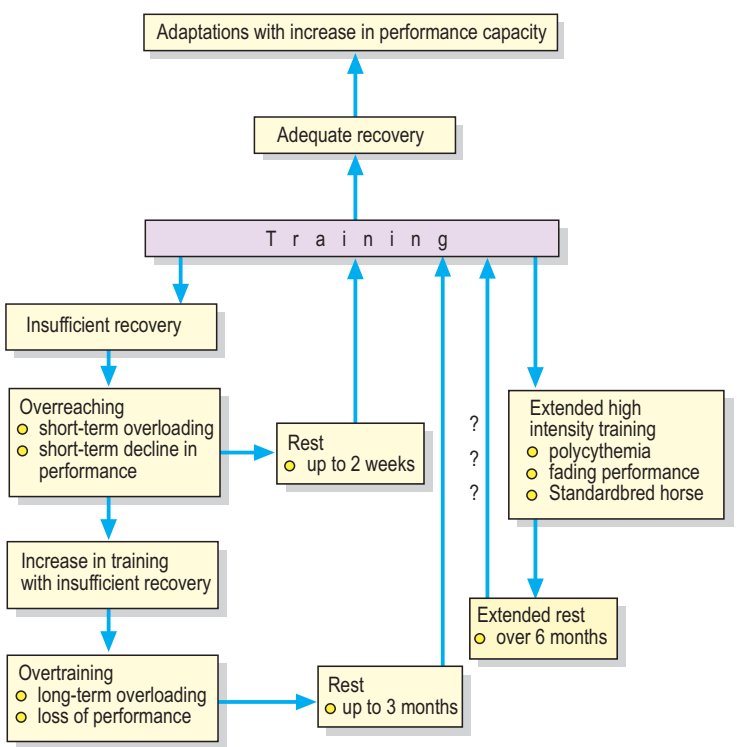

Fig. 37.6
A balanced training program leads to adaptation and increase in performance capacity while an overly strenuous training load, with insufficient recovery between training sessions, may cause loss of performance. In Standardbred trotters, training-induced red cell hypervolemia may signal the end of a successful racing career.

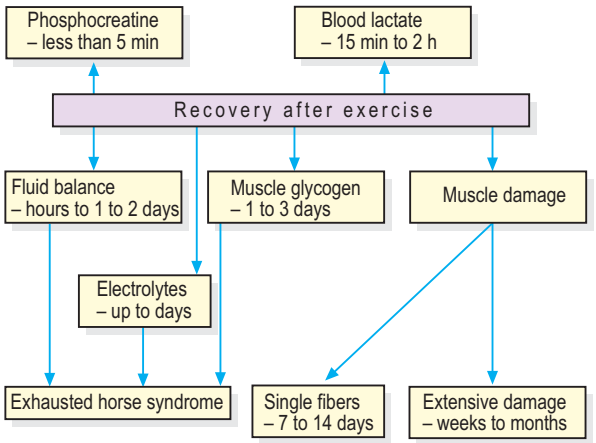

Fig. 37.7
Energy stores and fluid and electrolyte balance recover within minutes to 2–3 days following strenuous exercise, but repair of muscle damage may require weeks.

than in other species and may take up to 3 days.[57] For the most part, muscles repair themselves in up to 7–10 days and in doing so, produce an adaptation or training effect.

Etiology and pathophysiology

This condition occurs when the volume of training is too great or the interval between workouts is too short, resulting in acute or cumulative depletion of energy stores and damage to muscle cells. Recovery usually occurs within a few days.[58]

Epidemiology

Young horses at the beginning of their training are especially susceptible to this condition when too much is attempted too soon. It may, however, also occur in well-trained horses if training is dramatically increased or the workout routine altered.

Prevention

A new exercise program should begin slowly, with increases in intensity or duration of a workout schedule being accomplished gradually. As a general rule, to minimize the risk of over-reaching, horses should not perform the same type of strenuous conditioning exercise on consecutive days.

Overtraining (long-term training-competition recovery imbalance, staleness)

- Occurs due to long-term imbalance between training and recovery.
- Clinical signs include decreased performance capacity, weight loss and behavioral changes.
- Treatment consists of rest for up to 3 months.
- Training program needs to be evaluated to prevent recurrence.

Recognition

Overtraining is defined as a loss of performance ability, despite the maintenance of or an increase in training effort, which cannot be explained by any discrete pathology. Athletic performance deteriorates and affected horses must reduce or cease training for variable periods of time to allow recovery.[59]

History and presenting complaint

The syndrome has been characterized by decreased performance capacity and loss of weight, as well as behavioral changes (irritability), including a reluctance to exercise.[48] Affected horses often show clinical signs consistent with psychic stress, including a nervous demeanor, tachycardia, muscle tremor, sweating and diarrhea. These signs may occur before a race or in connection with training. Poor appetite is another common clinical sign in overtrained horses. Horses may also have increased susceptibility to infections, which in human athletes has been attributed to decreased concentrations of glutamine,[60] but no such decrease has been detected in horses.[61]

Laboratory examination

No single change occurs with sufficient consistency to identify the individual horse which is overtrained. Therefore, as yet no specific biological markers have been identified to help predict the onset of overtraining.[58,62] The serum activities of AST and CK are often increased due to muscle damage, but because muscle damage can occur in horses that have not been overtrained, an increase in AST or CK activity cannot be used as a definitive marker of overtraining.[58,62] In overtrained human athletes, increased concentrations of urea have been taken as an indication of increased protein catabolism, but such changes have not been detected in the horse, suggesting that in horses overtraining is not associated with proteolysis.[62]

Diagnostic confirmation

Signs of overtraining persist after 2 weeks of a reduced training load. However, because chronic fatigue can be the presenting symptom of many diseases, any medical conditions that cause chronic fatigue must be excluded.

Treatment and prognosis

An extended rest for 30–90 days is needed to reverse overtraining.

Etiology and pathophysiology

In training, the concept of progressive loading is applied to continually challenge body systems to adapt such that they are better able to perform the tasks demanded. Adaptation to any workload imposed at one point will not be seen until some point in the future, because the body requires time to respond. Overtraining is an imbalance between training and recovery, exercise and exercise capacity, stress and stress tolerance. Incorrect nutrition may contribute to the overtraining syndrome. Chronic fatigue, lack of training progress and injuries are common outcomes.

The physiologic features of overtraining are still poorly understood. In addition to depletion of energy stores and damage to muscle cells, it probably involves endocrine imbalance. Hormones are essential for physiologic reactions and adaptations during exercise and influence the recovery phase after exercise by modulating anabolic and catabolic processes. In overtrained human athletes, disorders of hormonal regulation at pituitary–hypothalamic level, adrenal exhaustion and a consequent reduction in blood cortisol, downregulation of peripheral and perhaps central β-adrenergic receptors and also downregulation of neuromuscular transmission have been claimed to occur.[63–65] Also in overtrained horses postexercise plasma cortisol concentration is reduced,[66] but both increased and decreased adrenocortical responsiveness to ACTH administration have been reported.[48,62]

Epidemiology

Overtraining is primarily related to a sustained high training load, such as that undertaken by Standardbred and Thoroughbred race horses.

Prevention

Increase in training load should be moderate, so that the horse has time to respond to the present load before any new requirement is imposed. Monotonous training should be avoided. After strenuous exercise, recovery is essential to allow time for training gains to take place and to permit further heavy work. Even when the training load is increased, the program for light exercise days should not be increased. Every third to fifth week should be considerably easier than the rest of the training program, to allow time for full recovery.

No two horses react the same to an equivalent exercise regimen. Each horse should therefore be monitored daily by measurement of resting heart rate and rectal temperature, by palpation of legs and muscles for swelling and soreness, by assessment of gait for any irregularities and by observance for any change in attitude or appetite. If any irregularities are noted, training volume should be reduced or a short rest period given. Adequate nutrition must be maintained.

Training-induced polycythemia (red cell hypervolemia, erythrocytosis)

- Occurs in association with long-term high-intensity training.
- Clinical signs may be absent except for a history of a rapid decline in performance after several years of racing.
- Blood samples show excessively high working hematocrit and hemoglobin values.
- Treatment consists of rest over 6 months, but polycythemia may signal the end of a successful racing career.

Recognition

Polycythemia has been described in Standardbred trotters. The condition is defined as a postexercise elevation of red blood cell count, packed cell volume and hemoglobin concentration above those levels considered normal.

History and presenting complaint

Horses are usually presented with a history of a rapid decline in racing performance after 3–4 years of racing.[67]

Physical examination

Polycythemic horses are often free from symptoms at rest, although Persson & Forssberg[68] have suggested an association between polycythemia and T-wave abnormalities in the electrocardiogram. The performance of affected horses in a submaximal standardized exercise test is similar to that of normovolemic horses, but polycythemic horses have reduced exercise capacity during racing.[67] Polycythemic horses and normovolemic horses show no differences in oxygen uptake, the maximum difference in arteriovenous oxygen content, heart rate, stroke volume, cardiac output or systemic arterial pressure, but polycythemic horses show higher pulmonary arterial pressure.[69] The latter may contribute to the high incidence of exercise-induced pulmonary hemorrhage in red cell hypervolemic horses.[69]

Laboratory examination

High postexercise values for hematocrit (> 65%) and hemoglobin concentration (> 240 g/L) suggest that polycythemia could be the problem. However, dehydration must be ruled out because a reduction in plasma volume will induce increases in red blood cell count, hematocrit and hemoglobin concentration.

Diagnostic confirmation

Diagnosis should be confirmed by measurement of total red cell volume. This involves measurement of postexercise hematocrit and plasma volume, the latter by use of the Evans blue dye dilution method.[70] For normovolemic adult trotters, red cell volumes are between 60 and 90 mL/kg[71] and for hypervolemic horses (4 years and older), between 90 and 115 mL/kg.[67]

Examination of middle gluteal muscle biopsy samples may yield useful information. Muscle capillary density is lower in red cell hypervolemic horses, while mitochondrial volume, estimated from NADH tetrazolium dehydrogenase activity in type II B muscle fibers, is higher in red cell hypervolemic when compared to normovolemic horses.[72,73]

Treatment and prognosis

As polycythemia seems to be a very persistent condition in Standardbred trotters, it has been suggested that its recognition may signal the end of a successful racing career.[67] Practitioners report that phlebotomy (4–5 L) will improve performance capacity of horses for only 2–3 weeks. Six months or more of rest without high-intensity training will usually reduce the red cell volume, but as training is resumed the condition frequently recurs. Castrating intact males to reduce circulating testosterone levels has also been suggested to be beneficial.

Etiology and pathophysiology

The etiology of this condition is not known. Intermittent hypoxia associated with regular strenuous exercise is thought to stimulate erythropoietin release and red cell production. This increase in red cell mass is presumably an important mechanism of training-associated increases in athletic capacity. Indeed, a significant correlation exists between blood volume and kilometer time in trotters. On the other hand, marked increases in blood viscosity associated with red cell hypervolemia may increase peripheral resistance, decrease cardiac output and impair tissue oxygenation.[74] These effects may underlie the reduction in athletic performance observed in trotters with polycythemia. Affected horses have lower muscle capillarization that may hamper the efflux of lactate from contracting skeletal muscle.[72,73]

Stallions are more likely to develop polycythemia than are mares and geldings, because on average they have a significantly higher red cell volume, due to high testosterone production. Abuse of erythropoietin and anabolic steroids may also cause or contribute to secondary polycythemia.[75,76]

Epidemiology

Polycythemia associated with prolonged fast work training has been reported in Standardbred trotters, but in other horse breeds it appears to be rare.[58,62,67,70,77] Training-induced polycythemia with impaired racing performance was first described in Scandinavia.[70] Typical features for the athletic career of these horses are intensive training with much high-intensity work, frequent racing (30 or more races per year) and a long racing career (up to 10 years).

References

1. Carlson GP. Thermoregulation, fluid and electrolyte balance. In: Snow DH, Persson, SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 291–309.
2. Chapman DI, Haywood PE, Lloyd P. Occurrence of glucosuria in horses after strenuous exercise. Equine Vet J 1981; 13:259–260.
3. Schott HC II, Hodgson DR, Bayly WM. Haematuria, pigmenturia and proteinuria in exercising horses. Equine Vet J 1995; 27:67–72.
4. Sloet van Oldruitenborgh-Oosterbaan MM. The treatment of the exhausted horse under field conditions. Equine Pract 1994; 16:27–33.
5. Geor RJ, McCutcheon LJ. Thermoregulatory adaptations associated with training and heat acclimation. Vet Clin North Am Equine Pract 1998; 14:97–120.
6. Schott HC II, Hinchcliff KW. Treatments affecting fluid and electrolyte status during exercise. Vet Clin North Am Equine Pract 1998; 14:175–204.
7. Foreman JH. The exhausted horse syndrome. Vet Clin North Am Equine Pract 1998; 14:205–219.
8. Essén-Gustavsson B, Karlström K, Lindholm A. Fiber types, enzyme activities and substrate utilisation in skeletal muscle of horses competing in endurance rides. Equine Vet J 1984; 16:197–202.
9. Flaminio MJBF, Rush BR. Fluid and electrolyte balance in endurance horses. Vet Clin Equine Pract 1998; 14:147–158.
10. White SL. Fluid, electrolyte, and acid-base balance in three-day, combined-training horses. Vet Clin North Am Equine Pract 1998; 14:137–145.
11. Andrews FM, Ralston SL, Sommerdahl CS, et al. Weight, water, and cation losses in horses competing in three-day event. J Am Vet Med Assoc 1994; 205:721–724.
12. Hyyppä S, Saastamoinen M, Pösö AR. Restoration of water and electrolyte balance in horses after repeated exercise in hot and humid conditions. Equine Vet J 1996; 22(Suppl): 108–112.
13. Schott HC II, Hichcliff KW. Fluids, electrolytes, and bicarbonate. Vet Clin North Am Equine Pract 1993; 9:577–604.
14. Kingston JK, Bayly WM. Effect of exercise on acid base status of horses. Vet Clin North Am Equine Pract 1998; 14:61–73.
15. Marlin DJ, Harris PA, Schroter RC, et al. Physiological, metabolic and biochemical responses of horses competing in the speed and endurance phase of a CCI**** 3-day-event. Equine Vet J 1995; 20(Suppl):37–46.
16. White SL, Williamson LH, Maykuth PL, et al. Heart rate response and plasma lactate concentrations of horses competing in the cross-country phase of combined training events. Equine Vet J 1995; 20(Suppl):47–51.
17. Sosa León LA. Treatment of exercise-induced dehydration. Vet Clin North Am Equine Pract 1998; 14:159–173.
18. Sloet van Oldruitenborgh-Oosterbaan MM, Arts F, Bryant J. Evaluation of the endurance ride. Equine Athlete 1996; 9:1–9.
19. Jansson A, Rytthammar Å, Lindberg JE, et al. Voluntary salt (NaCl) intake in Standardbred horses. Pferdeheilkunde 1996; 12:443–445.
20. Burdick DL, Hodgson D. Thermoregulation in the horse: derangements and associated clinical diseases. Equine Athlete 1990; 3:15–20.
21. Fenger CK. Disorders of calcium metabolism. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia, PA: Saunders; 1998; 925–934.

22. Freestone JF, Carlson GP, Harrold, DR, et al. Furosemide and sodium bicarbonate-induced alkalosis in the horse and response to oral KCL or NaCl therapy. Am J Vet Res 1989; 50:1334–1339.
23. Waldron-Mease E. Hypothyroidism and myopathy in racing Thoroughbreds and Standardbreds. J Equine Med Surg 1979; 3:124–128.
24. Sojka J. Factors which affect serum T_3 and T_4 levels in the horse. Equine Pract 1993; 15:15–19.
25. Sumano Lopez H, Hoyas Sepulveda ML, Brumbaugh GW. Pharmacologic and alternative therapies for the horse with chronic laminitis. Vet Clin North Am Equine Pract 1999; 15:495–516.
26. Vischer CM, Foreman JH, Constable PD, et al. Hemodynamic effects of thyroidectomy in sedentary horses. Am J Vet Res 1999; 60:14–21.
27. Lowe JE, Foote RH, Baldwin BH, et al. Reproductive patterns in cyclic and pregnant thyroidectomized mares. J Reprod Fertil 1987; 35(Suppl):281–288.
28. Frank N, Sojka JE, Latour MA, et al. Effect of hypothyroidism on blood lipid concentrations in horses. Am J Vet Res 1999; 60:730–733.
29. Thompson JC, Ellison RS, Kirk J. Serum thyroid hormone concentrations in New Zealand horses. New Zealand Vet J 1997; 45:11–14.
30. Duckett WM. Thyroid gland. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia, PA: Saunders; 1998; 916–925.
31. Suwannachot P, Verkleij CB, Kocsis S, et al. Prolonged food restriction and mild exercise in Shetland ponies: effects on weight gain, thyroid hormone concentrations and muscle Na(+), K(+)-ATPase. J Endocrinol 2000; 67:321–329.
32. González O, González E, Sánchez C, et al. Effect of exercise on erythrocyte β-adrenergic receptors and plasma concentrations of catecholamines and thyroid hormones in Thoroughbred horses. Equine Vet J 1998; 30:72–78.
33. Irvine CHG. Thyroxin secretion rates in the horse in various physiological states. J Endocrinol 1987; 39:313–320.
34. Ramirez S, Wolfsheimer KJ, Moore RM, et al. Duration of effects of phenylbutazone on serum total thyroxine and free thyroxine concentrations in horses. J Vet Intern Med 1997; 11:371–374.
35. Chen CL, Riley AM. Serum thyroxine and triiodothyronine concentrations in neonatal foals and mature horses. Am J Vet Res 1981; 42:1415–1417.
36. Oliver JW, Held JP. Thyrotropin stimulation test – new perspective on value of monitoring triiodothyronine. J Am Vet Med Assoc 1985; 187:931–934.
37. Held JP, Oliver JW. A sampling protocol for the thyrotropin-stimulation test in the horse. J Am Vet Med Assoc 1984; 184:326–327.
38. Frape D. Equine nutrition and feeding, 2nd edn. Oxford: Blackwell Science; 1998.
39. Lori DN, MacLeay JM. Hypothyroidism in the horse. J Equine Vet Sci 2001; 21:8–11.
40. Fahey JW, Zalcmann AT, Talalay P. The chemical diversity and distribution of glucosinolates and isothiocyanates among plants. Phytochemistry 2001; 56:5–51.
41. Irvine CHG. Hypothyroidism in the foal. Equine Vet J 1984; 16:302–306.
42. Allen AL, Fretz PB, Card CE, et al. Effects of partial thyroidectomy on the development of the equine fetus. Equine Vet J 1998; 30:53–59.
43. Bayly W, Andrea R, Smith B, et al. Thyroid hormone concentrations in racing Thoroughbreds. Pferdeheilkunde 1996; 12:534–538.
44. Alberts MK, McCann JP, Woods PR. Hemithyroidectomy in a horse with confirmed hyperthyroidism. J Am Vet Med Assoc 2000; 21:1051–1054.
45. Ramirez S, McClure JJ, Moore RM, et al. Hyperthyroidism associated with a thyroid adenocarcinoma in a 21-year-old gelding. J Vet Intern Med 1998; 12:475–477.
46. Irvine CHG. The role of hormones in exercise physiology. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 377–388.
47. Viru M, Litvinova L, Smirnova T, et al. Glucocorticoids in metabolic control during exercise: glycogen metabolism. J Sports Med Phys Fitness 1994; 34:377–382.
48. Golland LC, Evans GM, Stone GM, et al. The effect of overtaining on plasma cortisol concentrations at rest and in response to exercise and administration of synthetic adrenocorticotropin in Standardbred racehorses. Pferdeheilkunde 1996; 12:531–533.
49. Dowling PM, Williams MA, Clark TP. Adrenal insufficiency associated with long-term anabolic steroid administration in a horse. J Am Vet Med Assoc 1994; 204:329–330.
50. Wilson WD, Kingery S, Snow DH. The effect of training on adrenocortical function in Thoroughbred racehorses. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 482–489.
51. Persson SGB, Larsson M, Lindholm A. Effects of training on adreno-cortical function and red-cell volume in trotters. J Am Vet Med Assoc 1980; 27:261–268.
52. Bicknell AB. Identification of the adrenal protease that cleaves pro-gamma-MSH: the dawning of a new era in adrenal physiology? J Endocrinol 2002;172:405–410.
53. Rivas L. Diseases of the adrenal glands. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia, PA: Saunders; 1998; 934–936.
54. Couetil L, Paradis MR, Knoll J. Plasma adrenocorticotropin concentration in healthy horses and in horses with clinical signs of hyperadrenocorticism. J Vet Intern Med 1996; 10:1–6.
55. Reed S. Pituitary adenomas: equine Cushing's disease. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia, PA: Saunders; 1998; 912–916.
56. Roussel AJ, Carter GK. Polyuria and polydipsia. In: Brown CM, ed. Problems in equine medicine. Philadelphia, PA: Lea and Febiger; 1989; 150–160.
57. Hyyppä S, Räsänen LA, Pösö AR. Resynthesis of glycogen in skeletal muscle from Standardbred trotters after repeated bouts of exercise. Am J Vet Res 1997; 58:162–166.
58. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Equine Vet J 1999; 30(Suppl):621–625.
59. Evans DL. Training regimens: overview. In: Hodgson DR, Rose RJ eds. The athletic horse. London: Saunders; 1994; 387–392.
60. Parry-Billings M, Blomstrand E, McAndrew N, et al. A communication link between skeletal muscle, brain and cells of the immune system. Int J Sports Med 1992; 2(Suppl): S122–S128.
61. Pösö AR, Essán-Gustavsson B, Persson SGB. Metabolic response to standardised exercise test in Standardbred trotters with red cell hypervolaemia. Equine Vet J 1993; 225:527–531.
62. Bruin G, Kuipers H, Keizer HA, et al. Adaptation and overtraining in horses subjected to increasing training loads. J Appl Physiol 1994; 76:1908–1913.
63. Lehmann M, Foster C, Dickhuth HH, et al. Autonomic imbalance hypothesis and overtraining syndrome. Med Sci Sports Exerc 1998; 30:1140–1145.
64. Urhausen A, Gabriel H, Kindermann W. Blood hormones as markers of training stress and overtraining. Sports Med 1995; 20:251–276.

65. Budgett R. Fatigue and underperformance in athletes: the overtraining syndrome. Br J Sports Med 1998; 32:107–110.
66. Hamlin MJ, Sherman JP, Hopkins WG. Changes in physiological parameters in overtrained Standardbred racehorses. Equine Vet J 2002; 34:383–388.
67. Persson SGB, Österberg I. Racing performance in red blood cell hypervolaemic Standardbred trotters. Equine Vet J 1999; 30(Suppl):617–620.
68. Persson SGB, Forssberg P. Exercise tolerance in Standardbred trotters with T-wave abnormalities in the electrocardiogram. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 772–780.
69. Funquist P, Nyman G, Persson SGB. Haemodynamic response to exercise in Standardbred trotters with red cell hypervolaemia. Equine Vet J 2000; 32:426–431.
70. Persson SGB. On blood volume and working capacity in horses. Acta Vet Scand 1967; 19(Suppl):1–189.
71. Persson SGB, Funkqvist P, Nyman G. Total blood volume in the normally performing Standardbred trotter: age and sex variations. J Vet Med 1996; 43:57–64.
72. Ronéus M, Persson SGB, Essén-Gustavsson B, et al. Skeletal muscle characteristics in red blood cell normovolaemic and hypervolaemic Standardbred racehorses. Equine Vet J 1994; 26:319–322.
73. Karlström K, Essén-Gustavsson B, Persson SGB. Capillaries of muscle in red cell hypervolaemic versus normovolaemic Standardbred horses. Equine Vet J 1995; 18(Suppl):228–230.
74. Windberger U, Ribitsch V, Resch KL, et al. The viscoelasticity of blood and plasma in pig, horse, dog, ox, and sheep. J Exp Anim Sci 1993; 94:89–95.
75. Jaussaud P, Audran M, Gareau RL, et al. Kinetics and haematological effects of erythropoietin in horses. Vet Res 1994; 25:568–573.
76. Hyyppä S, Räsänen LA, Persson SGB, et al. Exercise performance indices in normal and anabolic steroid treated trotters. Equine Vet J 1995; 18(Suppl):443–447.
77. Persson SGB. Evaluation of exercise tolerance and fitness in the performance horse. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983; 441–457.

CHAPTER 38

Body fluids and electrolytes: responses to exercise and training

Kenneth Harrington McKeever

The exercising horse produces a tremendous amount of metabolic heat. This byproduct of the transduction of potential energy into kinetic energy can raise core body temperature in the horse from 37°C at rest to temperatures exceeding 42°C in a matter of minutes.[1–6] Normal cellular function, however, requires active and efficient ways to keep core body temperature within narrow limits. To do this a horse must move heat produced in the muscles to the periphery.[1,2,4–6] Other mammalian species, like the rabbit and dog, have an enhanced countercurrent brain bloodflow mechanism that couples with panting to provide for cooling of the brain while permissively allowing heat storage in the rest of the body and a rise in body temperature.[5,7,8] Horses and humans are the only species that cool primarily through the evaporation of sweat.[1,5,7,8] Sweating can produce tremendous fluid and electrolyte losses that, if uncompensated for, can lead to cardiovascular and thermoregulatory instability. These fluid deficits and their effects are even more pronounced during endurance exercise and exercise performed during periods of high environmental temperature and humidity.[1–3,5–7] Recent work focused on preventing thermal injuries in horses has documented findings similar to those published in the human sports medicine literature, namely that maintenance of fluid and electrolyte balance prevents dehydration and provides thermoregulatory and cardiovascular stability.[3–12] Data demonstrate that optimal fluid and electrolyte balance delays the onset of fatigue. The present chapter reviews the current literature on the effects of exercise on fluid balance and renal function in horses.

Body fluid compartments

Like all animals, the body of the horse is primarily composed of water and electrolytes. Those solutions are compartmentalized within and outside the cells. This combination of intracellular and extracellular water is referred to as the total body water (TBW). The TBW accounts for 50–70% of bodyweight, or 250–350 kg of the bodyweight of a typical 500-kg horse.[1,2,9] TBW can be measured using various indicator dilution techniques, stable isotope techniques, and bioelectric impedance technologies.[1,2,9] Each of these techniques has advantages and disadvantages, with the use of stable isotope infusion being one of the most accurate and bioelectric impedance technology the least reliable. The TBW is divided by cell membranes into two primary fluid compartments, the intracellular fluid compartment (ICF) and the extracellular fluid compartment (ECF).[1,2,8] Approximately two-thirds of the TBW (~200 L) is contained within the cells of the body leaving one-third of the water in the ECF space (~100 L). According to Carlson,[2] the latter is further compartmentalized into fluid contained within the vascular space, the interstitial fluid space, the lymphatics, and transcellular fluids. This last category includes the fluid content of the gastrointestinal tract, which represents a large reservoir of fluid.[2]

The vascular space or total blood volume is filled with a mixture of fluid and cells, the latter primarily red blood cells, but also including white blood cells and platelets. Thus, the total blood volume (BV) is the combination of the plasma

volume (PV) and the red cell volume (RCV) or stated as a formula:[2] BV = PV + RCV. Blood volume varies from breed to breed, with age, body composition, hydration status, and training status.[2,13] Across breeds, studies have reported total blood volumes ranging from 61 mL/kg in draft horses to 137 mL/kg in race horses.[1,2,9] In the average 450-kg horse, total BV would be about 36 L, PV ~16 L and RCV around 20 L.[1,2,13]

The eloquent work of Persson[13] and many others[2,14–16] has shown that there is a strong relationship between red blood cell volume and aerobic performance in the horse. Oxygen uptake and delivery is dependent on both optimal volume to insure cardiac filling pressure and an optimal number of red blood cells to carry oxygen. Much focus has been placed on the need to have red blood cells to carry oxygen to the working muscles. However, while RCV and PV are usually looked at independently; they are interdependent in the optimization of blood flow during exercise. Blood flow can be affected by changes in viscosity; thus, too many red blood cells and not enough plasma can cause a substantial change in viscosity, as well as other factors related to resistance to flow. The values for BV, PV, and RCV in the literature also vary with the differing methodologies used in different laboratories to measure and/or calculate total blood volume.[2,13–16] For the most part, studies of equine blood volume have not used direct measurement of BV. Instead, they have generally used dye or indicator dilution techniques to measure PV and then calculated (Formula 1) BV using the measured PV and hematocrit (HCT):[2,13–16]

$$BV = \left(\frac{PV}{100 - HCT} \right) \times 100$$

The measurement of PV using dye or indicator dilution techniques requires the use of an indicator that stays within the vascular compartment for a long enough time to reach full steady-state distribution without substantial removal through the metabolism of the dye by the tissues.[2,15] Ideally, this requires an indicator that binds to a large molecule that does not readily leave the vascular compartment. Two substances commonly used to measure PV in the horse are indocyanine green (IC-green or cardiac green) dye and Evans Blue dye.[2] While IC-green dye has been used to measure plasma volume in the horse, one must caution that because it is rapidly cleared from the vascular compartment, it is better suited for the repeated injections required for the measurement of cardiac output. The rather short half-life of IC dye means it can be cleared before reaching full distribution affecting the accuracy and repeatability of PV measurements in the horse. Evans Blue dye binds to albumin and thus, has a relatively long half-life and stays for the most part in the vascular compartment.[2,13,15] However, one must caution that albumin can shift out of the vascular compartment if there is an increase in hydrostatic pressure induced by manipulations such as exercise or adrenaline infusion. Thus, the measurement of PV using the Evans Blue dye dilution technique requires that a horse be standing relatively quietly and unperturbed by exercise or pharmacological manipulations for the 15- to 20-min mixing period between collection of a blank plasma sample and injection of the dye and the collection of a postinjection blood sample.[2,15] Anything that disturbs the steady-state of the cardiovascular system affects distribution of the dye; therefore, one should view with extreme caution published studies reporting PV, BV, and RCV values calculated using a postinjection sample obtained after exercise as the readings can be skewed in two ways.[13] First, decreases in PV due to water shifts out of the vascular compartment caused by increases in hydrostatic pressure that would give artificially high concentration of the dye and, second, errors caused by the loss of dye from the vascular compartment due to extrusion of albumin out of the bloodstream by the same increases in hydrostatic pressure.[3,17–20] Plasma volume can decrease 15–20% after only three 1-min steps of an incremental exercise test;[17] therefore, errors in the measurement of plasma volume due to non-steady-state sampling would also affect the calculation of BV and RCV using the above formula.

Another factor that must be considered in the calculation of total BV in the horse is the splenic reserve volume. The horse is somewhat unique compared to most other mammalian species in that the spleen is a very capacious and capricious organ, storing between 6 and 12 L of red-cell-rich blood at rest.[2,13,19,20] Splenic blood typically has a hematocrit of ~65–75%.[2,13] Thus, studies of total BV become somewhat problematic because measurement of the total circulating BV requires an accounting for the splenic reserve volume, a measurement that requires mobilization of the splenic red cell reserve. Most studies to date have utilized exercise or infusion of adrenaline or an α-adrenergic agonist drug to cause splenic contraction, with a blood sample obtained for the measurement of hematocrit after the accommodation and the mixing of the extra volume of blood. Complete mixing takes only 1–2 min; however, in many studies, the hematocrit used to calculate BV and RCV was taken at the end of or after an incremental exercise test.[13,16] While this is an accepted way to cause splenic contraction and a viable way to *estimate* the contribution of the splenic reserve to the total circulating blood volume, the resulting hematocrit values are skewed upward by the dynamic fluid shifts caused by the changes in flow and hydrostatic pressure induced by the exercise or pharmaceutical manipulation. Therefore, the hematocrit used to calculate total BV would reflect both the contribution of splenic reserve mobilization and reductions in plasma volume and would be an overestimation of total blood volume. This is essentially an offset error and, because acute reductions in PV caused by exercise-induced fluid shifts are linked to exercise intensity,[3,17–19] the fluid shifts that lead to this overestimation only become a problem if a study's experimental design uses different exercise intensities to measure the hematocrits used in comparisons between treatment groups or comparisons made before and after training. For example, if one calculates BV using a hematocrit obtained at the 10 m/s step of a treadmill test it will yield a different result than the value calculated using the hematocrit collected at the 11 or 12 m/s step of an incremental treadmill test.

As mentioned above, the absolute value for resting plasma volume can be determined using Evans Blue dye. However, measurement of PV during exercise and any resulting

Example 1 Calculation of the percent change in plasma volume using uncorrected hematocrit as in humans

$$\%\Delta PV = \left(\frac{100}{100 - HCTb}\right) \times \left[100 \times \frac{(HCTb - HCTa)}{HCTa}\right]$$

$$\%\Delta PV = \left(\frac{100}{100 - 43}\right) \times \left[100 \times \frac{(43 - 45)}{45}\right]$$

$$\%\Delta PV = \left(\frac{100}{57}\right) \times \left[100 \times \frac{(-2)}{45}\right]$$

$$\%\Delta PV = (1.8) \times [-4.4]$$

$$\%\Delta PV = -7.9$$

decreases are problematic because of mixing time, the requirement for steady-state conditions, and the potential for overwhelming the vascular space with dye through repeated injections. Percent changes in PV can be measured using changes in protein concentration.[17] However, because some protein leaves the vascular compartment, this method tends to underestimate the reduction in PV.[17] To get around these methodological problems, studies of human athletes[21–23] have utilized changes in hematocrit to calculate percent changes in PV (Example 1). Absolute volume changes in liters are then calculated using the previously measured absolute resting PV determined using Evans Blue dye.[21–23] The calculation of percentage change in PV using hematocrit is feasible because red blood cells do not leave the vascular compartment like protein molecules and any change in their concentration must be due to changes in plasma volume.[21–23] In humans, the calculation is simple and involves the use of a pre-exercise hematocrit (HCTb) and hematocrits measured during or after exercise (HCTa).[21–23] For example, if the hematocrit measured before exercise (HCTb) was 43 and the hematocrit measured in a blood sample obtained after 10 min of exercise was 45 then the change in plasma volume is –7.9%. Thus, one can see that a relatively small change in hematocrit represents a much larger change in plasma volume.

However, it is important to note that the use of this formula requires that there is no addition of red blood cells to the central circulation or change in the size of the cells.[21–23] The latter has been shown to not be a problem if exercise duration is less than 120 min.[23] The former makes the use of this formula problematic for those doing horse research because the spleen adds RBCs to the central circulation. Fortunately, McKeever et al. have developed a correction factor obtained after comparing sequential blood samples taken from splenectomized and intact horses.[17] These studies demonstrated that the spleen contracts very rapidly with both the extruded volume and cells accommodated and mixed with the central circulation within the first one to 1.5 min of exercise.[17] Changes in hematocrit from the point of full mixing onward paralleled each other in both groups of horses. Thus, the changes in hematocrit from that point on were due to decreases in plasma volume caused by fluid shifts and loss of water from the vascular compartment.[17] More importantly, the difference between the pre-exercise and the 2-min values for hematocrit in the intact horses represented an offset due to splenic reserve mobilization that could be used as a correction factor.[17]

Example 2 Calculation of the percentage change in plasma volume using corrected hematocrit in horses[17]

HCTb = 35

HCTraw = 58

HCT2min = 20

HCTa = HCTraw – HCT2 min = 58 – 20 = 38

$$\%\Delta PV = \left(\frac{100}{100 - HCTb}\right) \times \left[100 \times \frac{(HCTb - HCTa)}{HCTa}\right]$$

$$\%\Delta PV = \left(\frac{100}{100 - 35}\right) \times \left[100 \times \frac{(35 - 38)}{37}\right]$$

$$\%\Delta PV = \left(\frac{100}{65}\right) \times \left[100 \times \frac{(-3)}{37}\right]$$

$$\%\Delta PV = (154) \times [-5.41]$$

$$\%\Delta PV = -12.2$$

Example 2 demonstrates how to use hematocrit in the horse to calculate percent changes in PV. For example, if a horse had a resting hematocrit (HCTb) of 35 and the hematocrit measured at 2 min of exercise (HCT_{2min}) was 55 then the difference between the two would be the calculated correction factor (HCT_{2min}) to be used to correct all the hematocrits measured after the 2-min point of exercise onward. Thus, in Example 2, if the uncorrected hematocrit obtained at 15 min of exercise was 58 (HCT_{raw}), then the value for HCTa to be used in the formula would be obtained by subtracting the correction factor from the uncorrected hematocrit.

Plasma osmolality and the concentration of key electrolytes

Normal cellular function is vitally linked to maintenance of fluid, electrolyte and acid–base balance within a narrow range.[2,3,23–26] Thus, the composition of both the plasma within the vascular compartment and the fluid within the intracellular fluid space is tightly controlled.[2,3,23–26] Key to maintenance of the internal environment is a regulation of overall plasma osmotic concentration or osmolality as well as the concentration of key electrolytes such as sodium, potassium, chloride.[2,3,23–26] Sodium is the major anion contributing to osmolality and is the major cation in the extracellular fluid space.[2,3,23–26] Potassium on the other hand is the primary cation found within the cells.[2,3,23–26] Other important cations include calcium and magnesium, both primarily intracellular ions.[2,3,23–26] When considering exercise, it is the

Table 38.1 Electrolyte composition (mEq/L) of plasma, interstitial fluid, intracellular fluid (muscle), and sweat

Electrolyte	Plasma	Interstitial fluid	Skeletal muscle cell	Sweat
Cations				
Na^+	140	143	10	120 (range 115–150)
K^+	4	4.1	142	35 (range 25–50)
Ca^{2+} (ionized)	2.5	2.4	4	10 (range 3–20)
Mg^{2+} (ionized)	1.1	1.1	34	5
Anions				
Cl^-	100	113	4	150 (range 140–190)
$HCO3^-$	25	28	12	
$H_2PO_4^-$, HPO_4^{2-}	2	2	40	
Protein	14	0	50	
Other	7	7	84	

calcium found within the muscle in the tubular sarcoplasmic reticulum that is important.[2,3,23–26] This calcium plays a vital role in the process of excitation contraction coupling. Magnesium found within the cells is an important cofactor in many of the reactions involved in various metabolic pathways.[2,3,23–26] Major anions include chloride, bicarbonate, and the phosphates.[2,3,23–26] Normal values for resting concentrations of the major electrolytes found in plasma, interstitial fluid, intracellular fluid and sweat can be found in Table 38.1. All of the electrolytes contribute to the osmotic concentration of the body fluids, a variable that is tightly regulated to prevent cell dehydration or cell swelling.

The osmotic concentration or osmolality of the plasma is essentially the same as that of the rest of the interstitial fluids.[27,28] Normal plasma osmolality in the horse and most other mammals averages 290 mOsm/L.[2] Plasma osmolality is the total number of dissolved particles in solution, independent of the elemental species making up that solution.[27] Plasma osmolality reflects the osmolality of both the extracellular fluid space and the intracellular fluid space[27] and is important for two reasons. First, large molecules in solution exert osmotic force across semipermeable membranes such as capillaries and cell membranes. Thus, plasma osmolality is a measure of the total 'osmotic pull' or osmotic force that is exerted by the sum of freely-moving particles in solution exerting an effect on water in surrounding tissues.[27,28] Because water tends to move down a concentration gradient from an area of low concentration to an area of high concentration, an increase or decrease in plasma osmolality has the capacity to dramatically alter normal cellular function by causing fluid shifts into and out of the cells, shifts that can decrease cell function.[27,28] Second, a change in osmolality reflects expansion or contraction of the extracellular fluid compartment.[27,28] Optimal cardiovascular function is highly dependent on fluid volume status and mechanisms associated with the maintenance of plasma osmolality and extracellular fluid volume serve as one of the first lines of defense in the regulation of cardiac filling volume and pressure and ultimately mean arterial pressure and the ability to perfuse the tissues.[19,27,28]

During exercise the horse can lose tremendous volumes of hypertonic sweat presenting a serious challenge for maintaining the volume and the composition of the body fluids.[1,2,19] Dramatic changes can compromise cellular function.[28] It can also compromise cardiovascular stability through a reduction in venous return and cardiac output. Therefore, it is vitally important that the body regulates plasma osmolality within very narrow limits.[28] Defense of osmolality is vitally intertwined with the defense of extracellular fluid volume, plasma volume, and cardiac filling pressure.[19,28] Thus, defending plasma osmolality involves an integrative response of multiple systems including the cardiovascular, neural, endocrine, and renal systems.[6,10,19,27–30] Changes in plasma osmolality are sensed by specialized cells within the supraoptic and paraventricular nuclei of the hypothalamus.[19,27–29] These osmoreceptors are very sensitive and changes in plasma osmolality as small as 2 mOsm/L can evoke a change in the synthesis and secretion of the hormone arginine vasopressin (antidiuretic hormone) by the posterior pituitary.[29] Changes in circulating vasopressin concentration occur rapidly and can cause dramatic alterations in renal handling of water within minutes, thus correcting volume deficits and swings in the concentration of osmotically active substances through losses of plasma water or electrolytes in the sweat.[29,30] Vasopressin also stimulates thirst and drinking, which ultimately affects water balance and osmolality.[29]

Plasma concentration versus plasma content

When considering the effects of acute exercise on changes in key electrolytes one must distinguish between changes in the concentration versus changes in the total content of those electrolytes.[23,31] By definition, the concentration of a substance is the amount of solute in a given volume of solvent. Content, on the other hand, is the total amount of that solute in the fluid compartment or body depending on the focus of analysis. For example, normal plasma concentration sodium is 140 mEq/L or, put another way, there are 140 mEq of

sodium per liter of plasma. Plasma content of sodium would be obtained by multiplying the concentration of sodium by the plasma volume:[23,31]

$$\frac{140\ \text{mEq}}{\text{Liter}} \times \frac{26\ \text{Liters}}{1} = 3640\ \text{mEq}$$

Calculation of changes in the content of key electrolytes and other substances allows one to determine if changes in the concentration of a substance is the result of addition or loss of the substance or just due to changes in plasma water.[23,31] When viewed on a whole body level, changes in content allow one to make calculations giving insight into how concentrations of tightly regulated plasma constituents are affected through routes of intake or loss that affect whole body balance of said constituent.[23,31] Acutely, calculation of relative or percent changes in the content of plasma volume and the plasma constituents gives one insight into the dynamic changes that occur in response to the challenge of exertion.[23,31] To that end, human exercise physiologists for years have used key formulae to calculate percentage changes in plasma volume and percentage changes in the content of various plasma constituents during exercise (Example 3).[21–23] If one knows the resting plasma volume then once one calculates the percentage change in the content of a plasma constituent one can calculate the total amount of that substance lost during exercise from the vascular compartment.[23,31]

On a practical level, calculation of changes in the content of various plasma constituents can give insight into their disposition. An example of this would be an examination of sodium and chloride losses during short-term versus endurance exercise. Plasma sodium and chloride concentrations are held within vary narrow limits. During short-term exercise plasma sodium and chloride concentrations undergo minimal changes.[31] However, the plasma content of sodium and presumably chloride decreases suggesting the fluid shifts that occur during short-term exercise involve an isotonic shift of fluid.[31] During longer-term exertion there can be minimal changes in plasma sodium concentration but content can change dramatically.[23,31] With chloride there is a dramatic disproportional decrease both in the plasma concentration and content due to large amounts lost in the sweat.[23,31] Measuring total content lost gives a more complete picture of how much supplementation must occur to replenish exercise related losses. When one looks at changes in plasma potassium concentration and content one sees a different picture. Both the concentration and content of potassium go up during high-intensity exercise. When one looks at the change in content one can see that the change in concentration is due to both the loss of plasma water and the addition of potassium to the plasma when it leaks out of the contracting muscle cells.

Effects of acute exercise on fluid and electrolyte balance

Hypothetically, fluid and electrolytes can shift from the intracellular space to the extracellular space as well as between each of the compartments through active, passive, and facilitative mechanisms.[6–8,11,18,19,23,32,33] This dynamic exchange of fluid and electrolytes between compartments moves nutrients and waste products, provides fluid and electrolytes for the production of sweat and allows the horse to defend the internal environment of the cells.[6–8,11,18,19,23,32,33] To maintain cellular homeostasis the horse must regulate blood volume, blood pressure, and the osmotic composition of the intracellular and extracellular fluid compartments. Acute fluid and electrolyte shifts have differing functional significance related to the timing of the response during exercise. Early shifts appear more related to a system-wide redistribution of blood and fluid from capacitance vessels and the interstitial space so as to increase venous return and augment cardiac output.[6–8] Later responses provide fluid and electrolytes for the production of sweat and thermoregulation[6,11,17,23] Finally, decreases and depletion of fluid stores lead to dehydration, thermoregulatory, and cardiovascular instability and fatigue.[6,11,17,23] This latter challenge stimulates an expansion of plasma volume and the contents of the various electrolytes, a beneficial adaptive response known as a training-induced hypervolemia.[6,11,17,23]

Intercompartmental fluid shifts at the onset of exercise

Senay[34] demonstrated, in humans, that in the first seconds at the onset of exercise, there is a rapid net movement of protein

Example 3 Calculation of percent change in the content of a plasma constituent using corrected hematocrit[31]

HCTb = Resting hematocrit

HCTa = Corrected hematocrit

Cnb = Resting concentration

Cna = Postconcentration

Co = Content of soulute

$$\%\Delta Co = \frac{Cna - [HCTa\ (100 - HCTb) \times (Cnb)]/HCTb(100 - HCTa)}{HCTa(100 - HCTb) \times (Cnb)/HCTb(100 - HCTa)} \times 100$$

and fluid from the interstitial space and lymphatics into the vascular compartment.[34] This inward flux of protein and water causes a transient, short-lived increase in plasma volume, an intercompartmental shift of body fluids that couples with a redistribution of blood from the venous capacitance side of the vascular system to the arterial side to provide adequate venous return to maintain cardiac filling pressure.[6–8,34] This important redistribution of blood and fluid from the capacitance side of the vascular system is important because of the need for extra venous return at a time when there is rapid vasodilation in the working muscles.[6–8,34–36] Similar phenomena have been demonstrated in dogs and probably also occur in horses.[35,36] Studies[37] have demonstrated a shift in the albumin to globulin ratio in the horse consistent with an inward flux of fluid from the interstitial space. At rest albumin is the primary protein found in the vascular space and globulin represents the most prevalent protein found in the lymphatics.[37] This dramatic change in albumin to globulin ratio suggests that the horse experiences a similar influx in fluid at the onset of exercise as described in humans.[34,37] Plasma is also added to the central circulation upon mobilization of the splenic reserve.[13,17] Splenic blood is rich in red blood cells, with a hematocrit between 65 and 75%.[13,17] However, this also means that there is an addition of plasma to the central circulation. Splenic blood volume averages range from 8 to 12 L; thus, there is an addition of a 1.6 to 3.6 L plasma to the central circulation in addition to the volume added by intercompartmental fluid shifts.[13,17] This extra volume of plasma serves a role in cardiovascular control and it also increases circulating protein that provides extra buffering capacity to the central circulation.[13,17]

Plasma volume decreases rapidly after this initial intercompartmental redistribution of water and electrolytes.[6,17,18,23,32,33,38] These secondary fluid shifts are caused by significant increases in mean arterial pressure and consequentially capillary hydrostatic pressure that cause water, electrolytes, and a small amount of protein to be extruded from the vascular compartment.[6,23] Studies of horses[17,19,20] performing moderate incremental exercise have demonstrated that this decrease in plasma volume is rapid and intensity dependent with a 15 to 20% decrease observed after only four 1-min steps of an incremental exercise test (Fig. 38.1). This movement of water and salts bathes the interstitial space, where it can be taken up into the working muscles, used to form sweat, or returned to the vascular compartment.[17,19,20] In mammals there is a dynamic flux of fluid into and out of the vascular compartment that is governed by Starling forces (Fig. 38.2).[2,6–8,11] Net filtration and reabsorption across a vascular bed is the sum of forces affecting the movement of fluid and osmotically active substances in both the arterial and venous capillaries.[2,6–8,11] These forces include the capillary and interstitial hydrostatic pressures and the capillary and interstitial oncotic pressures. On the arterial side of the resting capillary bed, hydrostatic pressure and

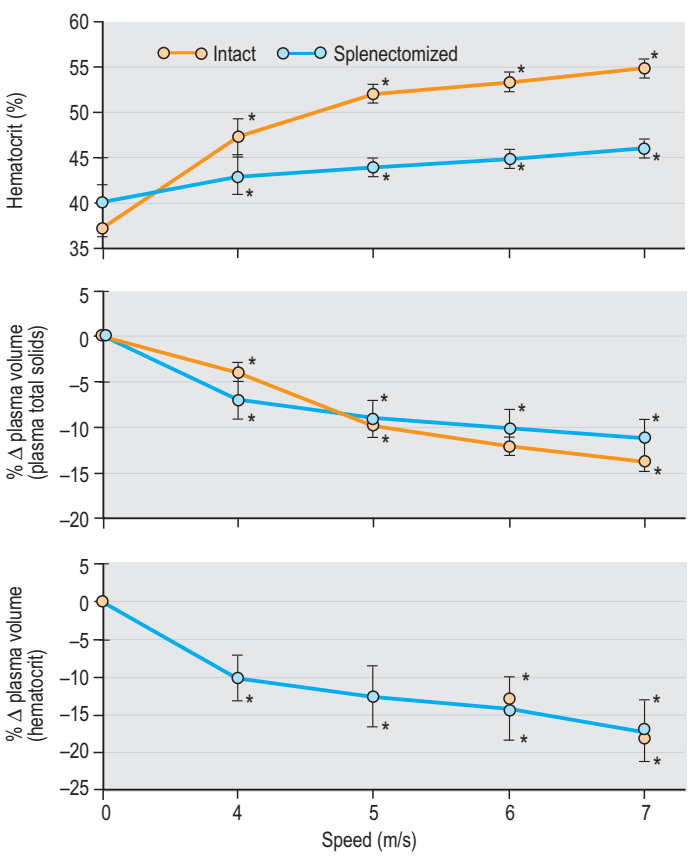

Fig. 38.1 Percentage change in plasma volume during incremental exercise. Values are means ± SE for hematocrit, percentage change in plasma volume calculated using total solids (i.e. protein) and percentage changes in plasma volume calculated using corrected hematocrit. (Reproduced with permission from McKeever et al.[17])

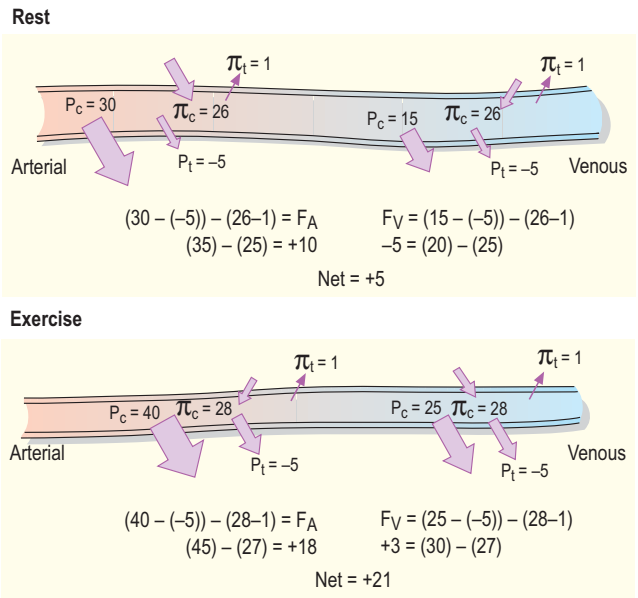

Fig. 38.2 Starling forces affecting the movement of fluid in and out of the vascular compartment. Rest: at rest, the balance of forces on the arterial side of the capillary bed is positive (+10), favoring an outward movement of fluid. On the venous side of the capillary bed the balance of forces is negative (–5), favoring the inward movement of fluid. However, the net difference between the arterial and venous sides of the capillary beds is positive (+5) and thus not all the fluid is returned to the bloodstream. The excess must be returned via the lymphatic system. Exercise: during exercise, hydrostatic pressure increases in both sides of the capillary bed enhancing the movement of fluid outward into the interstitial space for transport and for sweat production. Thus, during exercise, lymphatics play an important role in returning fluid not lost as sweat.

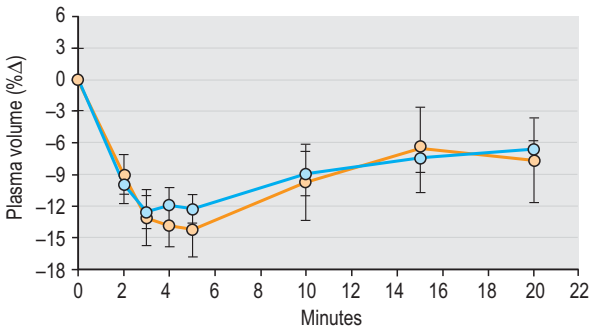

Fig. 38.3 Changes in plasma volume with steady-state exercise. Initial drop in plasma volume (0–3 min) due to fluid shifts, secondary changes due to fluid loses. (Reproduced with permission from McKeever et al.[17])

interstitial oncotic pressure outweigh interstitial pressure and intravascular oncotic pressure.[2,6–8,11] This favors a net movement of fluid out of the vascular compartment. However, resting venous oncotic forces outweigh the other forces and favor a movement of fluid back into the vascular space.[2,6–8,11] Some fluid is not returned via the influx into the venous capillaries and is returned through the lymphatic system.[2,6–8,11] During exercise, the balance of Starling forces is greatly affected by a larger increase in arterial hydrostatic pressure.[2,6–8,11] At the arteriole level this amounts to a ~20 mmHg increase in hydrostatic pressure enhancing the net force of fluid outward.[2,6–8,11] On the venous side of the capillary beds, hydrostatic pressure is also elevated with a tendency for a net positive outward force. This means that more fluid is shifted into the interstitial space when compared to rest. This extra dynamic outward flux of fluid has a functional significance and is beneficial as it can either be excreted as sweat or returned to the vascular compartment via the lymphatics. The net result is a decrease in plasma volume and a dynamic flux of fluid that provides for removal of metabolic waste products and for removal of heat produced during exercise.[2,17,20] The key here is that the decrease in plasma volume seen at the onset of exercise[2,17,20] is dynamic and intensity dependent (Fig. 38.3) and occurs before the onset of sweat losses.[17,20] However, plasma volume decreases seen after these initial fluid shifts are the result of reductions in total body water caused by sweating.[1,2]

Fluid and electrolyte losses associated with longer acute exercise

Exercise continued beyond a few seconds causes pronounced hemodynamic changes and, because of sweat production, fluid and electrolyte losses.[1,2,6] Evaporative cooling via sweating is by far the most efficient way to remove a large amount of heat from the body.[1,2,4–6,39] But this ability to maintain body temperature comes at a cost to the cardiovascular system. First, a portion of blood flow that could be used to supply the working muscles is redistributed to the skin to transport heat from the core to the surface.[5–8] At moderately heavy work intensities limited circulating blood volume and cardiac output cause transient alterations in cardiac filling volume and mean arterial pressure that are sensed respectively by the cardiopulmonary baroreceptors (volume receptors) and by the high pressure baroreceptors.[5–8] Optimal perfusion of working muscles requires that the cardiovascular system keeps mean arterial pressure within narrow limits.[5–8] However, there is an upward change in the set point during exercise that removes the check on the system that would tend to limit an increase in cardiac output. Rowell[7,8] has suggested that a feedforward mechanism allows blood pressure to increase during exercise via integrated responses of the above mentioned two layers of defense.[7,8] Control of mean arterial pressure during increasing exercise intensity necessitates shunting of blood away from non-obligate tissues.[6–8,35,36] These non-obligate tissues include the splanchnic and renal vascular beds.[6–8,35,36,40,41] The changes in vascular tone are so pronounced that they are facilitated by both nervous system and endocrine effector signals.[6–8,40,41] Interestingly, these neural

and endocrine factors (catecholamines, plasma renin activity, vasopressin etc.) influencing vascular tone in the splanchnic and renal vascular beds increase at intensities above 50–60% $\dot{V}O_{2max}$,[6–8,29,33,40,42–45] in most cases prior to any substantial loss of sweat. These adjustments in cardiovascular function and renal blood flow thus appear to be a response to the 's tress of exercise' itself rather than fluid and electrolyte imbalance.[40]

As exercise progresses, acute fluid shifts from the vascular compartment to the interstitial space provide water for sweat production.[6–8] Sweat loss causes a net reduction in total body water and a decrease in plasma volume that, if not replaced by water intake, eventually results in decreased venous return and cardiac filling pressure.[6–8] The horse has evolved to have a large reservoir of fluid in its digestive tract.[6] This is not an inconsequential amount as the horse can utilize fluid from the large colon as well as fluid contained in its cecum. Thus, in the wild the horse does not need to stop to drink while running from a predator. There are limits to these fluid reserves and the horse produces a huge volume of hypertonic sweat that eventually can lead to a compromised vascular volume. The cardiopulmonary volume receptors sense the drop in cardiac filling pressure and volume. To keep cardiac output constant the resultant fluid-loss-induced decrease in stroke volume must be countered by an increase in heart rate.[6–8] This tachycardiac adjustment to progressive fluid loss is referred to as cardiovascular drift.[6–8] More dramatic reductions in flow to non-obligate tissues can occur if increased heart rate cannot compensate for the decrease in cardiac filling pressure. Sweat-induced reductions in total body water initially come at the expense of plasma volume; however, as exercise progresses water loss causes a progressive cellular de-hydration.[1,2,4–6,9,39,45] The resultant cellular fluid deficit eventually leads to decreased cell function, fatigue, and a failure to thermoregulate properly.[46,47] Other problems can be caused by significant simultaneous electrolyte losses.[2,4,5,39,45–47]

Along with heavy sweat production comes loss of electrolytes which stimulates a variety of endocrine responses which function to correct the concentration of these vital substances.[6] Human sweat is hypotonic, that is, the concentration of sodium is less than that found in the plasma.[2] While prolonged exercise can result in severe electrolyte disturbances recent research has shown that they are much less frequent in humans compared to those seen in horses.[2,6,45–47] Equine sweat, on the other hand, is hypertonic and excessive sweat loss can rapidly result in severe problems related to both the hypovolemia and to the resulting electrolyte imbalance.[1,2,39] Several papers have documented that severe electrolyte loss can lead to weakness, muscle cramps, acid–base imbalance, and decreased performance.[2,5,6,45–47] Interestingly, trained humans appear to start sweating earlier and in greater amounts than untrained individuals exercising at similar relative work intensities.[6,26,48] Trained human athletes also appear to have a more hypotonic sweat[11,48] that results from aldosterone's action on the sweat glands.[19,20,25,26,48] Studies have not yet demonstrated similar training-induced adaptations in the neuroendocrine control of sweating and fluid balance in horses.

Sweat losses and the combined effects of exercise and environment

The transduction of potential energy into kinetic energy is a rather inefficient process with only 20–30% of potential energy effectively utilized for work.[5] The rest is heat that must be liberated from the body.[5] In general, the greater the exercise intensity of the event, the greater the heat load generated and the greater the need for heat dissipation.[5] Even under mild ambient conditions, the exercising horse is presented with a significant thermoregulatory challenge that requires an integrated response to transport heat from the core to be transferred to the environment.[5] The major method for the transfer of heat from the body involves sweating and evaporative cooling.[5] Evaporative cooling is several times more effective than other routes of heat exchange. Because evaporative cooling is so essential, the horse appears to have evolved with several species specific adaptations that enhance the ability to move fluid from the vascular compartment to the sweat glands and ultimately to the exterior as sweat.[5] First, as previously mentioned, increases in hydrostatic pressure during exercise enhance fluid shifts from the vascular compartment to the interstitial space, increasing the availability of fluid for sweat production.[5,6,19,20] Second, the sweat gland of the horse is very simple compared to the well-organized sweat glands seen in humans.[5,39] Therefore, sweat excretion is a less complex process. Additionally, the equine sweat gland, unlike the human sweat gland, is not responsive to aldosterone and thus it cannot conserve sodium.[39] Put simply, the equine sweat gland almost acts like a funnel to allow a hypertonic solution of electrolytes to move from the interstitial space to the surface. Teleologically, producing a hypertonic sweat may be beneficial as the solvent drag would tend to facilitate the movement of a greater amount of water outward. The extra salt in the sweat, as well as the protein lather in, also alters the evaporation point of the sweat possibly enhancing evaporative cooling. Functionally, this is significant as the horse has a less favorable surface area to volume ratio when compared to humans. The down side to these adaptations is the potential for large fluid and electrolyte deficits.

Recent articles have reported that during submaximal exercise, under conditions of high heat and humidity, sweat losses in horses can exceed rates of 12 L per hour.[5,39,45,49,50–56] This large volume of sweat results in proportional decreases in body weight, total body water, and plasma volume. This, in turn, can compromise venous return, cardiac filling pressure, cardiac output, and the ability to thermoregulate. Thermoregulatory stability requires a large cardiac output and peripheral blood flow to carry heat from the core of the body to blood vessels in the skin.[5] At the same time, the heart must pump blood to the working muscles, to the brain, and to other 'obligate' tissues that cannot suffer from reduced perfusion. To maintain cardiac output during intense exercise, baroreflexes

cause selective vasoconstriction and blood flow redistribution.[6–8] This reduces blood flow to non-obligate tissue beds like the viscera and kidneys and allows for increased blood flow to the working muscles.[7,8] As core heat accumulates, various feedback mechanisms cause blood flow to increase to the skin to enhance the transport of heat from deep in the core of the body to the surface.[5] If exercise proceeds for a long enough time, sweat loss leads to progressive dehydration and loss of plasma water from the bloodstream. Dehydration causes a decrease in circulating blood volume and cardiac stroke volume. A horse can keep going despite this reduction in vascular fluid volume; however, to maintain cardiac output, heart rate must increase ('cardiovascular drift').[5–8] When dehydration cannot be compensated for by cardiovascular adjustments, body temperature rises and is soon followed by decreased performance and fatigue. Maintaining cardiac output and mean arterial pressure (MAP) is vital to keeping perfusion pressure at the level needed to distribute flow to the working muscles, skin, and other obligate tissues. Thus, at the onset of exercise both mean arterial blood pressure and skin blood flow are defended.[5–8,19] However, as a horse becomes dehydrated MAP is defended preferentially at expense of skin blood flow and thermoregulation, adding to the resulting increase in body temperature.[5–8,19]

Several laboratories have observed that, even under cool conditions, endurance exercise performed in the field or on a treadmill laboratory will cause a substantial rise in core temperature, a substantial amount of sweat production, and a dramatic loss of total body water.[1,2,5,39,45,49,50–56] In field trials, it has been documented that even with the combination of proper hydration, adequate sweating, and maximal rates of evaporative cooling, a horse's body temperature can reach 105–106°F during endurance rides performed under moderate climatic conditions.[1,2,5,39,45,49,50–56] Under hot humid conditions, evaporative cooling becomes ineffective because sweat will not evaporate. The resulting hyperthermia can cause fatigue, cramps, heat stroke, and other thermal injuries.[1,4–6,10] Thus, in a hot and humid environment, even a well hydrated horse can encounter potential life-threatening situations in a relatively short time. However, most of these injuries can be prevented with proper feeding, adequate watering, and advanced planning of exercise training sessions and athletic events.

Almost all studies reporting sweat electrolyte concentrations in horses during exercise demonstrate that the horse loses a large amount of key electrolytes.[1,2,5,39,45,49,50–56] The range of sweat electrolyte concentrations varies with older studies suggesting tremendous sodium and chloride losses.[2] The magnitude of electrolyte loss reported in some studies is questionable and most likely is a function of the methodologies utilized. Older studies relied on sweat scrapings and other sampling techniques that overestimate actual losses. Several newer papers have utilized more refined methods adapted from human research, preventing the errors due to evaporation of water or addition of salt from areas already contaminated by prior sweating.[49,50–56] Nevertheless, more recent studies still demonstrate that equine sweat is hypertonic to plasma and that without replacement there are substantial electrolyte deficits in horses competing in endurance activities. While sodium and chloride are the primary electrolytes lost in equine sweat, other key electrolytes like magnesium and calcium are lost.[39] Most important is a disproportional loss of chloride ions that can potentially lead to a serious metabolic alkalosis.[9,39] The loss of sodium can become an even greater problem during recovery if a horse drinks too much water.[9] As with human marathon runners, some endurance horses can develop a hyponatremia that, if untreated, can lead to collapse and death.[47] Thus, provision of water as well as electrolyte supplements is warranted after endurance activities accompanied by large fluid and electrolyte losses.

Thirst, drinking, and electrolyte intake

Hormonal changes stimulate thirst and drinking and it is well recognized that the horse has a finely tuned regulatory system to maintain fluid and electrolyte balance.[1,2,6,19] Mechanistically, thirst can be stimulated by increases in circulating concentrations of angiotensin, arginine vasopressin (AVP), and by changes in the concentration of calcium and other electrolytes in the cerebrospinal fluid.[6,24–26,28,57–60] These systems are modulated by changes in osmolality sensed by the paraventricular and supraoptic nuclei of the hypothalamus.[6,24–26,28,57–60] Thus, a small increase in plasma osmolality will result in the release of AVP by the posterior pituitary.[6,24–26,28,57–60] These drives for thirst and drinking are finely tuned for the resting horse; however, it has been documented that strenuous, high intensity, exercise can paradoxically suppress thirst and the central drive for drinking behavior in humans, dogs, and more recently horses.[6,24–26,28,57–60] Mechanistically, it appears that early in exercise there is a suppression of AVP release associated with the role the cardiopulmonary baroreceptors play in the accommodation of fluid shifts and the mobilization of the splenic reserve.[19,61] Comparative studies of dogs, humans, and other species have also shown that there is a general suppression of the drive for drinking, as well as additional suppression of thirst and drinking during exercise when cold hypotonic water passes by nerves in the mouth and throat.[6,24–26,28,57–60] This suppression of drinking behavior may be a protective mechanism – an ingrained defensive behavior that prevents an individual from stopping for water while on the run from a predator. Horse owners and veterinarians monitoring endurance events have reported a similar suppression of drinking in horses.[6,9,10,23] In many cases, endurance horses will not drink at the end of a race and some clinicians have reported that this suppression of thirst and drinking behavior can last for several hours after exercise.[1,2,10,23] Unfortunately, this is the time when rehydration should be taking place. In some cases, it is the horse

with the most severe fluid and electrolyte deficit that is the one that will not drink right away or is the one that will consume a volume that is not sufficient to replace the amount of water lost during competition.[10,23] Some researchers have speculated that there is a threshold where severe dehydration itself accentuates this paradoxical suppression of drinking.[26,28,57–60] Interestingly, recent research demonstrated that endurance horses could be taught to drink warm water with electrolytes during competition without a resulting suppression of thirst and drinking.[62–66]

An equine athlete can usually recover from moderate acute exercise-induced fluid and electrolyte losses. And, in most cases, fluid and electrolyte losses following acute exercise can be compensated for through the provision of adequate water, a normal diet, and a salt and mineral supplement.[10,67] However, some scenarios can potentially cause problems for competing animals.[10,67] One scenario might result from larger-than-normal fluid and electrolyte losses resulting from exercise in hot or hot and humid conditions. In this case, fluid losses may need to be replaced rapidly to avoid thermal injuries.[10] Competition following long periods of trailering to an event with limited amount of water supplied for drinking while in transit presents another scenario for problems.[10] In this case, a horse owner should provide access to water prior to competition.[10] If the distance to the event is long, one should consider providing opportunities for drinking at rest stops along the way.[10] Another situation that can result in severe dehydration can occur when there is limited recovery time between phases during three-day competitions or other multiple event competitive formats.[10] Logistics of these events may prevent an animal from drinking enough water or prevent a horse from getting adequate electrolytes via dietary replacement.[10] Clinicians monitoring the status of competing horses should insure that all animals have had an ample opportunity to recover between days, phases, or heats of a competition.[10]

The amount of water consumed by a horse varies with the individual, diet, climate, and amount of exercise.[10,66] The National Research Council guidelines for feeding horses recommend 2–4 L of water per kilogram of dry matter feed intake.[10,67] This amount can increase 15–20% for horses in warm environments.[10,66] For example, a recent paper reported that non-exercised horses in Arizona consumed between 30 and 40 L of water in the hot months of June and July.[14] Water intake may increase 300% or more with prolonged exercise and some studies have documented that an active horse can consume 100 liters of water per day under some conditions.[1,2,39,62]

Renal function during exercise

Alterations in renal blood flow and renal function vary with both the duration and the intensity of exercise.[6,40,68–70] In general, exercise affects both renal blood flow and the delivery of water and electrolytes to the kidney and it affects

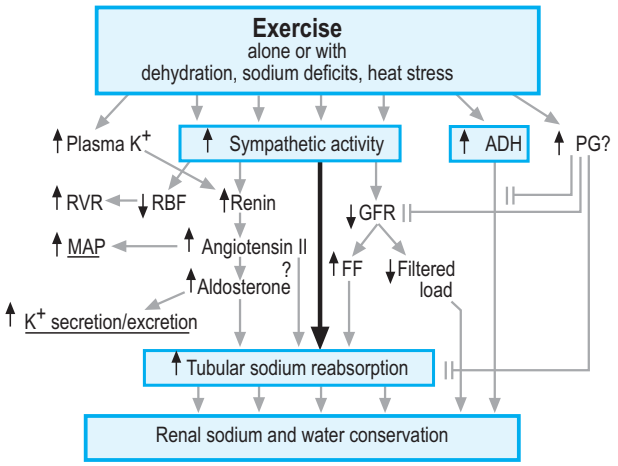

Fig. 38.4 Renal response to high-intensity exercise. (Reproduced with permission from Cooper Publishing Group, Traverse City, MI[40]). FF, filtration fraction; GFR, glomerular filtration rate; MAP, mean arterial pressure; PG, prostaglandins; RBF, renal blood flow; RVR, renal vascular resistance

mechanisms associated with the tubular reabsorption of water and electrolytes.[6,40] Acute and chronic renal responses to exercise are part of an integrative defense of blood volume, blood pressure, and osmolality.[6,40] Zambraski[40] suggests that the alterations in renal function are both a response to the stress of exercise alone and also to perturbations in fluid and electrolyte balance (Fig. 38.4). Acute demands of exercise result in a decrease renal blood flow, sparing cardiac output so as to allow the cardiovascular system to meet the increased circulatory demand associated with exertion.[40] Post-exertional changes in renal function, on the other hand, are part of a long-term mechanism to restore lost water and electrolytes.[6,40] The kidneys also function as major effector organs in the adaptive expansion of plasma volume and electrolyte content balance referred to as the hypervolemic response to exercise training.[6,40]

Effects of exercise on renal blood flow

During submaximal exercise absolute renal blood flow (RBF) is not reduced in humans or horses.[40,71] However, it has been documented that low- intensity exercise results in a reduction of renal blood flow as a percentage of cardiac output.[40,71] For example, Hinchcliff et al.[71] reported that renal blood flow averaged 15 mL/kg/min and did not change during exercise. However, because cardiac outpit increased, RBF did decrease as a percentage of cardiac output, dropping from 23% at rest to 6% during exercise.[71] High-intensity exercise, on the other hand, causes substantial reductions in absolute renal blood flow in swine, horses and humans, but not in normal dogs.[6,40,72,73] Renal vasoconstriction appears to occur when work intensities exceed a threshold of 50–60% of $\dot{V}O_{2max}$,[6,40] a point coincident with detectable increases in renal nerve activity, circulating catecholamines, and plasma renin activity.[6,40–42]

Schott and co-workers[72] were the first to demonstrate that high- intensity exertion causes a reduction both in absolute RBF and relative RBF (i.e. RBF expressed as a percentage of cardiac output) in the horse. Absolute RBF decreased from 9.0 L/min to 2.4 L/min when horses were exercised at a speed shown to produce an oxygen uptake that was 100% of $\dot{V}O_{2max}$.[72] Amazingly, RBF decreased as a percentage of cardiac output from 22% at rest down to 0.09% during maximal exercise.[72] This reduction in RBF resulted in a substantial drop in glomerular filtration rate and subsequently a drop in urine flow, and the excretion of solute-free water and various electrolytes. Interestingly, a follow-up study demonstrated that phenylbutazone and furosemide did not appear to alter the renal response to high-intensity exercise.[73]

Effect of exercise on glomerular filtration rate, filtration fraction

Blood flowing through the renal artery is filtered through millions of glomeruli in the kidney.[40] The glomerulus is part of the nephron, the basic structural unit of the kidney.[40] It is a complex structure made up of the afferent artery, Bowman's capsule, and the efferent artery.[40] Algebraically, glomerular filtration rate is representative of the sum of the action of all the nephrons, and is autoregulated over a wide range of kidney blood flow. As with RBF, the effects of exercise on glomerular filtration rate (GFR) in the horse varies with the intensity of the exercise.[71–73] GFR has been shown to increase or decrease during submaximal exercise depending on hydration status.[40] In studies where the subjects were hyperhydrated, GFR did not change during submaximal exertion.[40] However, when individuals were euhydrated or hypohydrated, changes in GRF were intensity and/or duration dependent, changing the most when individuals performed high-intensity exercise.[40] Interestingly, while RBF can be dramatically reduced during exercise, studies of humans show that decreases in GFR do not necessarily parallel the decreases in RBF.[40] Thus, glomerular filtration is somewhat protected in the face of exercise-induced reductions in RBF with a resultant increase in filtration fraction (i.e. the ratio GFR/RBF).[40]

Zambraski[40] has suggested some possible mechanisms to explain the exercise-induced increase in filtration fraction (FF) observed in humans and other species. First, maintenance of glomerular hydrostatic pressure and preservation of GFR through greater constriction of the efferent arteriole relative to the afferent arteriole.[40] However, data from comparative species are lacking or have not fully supported this hypothesis. A second hypothesis for exercise-induced increases in FF postulated that changes in glomerular capillary Kf simultaneous to decreases in glomerular capillary hydrostatic pressure would 'assist in maintaining GFR'.[40] While not directly tested, this mechanism fits teleologically with data from human and animal studies documenting exercise-induced increases in substances that affect Kf, such as vasopressin, the prostaglandins, and angiotensin II.[40]

The effects of exercise on GFR and FF appear to be similar in the exercising horse and in exercising humans. Hinchcliff and co-workers[71] reported that, as in humans, there appear to be no alterations in GFR or FF during standing control or submaximal (50–60% $\dot{V}O_{2max}$) exercise in horses. In that study, creatinine clearance (GFR) ranged between 2.0 and 2.5 mL/min/kg and FF averaged 23%.[71] High-intensity exercise, on the other hand, produces a significant decrease in GFR and a significant increase in FF in the horse.[72] Schott and co-workers[72] demonstrated that GFR decreased 73% from a mean of 1.9 mL/kg/min to 0.5 mL/kg/min during exercise performed at an intensity shown to produce $\dot{V}O_{2max}$. As with humans, horses performing high-intensity exercise had significant increases in FF from 16% at rest to 23.2% following running.[72] While drugs like furosemide and phenylbutazone affect renal blood flow, they do not appear to alter GFR and FF in the horse during submaximal or maximal exercise.[73] These observations were interpreted to suggest that the renal prostaglandins play a minimal role in mediating changes in GFR and RBF in the horse during exercise.[73]

Renal tubular function and excretion during exercise

In simple terms, the kidneys filter the blood at the glomerulus and then selectively reabsorb or secrete essential and non-essential substances in the tubules.[6,40] Normal fluid and electrolyte homeostasis requires the kidneys to eliminate excess water and electrolytes or if there is a deficit, to reabsorb those vital components of the blood.[6,40] Alterations in GFR and/or tubular handling of water and solutes ultimately affects the volume of urine produced and the rate volume of essential electrolytes excreted over a given period of time.[6,40] Studies of humans, dogs, and horses have demonstrated that changes in tubular handling of water and solutes varies with work intensity.[6,40] These changes appear to be secondary to alterations in renal blood flow, GFR, and the filtered load of a given substance.[6,40] We are aware of only a few studies of the effects of exertion on renal tubular function. One study (Fig. 38.5) examined the effects of 1 h of submaximal exercise on endocrine changes and renal tubular function[74] and the others examined the effects of high intensity exercise on renal function during and after exercise.[72]

During submaximal exercise, performed at an intensity below 60% $\dot{V}O_{2max}$, urine flow increases in humans and horses.[40,69,71] However, in horses, while low intensity exercise resulted in a significant 45% increase in urine production, the total volume of extra water lost (~6 mL/min) was reported to be small compared with the increased volume lost as sweat.[72] McKeever et al.[74] reported that the increase in urine flow was due to an exercise-induced increase in osmotic clearance induced primarily by a natriuresis and a kaliuresis.[74] The increase in sodium excretion appeared to be medi-

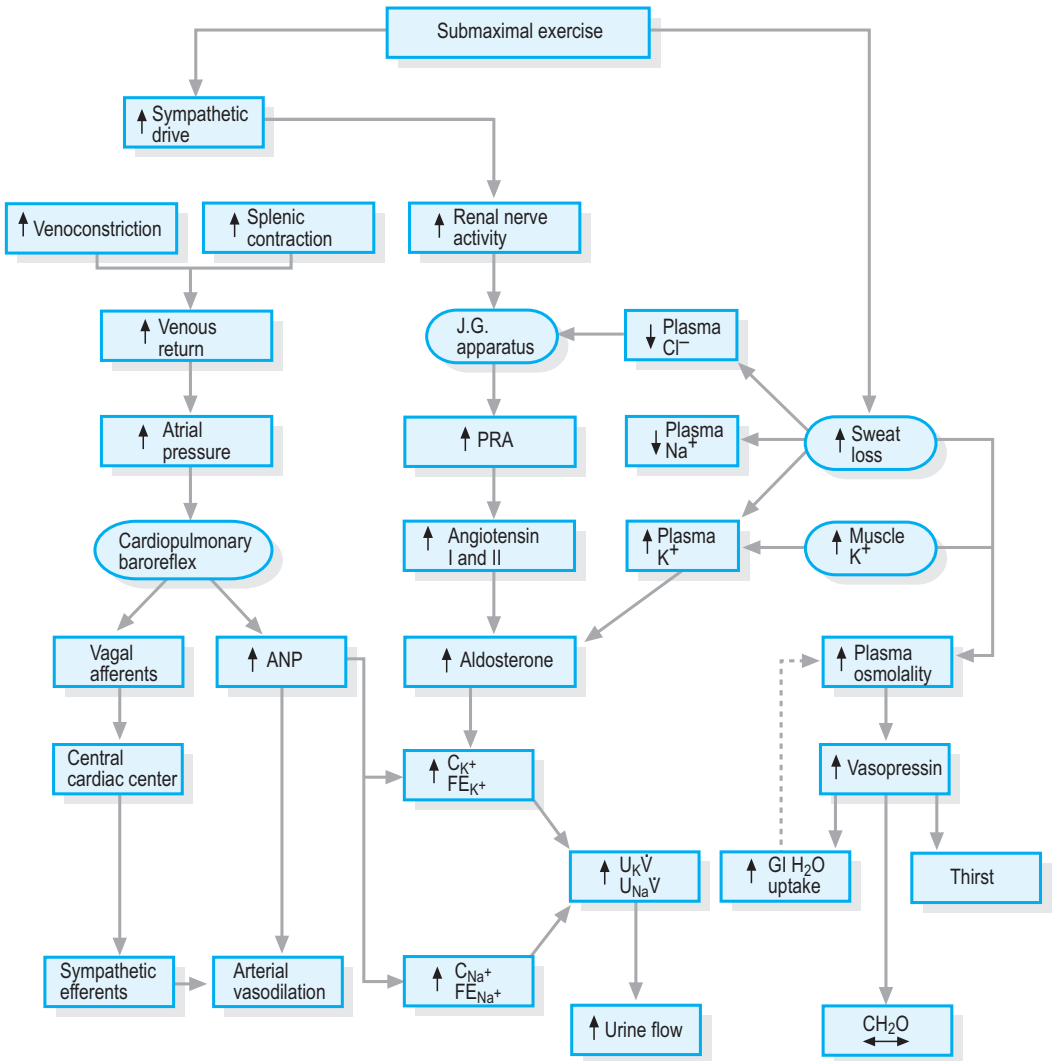

Fig. 38.5 Renal, cardiovascular, and endocrine response to low-intensity exercise in the horse. ANP, atrial natriureteric peptide; C_{K^+}, potassium clearance; C_{Na^+}, sodium clearance; FE_{K^+}, fractional excretion of potassium; FE_{Na^+}, fractional excretion of sodium; GI, gastrointestinal, JG, juxtaglomerular (apparatus); PRA, plasma renin activity; $U_K\dot{V}$, potassium excretion; $U_{Na}\dot{V}$, sodium excretion. (Reproduced with permission from McKeever et al.[74])

ated by a concomitant increase in plasma atrial natriuretic peptide (ANP).[74] Even so, the total amount of sodium lost via renal excretion was minimal. The authors suggested that, during exercise, ANP (a potent vasodilator) functioned primarily to facilitate decreased vascular resistance in the working muscles[74] so as to accommodate increased atrial pressure caused by exercise-induced increases in venous return. The relatively small but significant increase in sodium excretion observed in horses and humans during the early part of a bout of endurance exercise appeared to be a minor secondary response to the potent cardiovascular action of this hormone.[74]

Interestingly, the authors of that same study demonstrated that there was a significant kaliuresis as well as the aforementioned natriuresis and suggested that the increase in potassium excretion was due primarily to a rise in plasma aldosterone concentration.[74] The increase in plasma K^+ concentration seen in submaximally exercised horses coincided with an increase in plasma aldosterone concentration.[74] The authors speculated that because there were limited decreases in plasma Na^+ concentration, the increases in aldosterone release may have been primarily in response to the rise in plasma K^+ concentration.[74] This phenomenon has been demonstrated by other researchers, who have shown that the most potent stimulus for aldosterone secretion is an increase in circulating potassium.[74] Functionally, this prevents excessive increases in plasma K^+ concentration, which can alter electrophysiological gradients in the muscles and other tissues.[74] Several studies have documented that excessive increases in plasma K^+ concentration appear to be one of many factors contributing to the onset of muscle fatigue.[6,74] Thus, the reported increase in plasma aldosterone release and the kaliuretic action of ANP may function to limit an excessive rise in plasma K^+ concentration during lower-intensity exercise.[74]

Another major problem associated with exercise in the horse is an excessive and disproportional loss of chloride via the sweat.[74] McKeever et al[74] demonstrated that renal chloride losses decrease when plasma chloride concentrations fall. Similar reductions in chloride excretion are also seen in exercising humans.[6,40] As Na^+ and K^+ excretion increased in submaximally exercised horses, the authors suggested that mechanisms affecting the conservation of those electrolytes could not have been responsible for the increase in Cl^- reabsorption.[74] Interestingly, the same horses became alkalotic during the hour-long bout of exercise.[74] Thus, the authors suggested that based on other reports,[40,74] renal mechanisms affecting reabsorption of Cl^- and secretion of HCO_3^- by the antiporter in the apical membrane of the intercalated cell of the cortical collecting duct may have led to conservation of chloride.[40]

Lastly, solute-free water clearance does not appear to be altered by submaximal exercise in the horse despite significant increases in plasma osmolality and plasma vasopressin concentrations.[74] Similar observations have been made in exercising humans.[40] This paradox has several possible explanations. First, a decrease in renal blood flow potentially could decrease the filtered load of solute-free water available for reabsorption by the action of AVP on the collecting ducts.[40] This explanation would not be supported by the observation that submaximal exercise does not affect absolute RBF or GFR.[6,71] It may, however, be possible that the extrarenal functions of vasopressin are more important during exercise and actions on the kidneys are overridden. Such functions may include vasopressin's role in vasoconstriction of vascular beds in non-obligate tissues, its role in central mechanisms that stimulate thirst and drinking, and its action on the gut.[6,25,75,76] In the gut, vasopressin appears to act on the epithelium of the large intestine enhancing the uptake of sodium and water.[75] This protective effect would aid in the limitation of exercise-related fluid deficits more than potential reductions in free water clearance.

High-intensity exercise appears to have effects that are dramatically different from submaximal exertion. Sodium excretion is dramatically reduced during high-intensity exercise in horses, pigs, and humans.[6,40,71] Inconsistent changes in sodium excretion have been observed in the exercising dog.[40] Several mechanisms could be responsible for the decrease in sodium excretion including: (i) a decrease in filtered load of sodium; (ii) activation of the renin–angiotensin cascade; (iii) elevation of plasma aldosterone concentration; and (iv) direct neurogenic control.[40] In the first instance, a change in filtered load sodium would mean that less solute would be presented to the tubules for reabsorption. This would require a reduction in GFR; as this does not change in humans, pigs, or horses,[6,40,71] it does not appear to be a viable mechanism for the decrease in sodium excretion. More recent information has been published that shows that the decrease in sodium excretion is not blocked by pharmacological blockade of the renin–angiotensin cascade.[40] Aldosterone concentration increases in the horse without a change in sodium excretion.[74] In other species, the observation that sodium excretion rapidly returns to baseline after exercise suggested that aldosterone was not the mediator of the antinatriuresis seen during exercise.[40] The speed of the recovery has been further interpreted to suggest a neural mechanism.[40] This theory is consistent with a reported intensity-dependent increase in renal sympathetic nerve activity during exercise.[40] Zambraski[40] and others have suggested that, based on all the current evidence, the mechanism behind exercise-induced increases in sodium reabsorption is primarily direct neurogenic control.

Schott et al.[72,73] reported that urine flow almost stopped during supramaximal exercise and was still below pre-exercise levels in the period immediately after exercise. High-intensity exercise also caused a decrease in urine osmolality and osmotic excretion.[72,73] Interestingly, one would have predicted a significant reduction in electrolyte excretion; however, there were only non-significant reductions in the bulk excretion of K^+ and Cl^- during exercise and no change in Na^+ excretion, despite a reduction in urine flow.[72] This response contrasts with changes observed in other species.[40] One explanation for this aberrational finding may be the design of the experiment. In the experiment, exercise was performed during part of one of the 15-min collection periods.[72] Data for the entire 15-min collection period were pooled and included a postexercise period characterized by diuresis, natriuresis, and kaliuresis (see below). These post-exercise changes may have offset any exercise-induced decreases in electrolyte excretion that should have occurred with a reduction in RBF and urine flow.

High-intensity exercise appears to also affect urinary pH, an observation of interest to racing chemists.[77] Gerken et al[77] reported that high-intensity exercise caused a transient reduction in urine pH that lasted for up to 60 min of recovery. The authors suggested that the more acidic urine may affect the results of the battery of tests used to detect foreign substances.[77] More interestingly, they suggested that alkalinizing agents like sodium bicarbonate may alter postexertion pH, thus further complicating drug detection efforts.

Post-exercise changes in renal function

While the studies of Schott et al.[72,73] did not document a change in tubular function, the authors did report a substantial postexercise increase in urine flow. Data were consistent with a diuresis, kaliuresis, and natriuresis.[72,73] Excretion rates for these substances returned to baseline by 30 min of recovery. The authors suggested that the increase in sodium and potassium excretion was most likely due to an increase in atrial natriuretic peptide, which had been shown to increase during exercise in the horse.[72] Long term, the adaptations to exercise training involves reduction in 24-h urine output and an expansion of plasma volume with a concomitant increase in the content of sodium in the vascular compartment.[14,78]

Adaptive response to repeated exercise (training)

Training-induced hypervolemia

Repeated exercise or training usually evokes an adaptive response that better prepares the horse's various physiological systems for subsequent bouts of acute exertion.[6,11,14,48,79] Disturbances in fluid and electrolyte balance require a two-phase response, with the early phase resulting in the replenishment of acute fluid and electrolyte losses and a secondary or adaptive phase that results in an enhanced ability to cope with future systemic disturbances.[6,11,14,48] This 'hypervolemic' response to training is an adaptive response that involves a beneficial increase in blood volume due to an increase in plasma volume.[48] The training-induced hypervolemia is beneficial because it enhances both cardiovascular and thermoregulatory stability during the challenge of acute exercise.[48,80] The increase in total body water provides extra fluid that insures cardiovascular stability by providing the extra volume needed to maintain venous return and thus cardiac output.[6,48] Thermoregulatory benefits are two-fold, including an increase in the ability to increase skin blood flow to enhance transport of heat from the core to the surface and an increase in the amount of fluid available for sweat production and evaporative cooling.[48] Functional evidence for the latter benefit can be seen in studies of humans that have demonstrated that trained individuals have an earlier onset to sweating and produce more sweat compared to untrained individuals exercising at the same relative submaximal work intensity.[48] It is likely that there are similar training-induced changes in cardiovascular function and thermoregulation in the horse.[80]

Mechanistically, the retention of water and electrolytes that leads to a training-induced hypervolemia reflects the effort of multiple systems to defend volume, plasma osmolality, and blood pressure.[6,11,14,19,48] Comparative studies have demonstrated that approximately 60% of the mechanism behind the hypervolemic response is related to stimuli associated with the demands of thermoregulation[48] The remaining 40% of the response appears to be related to mechanisms directly associated with exertion.[48] These mechanisms counter acute fluid and electrolyte losses by stimulating the intake of water and by reducing renal losses of water and electrolytes (Fig. 38.6).

Interestingly, rats, humans, dogs, and horses all expand their plasma volume in response to exercise training.[14,48,79,81] However, there are profound species differences in the mechanism behind the hypervolemic response to exercise training. Dogs expand their total body water through drinking, in fact, water is consumed at a greater rate than an observed training-induced natriuresis and diuresis.[81] Cooling in dogs involves a large loss of respiratory water and saliva, which results in acute increases in plasma tonicity and osmolality.[81] Thus, dogs must either drink to take in water to dilute the hyperosmotic hypertonic plasma or they must use renal mechanisms to excrete the excess electrolytes sensed in the plasma.[81] Humans and horses on the other hand, lose a large amount of electrolytes in their sweat; therefore, there is a drive to replenish fluid and electrolytes to defend both volume and tonicity.[14,48,78]

In horses and humans, drinking during and immediately after exercise at best only slows or partially counters the development of a fluid deficit, but does not counter any electrolyte deficit.[14,48,78] Studies of horses and humans are mixed as to the role of water and electrolyte intake in the long-term response to exercise training.[14,48,78] Humans use both an increase in thirst and drinking and renal mechanisms to increase net fluid retention.[48] Drinking in humans, however, does not account for all of the net water retention, with most of the actual expansion of total body water coming through renal mechanisms.[48] One recent study of the horse reported that water intake increased with training; however, the authors did not measure renal losses or conduct a balance study that would determine if the amount ingested contributed to an expansion of plasma volume.[6] Other studies have shown that exercise training does not alter water intake in the horse.[14,78] Instead, they reported that the horse appears to rely on renal mechanisms and an overall reduction in urine water loss[14,78] to retain the sodium and water needed to expand plasma and blood volume.

In both humans and horses, this decrease in urine output seen with training is due to alterations in postglomerular mechanisms rather than a change in filtration rate.[14,48,78]

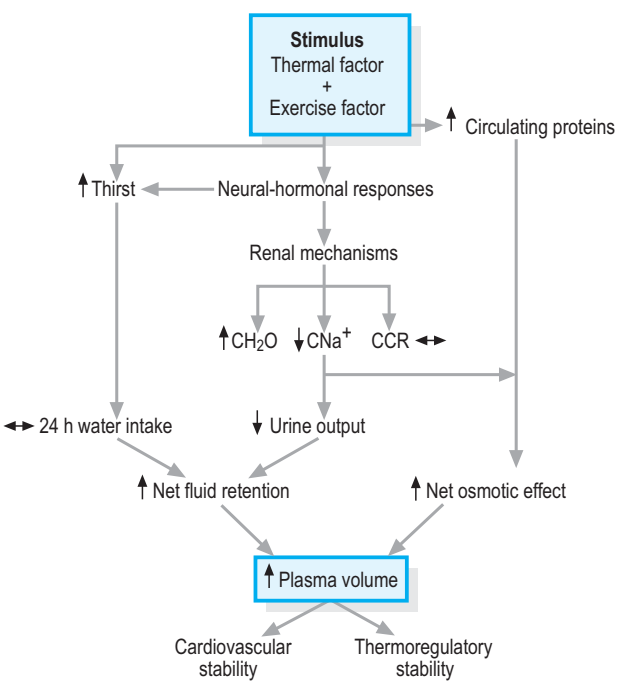

Fig. 38.6 Suggested mechanisms for the exercise training-induced hypervolemia seen in horses. CCR, creatinine clearance. (Adapted from Convertino.[48])

These renal adjustments are an adaptive or training response rather than a countermeasure to the perturbations of acute exercise. In humans an aldosterone-mediated retention of sodium and water seems to cause a net retention of water.[82–84] Until recently, the mechanism behind the hypervolemic response was not as clear in the horse. An early study did not demonstrate any change in renal mechanisms affecting the retention of sodium and water, and instead suggested that urea rather than sodium may be the solute responsible for the renal retention of water that leads to a training-induced expansion of plasma volume in the horse.[14] However, the authors paradoxically demonstrated that there was a highly significant increase in plasma sodium content that paralleled the increase in plasma volume.[14] Interestingly, this net increase in retained sodium and water occurred despite increased losses via sweating.[14] As the rate of sodium intake was held constant, the only other routes for a training-induced retention of sodium would have been either a more efficient uptake of electrolytes and water from the gut and/or a net retention by the kidneys early in the first days of training, as seen in humans, where most of the response occurs in the first days of training. To solve this mystery, a more recent paper[78] focused on the first days of training and demonstrated dramatic reductions in urine output and excretion of sodium during the first days of training. Thus, like humans, the horse appears to undergo a similar aldosterone-mediated retention of sodium and water by the kidneys.[78]

However, it was also found that renal retention of sodium and water did not fully counter losses seen in the sweat during the first days of training and the authors suggested that an enhanced aldosterone-mediated uptake of sodium and water from the large intestine may also contribute to the retention of electrolytes and water.[78] This makes sense because the horse's large intestine serves as a fluid reservoir. Such an additional response in the horse may be a warranted species-specific adaptation in response to the relatively larger electrolyte deficits associated with the production of hypertonic sweat. Enhanced intestinal uptake of sodium and water is supported by other published studies[85] demonstrating that aldosterone may enhance the transport of electrolytes and water from the digestive tract of the horse.

Concurrent with the aforementioned retention of water, sodium, and other vital electrolytes (which keeps the retained fluid isotonic), is an increase in the plasma protein content.[14,48,78] This increase in protein functions to keep the plasma iso-oncotic; thus, holding water within the vascular space. Human studies suggest that the early increase in plasma protein content comes about from inward shifts of protein from the lymphatics and interstitial space, and later from an overall net increase in plasma protein synthesis.[48] The hypervolemic response to training in the horse also appears to involve an increase in the content of plasma protein, most likely through a net increase in synthesis.[14,78]

One aspect of the effect of training yet to be studied in the horse is whether there are alterations in the cardiopulmonary baroreceptors that allow for the retention of the extra vascular volume. Human studies have shown that training results in a down regulation of the ANP and neuroendocrine response to exercise, quite possibly to accommodate the hypervolemia associated with exercise training.[48] Future research should determine if down regulation of these important control mechanisms also occurs in horses.

It is important to note that short term horizontal studies of humans, dogs, and horses have demonstrated that the increase in plasma volume occurs early in training and is followed by a subsequent slow increase in red blood cell volume (Fig. 38.7).[86] Thus, early in training, if one only looks at hematocrit there is a false impression of a 'sports anemia'.[86] Interestingly, in humans there appears to be an overshoot in the expansion of plasma volume.[86] As red cell volume slowly increases, the early increases in plasma volume appear to level off and even decrease.[86] Thus, after weeks and months of training there is a greater blood volume, with both plasma and red cell volume remaining greater than pretraining levels,[86] most likely at a level that optimizes both blood viscosity and oxygen-carrying capacity.[87]

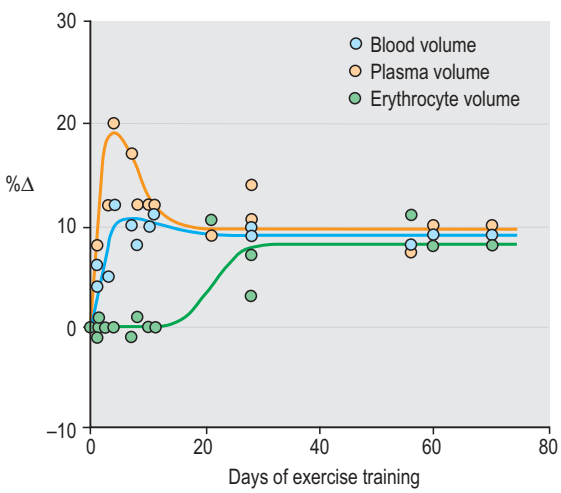

Fig. 38.7 Estimated time course of relative (%) changes in blood volume (blue line), plasma volume (orange line), and erythrocyte volume (green line) during exercise. Each point represents the average change reported in a group of (human) subjects from one investigation. Data were extracted from 18 investigations in which all three vascular volumes were reported. (Reproduced with permission from Sawka et al.[86])

Effects of aging on the acute and chronic response to exercise

A limited number of data have been reported comparing the thermoregulatory responses of older and younger men and

women during exercise in the heat.[88,89] It has been concluded that age influences thermoregulatory function during exercise.[88] Suggested reasons for this age-related decline in the ability to thermoregulate properly during exercise in humans include lower cardiovascular capacity due to the age-related decrease in cardiac output, alterations in mechanisms associated with the control of skin blood flow, and a possible state of hypohydration in the elderly.[88]

While there are an abundance of papers that have examined thermoregulation in young horses, few studies have addressed the effects of age on the thermoregulatory response to exercise in the horse.[90,91] McKeever and co-workers[90,91] exercised young and old horses at the same submaximal absolute work intensity of 1625 watts until they reached a core body temperature of 40°C. Older horses reached a core temperature of 40°C in almost half the time required by the younger mares.[90,91] The heart rates of the older mares were also substantially higher than the heart rates of the younger mares at 40°C.[90,91] Interestingly, both groups had similar heart rates and core temperatures by 10 min after exercise.[90,91] Even with the more rapid heart rate, older horses were still unable to dissipate the heat generated from exercise as quickly as younger mares, therefore leading to a faster increase in core temperature after the onset of exercise. Age-related changes in fluid and electrolyte balance and cardiovascular function may contribute to the impaired thermoregulatory capacity. Older humans commonly have lower total body water, plasma volume and reserves of fluid for sweating. [88] In the above mentioned studies of aged horses the changes in markers of fluid status suggested that acute fluid shifts were of a similar magnitude when compared to younger animals. However, a subsequent study[92] demonstrated that older horses had a substantially lower pre-exercise plasma volume compared to younger animals. A lower plasma volume could result in lower venous return, stroke volume, and cardiac output and a compromise of thermoregulatory stability.

Summary

Exercise places large demands on the cardiovascular system, and is further complicated by environmental factors. Performance is limited in many respects by fluid and electrolyte stores and the ability to maintain cardiovascular and thermoregulatory stability in the face of severe sweat losses. Studies of the exercising horse have been primarily descriptive and/or associative with only a limited number seeking to identify physiological mechanisms associated with the control of fluid and electrolyte balance. More mechanistic studies are needed to fully understand the integration of the cardiovascular, endocrine and renal systems in the defense of plasma osmolality, blood volume, and blood pressure.

References

1. Carlson, GP. Thermoregulation and fluid balance in the exercising horse. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge, Granta Editons, 1983; 291
2. Carlson GP. Hematology and body fluids in the equine athlete: a review. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology vol 2. Davis, CA: ICEEP Publications; 1987; 393–425.
3. Greenleaf JE, Morimoto T. Mechanism controlling fluid ingestion: thirst and drinking. In: Buskirk ER, Puhl SM, eds. Body fluid balance: exercise and sport. New York: CRC Press; 1996; 3–17.
4. Geor RJ, McCutcheon LJ. Thermoregulatory adaptations associated with training and heat acclimation. In: Hinchcliff KW, ed. Veternary Clinics of North America: equine practice; fluids, electrolytes and thermoregulation in horses. Philadelphia: WB Saunders; 1998; 97–120.
5. McConaghy F. Thermoregulation. In: Hodgson DR, Rose RJ eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994; 181–204.
6. McKeever KH. Fluid balance and renal function in exercising horses. In: Hinchcliff KW ed. Veterinary Clinics of North America: Equine practice; fluids, electrolytes and thermoregulation in horses, Philadelphia: WB Saunders; 1998; 23–44
7. Rowell LB. Human cardiovascular control. New York: Oxford University Press; 1993; 441–479.
8. Rowell LB. Cardiovascular adjustments to thermal stress. In: Handbook of physiology. The cardiovascular system. Peripheral circulation and organ blood flow, section 2, vol. 111, part 2, Chapter 27. Bethesda, MD: American Physiological Society; 1983; 967–1023.
9. Schott HC, Hinchcliff KW. Fluids, electrolytes, and bicarbonate. In: Hinchcliff KW, Sams RA, eds. Veterinary Clinics of North America: equine practice – drug use in performance horses. Philadelphia: WB Saunders; 1993; 577–604.
10. McKeever KH. Electrolyte and water balance in the exercising horse. In: Nutrition manual for veterinarians. AAEP and Purina Mills, St Louis, 1997; 79–86.
11. Convertino VA. Fluid shifts and hydration status: effects of long-term exercise. Can J Sport Sci 1987; 12:136S–139S.
12. Eichner E. Other medical considerations in prolonged exercise. In: Perspectives in exercise science and sports medicine, vol 1, prolonged exercise. Indianapolis: Benchmark Press; 1988; 415–442.
13. Persson SGB. On blood volume and working capacity. Acta Vet Scand Suppl 1967; 19:1–189.
14. McKeever KH, SH Jarrett, WA Schurg, et al. Exercise training-induced hypervolemia in the horse. Med Sci Sport Exerc 1987; 19:21–27.
15. McKeever KH, Schurg WA, Convertino VA. A modified Evans Blue dye method for the measurement of plasma volume in the horse. J Equine Vet Sci 1988; 8:208–212.
16. Rose RJ, Hodgson DR. Hematology and biochemistry. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994; 63–78.
17. McKeever KH, Hinchcliff KW, Reed SM, et al. Role of decreased plasma volume in hematocrit alterations during incremental treadmill exercise in horses. Am J Physiol 1993; 265:R404–R408.

18. Nose H, Mack GW, Shi X, et al. Shift in body fluid compartments after dehydration in humans. J Appl Physiol 1988; 65:318–324.
19. McKeever KH, Hinchcliff KW. Neuroendocrine control of blood volume, blood pressure, and cardiovascular function in horses. Equine Vet J Suppl 1995; 18:77–81.
20. McKeever KH, Hinchcliff KW, Reed SM, et al. Splenectomy alters the hemodynamic response to incremental exercise in the horse. Am J Physiol 1993; 265:R409–R413.
21. Dill DB, Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. J Appl Physiol 1974; 37:247–248.
22. Van Beaumont W, Greenleaf JE, Juhos L. Disproportional changes in hematocrit, plasma volume, and proteins during exercise and bed rest. J Appl Physiol 1972; 33:55–61.
23. Harrison MH. Effects on thermal stress and exercise on blood volume in humans. Physiol Rev 1985; 65: 149–209.
24. Nadel ER, Mack GW, Takamata A. Thermoregulation, exercise and thirst: interelationships in humans. In: Gisolfi CV, Lamb DR, Nadel ER, eds. Perspectives in exercise science and sport medicine, vol. 6. Exercise, heat, and thermoregulation. Carmel, IN: Brown and Benchmark; 1993; 225–256.
25. McKeever KH. The endocrine system and the challenge of exercise. In: Messer NT, Johnson PJ, eds. Veterinary Clinics of North America: equine practice; endocrinology. Philadelphia: WB Saunders; 2002; 321–353.
26. Wade CE, Freund BJ, Claybaugh JR. Fluid and electrolyte homeostasis during and following exercise: hormonal and non-hormonal factors. In: Claybaugh JR, Wade CE, eds. Hormonal regulation of fluid and electrolytes. New York: Plenum; 1989; 1–44.
27. Johnson PJ. Physiology of body fluids in the horse. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids, electrolytes and thermoregulation in horses. Philadelphia: WB Saunders; 1998; 1–22.
28. Szlyk-Modrow PC, Francesconi RP, Hubbard RW. Integrated control of body fluids. In Buskirk ER, Puhl SM eds. Body fluid balance: exercise and sport. New York: CRC Press; 1996; 117–136.
29. Wade CE, Freund BJ. Hormonal control of blood volume during and following exercise. In: Gisolfi CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3: fluid homeostasis during exercise. Carmel, IN: Benchmark, 1990; 207–245.
30. Convertino VA, Keil LC, Bernauer EM, et al. Plasma volume, osmolarity, vasopressin, and renin activity during graded exercise in man. J Appl Physiol 1981; 50:123–128.
31. McKeever KH, Hinchcliff KW, Reed SM, et al. Plasma constituents during incremental treadmill exercise in intact and splenectomised horses. Equine Vet J 1993; 25:233–236.
32. Freund BJ, Claybaugh JR, Dice MS, et al. Hormonal and vascular fluid responses to maximal exercise in trained and untrained males. J Appl Physiol 1987; 63:669–675.
33. Freund BJ, Shizuru EM, Hashiro GM, et al. Hormonal, electrolyte, and renal responses to exercise are intensity dependent. J Appl Physiol 1991; 70:900–906.
34. Senay LC. Early response of plasma contents on exposure of working men to heat. J Appl Physiol 1978; 44:166–170.
35. Delgado R, Sanders TM, Bloor CM. Renal blood flow distribution during steady-state exercise and exhaustion in conscious dogs. J Appl Physiol 1975; 39:474–478.
36. Musch TI, Friedman DB, Pitetti KH, et al. Regional distribution of blood flow of dogs during graded dynamic exercise. J Appl Physiol 1997; 63:2269–2277.
37. Coyne CP, Carlson GP, Spensley MS, et al. Preliminary investigation of alterations in blood viscosity, cellular composition, and electrophoresis plasma protein fraction profile after competitive racing activity in thoroughbred horses. Am J Vet Res 1990; 5:1956–1963.
38. Convertino VA, Keil LC, Greenleaf JE. Plasma volume, renin, and vasopressin responses to graded exercise after training. J Appl Physiol 1983; 54:508–514.
39. McCutcheon LJ, Geor RJ. Sweating. Fluid and ion losses and replacement. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids, electrolytes and thermoregulation in horses. Philadelphia: WB Saunders 1998; 14:75–95.
40. Zambraski EJ. Renal regulation of fluid homeostasis during exercise. In: Gisolfi CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3. Fluid homeostasis during exercise. Carmel, IN: Benchmark; 1990; 245–280.
41. Zambraski EJ, Tucker MS, Lakas CS, et al. Mechanism of renin release in exercising dog. Am J Physiol 1984; 246:E71–E76.
42. Jimenez M, Hinchcliff KW, Farris JW. Catecholamine and cortisol responses of horses to incremental exertion. Vet Res Commun 1998; 22:107–118.
43. McKeever KH, Hinchcliff KW, Schmall LM, et al. Changes in plasma renin activity, aldosterone, and vasopressin, during incremental exercise in horses. Am J Vet Res 1992; 53:1290–1293.
44. McKeever KH, Hinchcliff KW, Schmall LM, et al. Atrial natriuretic peptide during exercise in horses. In: Persson, SGB, Lindholn A, Jefffcott L, eds. Equine exercise physiology 3, Davis, CA: ICEEP Press; 1991; 368–373.
45. Lindinger MI, Ecker GL. Ion and water losses from body fluids during a 163 km endurance ride. Equine Vet J Suppl 1995; 18:314–322.
46. Sawka MN, Pandolf KB. Effects of body water loss on physiologic function and exercise performance. In: Gisofli CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3. Fluid homeostasis during exercise. Carmel, IN: Benchmark Press; 1990; 1–38.
47. Sejersted OM. Electrolyte imbalance in body fluids as a mechanism of fatigue during exercise. In: Lamb DR, Gisolfi CV, eds. Perspectives in exercise science and sports medicine, vol. 5. Energy metabolism in exercise and sport. Dubuque, IA: Brown & Benchmark; 1992; 149–206.
48. Convertino VA. Blood volume: its adaptation to endurance training. Med Sci Sport Exerc 1991; 23:1338–1348.
49. Geor RJ, McCutcheon LJ, Lindinger MI. Adaptations to daily exercise in hot and humid ambient conditions in trained thoroughbred horses. Equine Vet J Suppl 1996; 22:63–68.
50. Geor RJ, McCutcheon LJ. Hydration effects on physiological strain of horses during exercise-heat stress. J Appl Physiol 1998; 84:2042–2051.
51. Kingston JK, McCutcheon LJ, Geor RJ. Comparison of three methods for estimation of exercise-related ion losses in sweat of horses. Am J Vet Res 1999; 60:1248–1254.
52. Kingston JK, Geor RJ, McCutcheon LJ. Rate and composition of sweat fluid losses are unaltered by hypohydration during prolonged exercise in horses. J Appl Physiol 1997; 83:1133–1143.
53. McCutcheon LJ, Geor RJ. Influence of training on sweating responses during submaximal exercise in horses. J Appl Physiol 2000; 89(6):2463–2471.

54. McCutcheon LJ, Geor RJ, Ecker GL, et al. Equine sweating responses to submaximal exercise during 21 days of heat acclimation. J Appl Physiol 1999; 87:1843–1851.
55. McCutcheon LJ, Geor RJ. Sweat fluid and ion losses in horses during training and competition in cool vs hot ambient conditions: implications for ion supplementation. Equine Vet J Suppl 1996; 22:54–62.
56. McCutcheon LJ, Geor RJ, Hare MJ, et al. Sweating rate and sweat composition during exercise and recovery in ambient heat and humidity. Equine Vet J Suppl 1995; 20:153–157.
57. Hubbard RW, Szlyk PC, Armstrong LE. Solute model or cellular energy model? Practical and theoretical aspects of thirst during exercise. In: Marriott BM, ed. Fluid replacement and heat stress. Washington, DC: National Academy Press; 1994; 169–193.
58. Hubbard RW, Szlyk PC, Armstrong LE. Influence of thirst and fluid palatability on fluid ingestion during exercise. In: Gisofli CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3. Fluid homeostasis during exercise. Carmel, IN: Benchmark Press; 1990; 39–86.
59. Thrasher TN, Nistal-Herrera JF, Keil LC, et al. Satiety and inhibition of vasopressin secretion after drinking in dehydrated dogs. Am J Physiol 1981; 240:E394–E401.
60. Greenleaf JE. Environmental issues that influence intake of replacement beverages. In: Marriott BM, ed. Fluid replacement and heat stress. Washington, DC: National Academy Press; 1994; 194–214.
61. McKeever KH, Hinchcliff KW, Cooley JL. Acute volume load during exercise in horses: atrial natriuretic peptide, vasopressin, and hemodynamics. Med Sci Sport Exerc 1991; 23:S104.
62. Sosa Leon LA. Treatment of exercise-induced dehydration. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids, electrolytes and thermoregulation in horses. Philadelphia: WB Saunders; 1998; 159–173.
63. Sosa Leon LA, Hodgson DR, Carlson GP, et al. Effects of concentrated electrolytes administered via a paste on fluid, electrolyte, and acid base balance in horses. Am J Vet Res 1998; 59:898–903.
64. Sosa Leon LA, Hodgson DR, Rose RJ. Gastric emptying of oral rehydration solutions at rest and after exercise in horses. Res Vet Sci. 1997; 63:183–187.
65. Sosa Leon LA, Davie AJ, Hodgson DR, et al. The effects of tonicity, glucose concentration and temperature of an oral rehydration solution on its absorption and elimination. Equine Vet J Suppl 1995; 20:140–146.
66. Butudom P, Schott HC, Davis MW, et al. Drinking salt water enhances rehydration in horses dehydrated by frusemide administration and endurance exercise. Equine Vet J (Suppl) 2002; 34:513–518.
67. Lawrence L. Nutrition and the athletic horse. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994; 205–230.
68. Poortmans JR. Exercise and renal function. Sports Medicine 1984; 1:125–153.
69. Kachadorian WA, Johnson NE. Renal responses to various rates of exercise. J Appl Physiol 1970; 28:748–752.
70. Grimby, G. Renal clearances during prolonged supine exercise at different loads. J Appl Physiol 1965; 20:1294–1298.
71. Hinchcliff KW, McKeever, KH, Schmall LM, et al. Renal and systemic hemodynamic responses to sustained submaximal exertion in horses. Am J Physiol 1990; 258:R1177–R1183.
72. Schott HC, Hodgson DR, Bayly WM, et al. Renal responses to high intensity exercise. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991; 361–367.
73. Schott HC, Ragle CA, Bayly WM. Effects of phenylbutazone and frusemide on urinary excretory responses to high intensity exercise Equine Vet J Suppl 1995; 18:426–431.
74. McKeever KH, Hinchcliff KW, Schmall LM, et al. Renal tubular function in horses during submaximal exercise. Am J Physiol 1991; 261:R553–R560.
75. Bridges RJ, Rummel W. Vasopressin-stimulated Na^+ transport in rat colon descendens. In: Skadhauge E, Heintze K, eds. Intestinal absorption and secretion. Boston, MA: MTP Press; 1984; 265–272.
76. Gisolfi CV, Summers RW, Schedl HP. Intestinal absorption of fluids during rest and exercise. In: Gisofli CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3. Fluid homeostasis during exercise. Carmel, IN: Benchmark Press; 1990; 129–180.
77. Gerken DF, Sams RA, McKeever KH, et al. Urinary pH effects on the renal clearance of lidocain and phenylbutazone in exercising horses. Toxicologist 1991; 11:96.
78. McKeever KH, Scali R, Geiser S, et al. Plasma aldosterone concentration and renal sodium excretion are altered during the first days of training in horses. Equine Vet J Suppl 2002; 34:524–531.
79. Lindinger MI, McCutcheon LJ, Ecker GL, et al. Heat acclimation improves regulation of plasma volume and plasma Na(+) content during exercise in horses. J Appl Physiol 2000; 88:1006–1013.
80. Kearns CF, McKeever KH, John-Alder H, et al. Body composition and other predictors of maximal oxygen uptake. Equine Vet J Suppl 2002; 34:485–490.
81. McKeever KH, Schurg WA, Convertino VA. Exercise training-induced hypervolemia in greyhounds: role of water intake and renal mechanisms. Am J Physiol 1985; 248:R422–R425.
82. Costill DL, Branum G, Fink W, Nelson R. Exercise-induced sodium conservation changes in plasma renin and aldosterone. Med Sci Sport Exerc 1976; 8:209–213.
83. Kirby CR, Convertino VA. Plasma aldosterone and sweat sodium concentrations after exercise and heat acclimation. J Appl Physiol 1986; 61:967–970.
84. Luetkemeier MJ, Flowers KM, Lamb DR. Spironolactone administration and training-induced hypervolemia. Int J Sports Med 1994; 15:295–300.
85. Jansson A, Lindholm A, Dahlborn K. Effects of acute intravenous aldosterone administration on Na(+), K(+), and water excretion in the horse. J Appl Physiol 2002; 9:135–141.
86. Sawka MN, Convertino VA, Eichner ER, et al. Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. Med Sci Sports Exerc 2000; 32:332–348.
87. Birchard GF. Optimal hematocrit: theory, regulation, and implications. Amer Zool 1997; 37:65–72.
88. Kenney WL. Body fluid and temperature regulation as a function of age. In: Lamb DR, Gisolfi CV, Nadel ER, eds. Perspectives in exercise and sports medicine, vol. 8. Exercise in older adults. Carmel, IN: Cooper Publishing, 1995; 305–352.
89. Armstrong CG, Kenney WL. Effects of age and acclimation on responses to passive heat exposure. J Appl Physiol 1993; 75:2162–2167.

90. McKeever KH. Exercise physiology of the older horse. In: MacLeay JM, ed. Veterinary clinics of North America: equine practice; geriatrics. Philadelphia: WB Saunders, 2002; 469–490.
91. McKeever KH, Eaton TL, Geiser S, et al. Thermoregulation in old and young horses during exercise. Med Sci Sport Exerc 2000; 32:S156.
92. McKeever KH, Kearns CF. Aging-induced alterations in plasma volume in horses. Med Sci Sport Exerc 2001; 33:S257.

CHAPTER 39

Acid–base physiology during exercise and in response to training

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Introduction

The aim of this chapter is to provide an introduction to acid–base assessment in clinically normal horses at rest and performing exercise of different intensities and durations. The physicochemical approach to acid–base assessment will be introduced and used to exemplify the origins of acid–base disturbances during exercise. Also, the impact of diet, alkalinizing agents, frusemide, and selected clinical conditions on acid–base status will be explored briefly. An update on acidosis and skeletal muscle fatigue will be provided and it is hoped that this will help to dispel some of the myths and confusion surrounding lactate, H^+, and muscle fatigue. At the outset, it is also important to dispel another myth. We often read that plasma and intracellular pH are maintained within narrow limits. This contention is not supported by the research literature in any animal so far studied, including horses. In clinically normal humans and horses, plasma pH can vary from 7.0 to 7.6, although the norm lies close to 7.4. The large range of change in pH represents a four-fold change in $[H^+]$, specifically 25 to 100 nEq/L, with normal plasma $[H^+]$ of 40 nmol/L. While this range of plasma $[H^+]$ can be tolerated, it is true that such changes are eventually accompanied by the activation of mechanisms that return $[H^+]$ back towards 40 nEq/L. Let us now consider reasons for the changes in acid–base status in the horse at rest and during exercise.

Overview of acid–base responses to exercise

Moderate- to high-intensity muscular exercise results in acidification of muscles and blood. The acidification that occurs primarily results from the generation of protons (H^+) within contracting skeletal muscle. The protons are generated from a series of biochemical and physicochemical reactions associated with increased rates of anaerobic energy production. These proton-generating reactions will be detailed below. The protons that are generated continue to be involved in a series of chemical reactions involving carbonic anhydrases and membrane transport proteins that results in the net movement of acid-equivalents out of the contracting muscle cells into the interstitium, and from there into the lymphatic system and venous capillary circulation. It is this large and rapid efflux of acid equivalents from contracting muscle that produces the systemic metabolic acidosis associated with moderate- to high-intensity exercise.

In the exercising horse, whole-body acid–base balance is dependent on the integrated responses of the muscular, respiratory, vascular, hepatic, cutaneous, and renal systems. The muscular system, in addition to providing the locomotory force requirement for activity, generates considerable amounts of acid equivalents, resulting in acidification of the intracellular and extracellular fluid compartments. Non-contracting skeletal muscle also provides the largest tissue mass within the body for the removal of lactate and acid equivalents during high-intensity exercise and the initial recovery period. The respiratory system plays a key role in eliminating acid equivalents as CO_2 at the lung, in addition to extracting the O_2 needed to fuel aerobic cellular metabolism. The vascular system plays an integral role in the transport and distribution of acid and base equivalents throughout the

body – this system provides for the 'buffering' of the acid–base disturbance by distributing acid equivalents from acid-generation sites (contracting skeletal muscle) to other sites (non-contracting skeletal muscle and other tissues). Within the vascular system itself, bicarbonate, plasma proteins and hemoglobin within red blood cells are also involved in the transport and temporary storage (buffering) of acid equivalents. The hepatic system is a major tissue mass involved in the removal of lactate from the vascular system, thereby removing acid equivalents from the circulation. The cutaneous system is heavily involved in the production and secretion of sweat to the surface of the skin during and immediately following moderate to high intensity exercise. Sweat contains large amounts of Na^+, K^+ and Cl^- and different rates of excretion of each ion affects acid–base state of blood leaving the skin. The kidneys are capable of excreting H^+ and lactate at greatly elevated rates during recovery from high intensity exercise, aiding in the process of recovery from the acidosis of exercise.

Each of the systems described above is capable of modifying the water, electrolyte and acid–base composition of the extracellular (blood plasma, lymph, interstitial fluids) and intracellular fluid compartments. It must therefore be appreciated that the acid–base status of the blood depends greatly on where and when the blood is sampled. Blood draining intensely contracting skeletal muscle has very high concentrations of H^+, lactate, K^+, and CO_2, whereas blood that drains relatively inactive tissues (jugular venous blood, for example) has markedly lower concentrations of these metabolites and ions; arterial blood is intermediate in composition. Also, the magnitude of change is proportional to the intensity and duration of exercise, and the concentrations of these and other substances change with time of exercise and recovery.

Why is acid–base balance important? A detailed analysis of acid–base balance provides a biochemical and physicochemical description of the state of the organism, or of individual organs and tissues within the body. Furthermore, severe acid–base disturbances are often associated with high-intensity exercise, with prolonged duration exercise, and with many pathologies. Therefore an understanding of the origins of acid–base disturbances is of interest to both basic and clinical physiologists. Within the context of the present chapter, exercise physiologists remain keenly interested in acid–base balance because of a close association between acidification and muscle fatigue.[1,2] Considerable research over the past century has identified many effects of increased $[H^+]$ within skeletal muscle (Box 39.1; for reviews see Jones and Heigenhauser,[3] Fitts[4]). The content of this chapter is primarily directed to moderate- to high-intensity exercise because exercise at these intensities produces a significant acid–base disturbance, while exercise at low intensities does not (unless markedly prolonged with underlying dehydration and metabolic abnormalities). Hultman and Sahlin's 1980 paper still provides the best, detailed review of skeletal muscle acid–base balance during exercise.[5] Previous treatments of muscle acid–base balance emphasizing a physicochemical approach include Lindinger[6] and Lindinger and Heigenhauser.[7,8]

Box 39.1 Effects of increased intramuscular $[H^+]$ and functional consequence(s) in muscle

Decreased glycogenolytic (phosphorylase) activity[33,162] → decreased anaerobic ATP production → ATP supply is limited → fatigue

Decreased glycolytic (phosphofructokinase) activity[33,163,164] → decreased anaerobic ATP production → ATP supply is limited → fatigue

Decreased pyruvate dehydrogenase activity[33] → decreased aerobic ATP production → ATP supply is limited → fatigue

Decreased sarcolemmal and sarcoplasmic reticulum Ca^{2+} ATPase activity[59,165,166] → elevated cytosolic $[Ca^{2+}]$ → decreased myosin ATPase activity[59] → decreased rate of actin–myosin cross-bridge cycling → slowed rate of muscular contraction → fatigue

Increased $[H^+]$ increases the [diprotonated inorganic phosphate] → Inhibition of actin–myosin cross-bridge interaction resulted[36,167,168]

Inhibition of Ca^{2+} binding to troponin C,[59,169,170] resulting in decreased number of actin–myosin cross-bridges formed → decreased strength of force production → fatigue

Increased acetyl CoA, indicative of increased intramuscular triacylglycerol hydrolysis[33] → increased citric acid cycle dehydrogenase activities → stimulate aerobic metabolism

Decreased lactate efflux from muscle cells[171] → prolongation of intracellular acidification by retaining a strong acid anion

Thorough reviews on plasma acid–base status have been provided by Constable,[9] Kowalchuk and Scheuermann,[10] Lindinger et al[11,12] and Johnson et al.[13] Clinical primers on assessing and treating acid–base disturbances are provided by Whitehair et al,[14] Constable,[15] Carlson,[16] and Corley and Marr.[17] Hyyppä and Pösö[18] and Kingston and Bayly[19] provide brief reviews on the effects of exercise on acid–base status in horses.

In traditional terms, many of us remember being taught that acid–base balance is represented by the relationships among P_{CO_2}, pH and the HCO_3^- in blood plasma.[20,21] While this is true, using only these three variables provides for only a very limited understanding of the factors that contribute to acid–base imbalances. The approach taken within this chapter is to use a comprehensive, physicochemical approach to identify the causes or origins of acid–base disturbances during exercise, and to discuss how the disturbance is resolved during recovery from exercise.

While the traditional variables of acid–base – P_{CO_2}, pH and the HCO_3^- – are useful in identifying whether an acid–base disturbance is metabolic or respiratory in nature,[20–22] they are insufficient to identify the physicochemical origins of the acid–base disturbance. It is nonetheless important for the student of acid–base physiology to be familiar with the concepts presented using the traditional approach, and to be able to use these concepts as an important foundation on which to apply the physicochemical approach. This chapter will emphasize the use of the physicochemical approach as this method provides for a detailed physiological and clinical

assessment of acid–base disturbances. It is worth pointing out that the traditional approaches to assessing acid–base status are not incorrect, but rather they were a simplification introduced in the 1960s to make use of readily available and relatively simple measurements of Pco_2 and pH. Technological developments from the 1970s have simplified the measurements of the other important acid–base variables in blood plasma and skeletal muscle, allowing us to take a more comprehensive approach.

The physicochemical approach presented here was detailed by Peter Stewart,[23,24] bears many similarities to earlier work by Peters and Van Slyke,[25] and builds on the work of many others, including Hastings, Dill, Lawrence, Henderson, and Siggaard-Andersen. This approach is based on the defined physicochemical properties of electrolyte solutions as detailed in textbooks of physical chemistry.[26] Helpful books and reviews include those by Stewart,[23,24] Kowalchuk and Scheuermann,[10] Lindinger,[6] Heigenhauser,[27] Jones and Heigenhauser,[28] Constable[15] as well as software developed by Watson.[29]

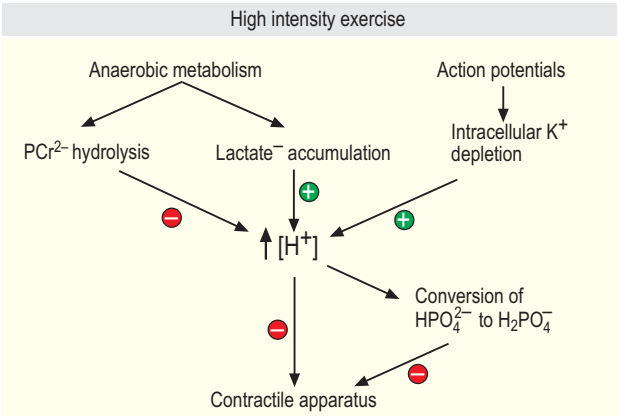

Fig. 39.1
Overview of events contributing to the intracellular acidosis and fatigue of skeletal muscle during high intensity exercise. A – indicates a decrease in accumulation of function, while a + indicates a positive contribution to the increase in $[H^+]$.

Acidosis and skeletal muscle fatigue

There is no question that high-intensity muscle contraction results in intracellular acidification[2,30] that generates an extracellular, systemic acidosis in the whole organism that can be very pronounced and long lasting.[11] It is also clear that intracellular acidosis and fatigue are associative during high-intensity exercise, with mounting evidence that increased $[H^+]$ reduces the calcium sensitivity of the contractile proteins.[30] Furthermore, acidosis imposed prior to the period of high-intensity exercise results in an earlier onset and more pronounced skeletal muscle fatigue.[31,32] Intracellular acidosis may, however, only exert these effects during high-intensity muscle contraction and recent evidence has shown that the contributions of intracellular acidosis to fatigue process have yet to be fully understood.[30,33–35] Indeed, Westerblad and colleagues[36] have suggested that increased intracellular concentrations of inorganic phosphate may be a more important contributor to muscle fatigue than the increase in $[H^+]$.

Skeletal muscle fatigue is also associated with an increased interstitial $[K^+]$ as a result of rapid rates of K^+ loss through sarcolemmal K^+ channels during the recovery phase of action potentials.[37] This increase in interstitial $[K^+]$ results in a marked depolarization of the sarcolemma and decreased contractile force.[38,39] In contrast to the dogma that we have long been taught, Nielsen et al[34] demonstrated that the loss in both sarcolemmal excitability and tetanic force resulting from elevated interstitial $[K^+]$ (8–12 mEq/L) was actually *reversed* when intracellular acidosis (either 20 mmol/L lactic acid or 50% CO_2) was imposed![34] While these muscles were only stimulated to perform one contraction every 10 min, this allowed a separation between the fatigue associated with repetitive contraction versus that associated with sarcolemmal depolarization and intracellular acidification.

As summarized by Fitts[4] and Chin and Allen,[30] increased $[H^+]$ does contribute to decreased force production during high-intensity muscle contraction (Fig. 39.1), and there is reasonably good evidence that these effects occur at the level of: (i) impaired Ca^{2+} binding to troponin C, which therefore impairs the ability of actin to form cross-bridges with myosin; (ii) slowing sarcoplasmic reticulum (SR) Ca-ATPase activity; (iii) increasing the leak of Ca^{2+} from the SR; and (iv) a key site of biochemical control within glycogenolysis (decreased glycogen phosphorylase a activity) and glycolysis (decreased phosphofructokinase activity).[33] The latter study also demonstrated an increased reliance on fat metabolism to meet the energy demands of contracting muscle during exercise in humans made acidotic by ingestion of 0.3 g/kg ammonium chloride.

It may be concluded that intracellular acidosis may have two main effects that, when taken together, are of long-term benefit for muscle function and survival (prevention of destruction resulting from over use). First, acidification restores the sarcolemmal excitability and contractility resulting from elevated interstitial $[K^+]$, and the former is very important for cells maintaining the composition of their intracellular environment within physiological limits. Second, the muscle retains the ability to contract while the force and rate of contraction and rates of glycogenolysis/glycolysis are slowed as a result of the acidosis. This in turn slows the demand for energy and the production of acid equivalents, while allowing the animal to continue to move if need be.

Assessment of acid–base balance and factors that affect acid–base regulation

The only method capable of fully assessing acid–base balance is the physicochemical approach, therefore it is this system that is detailed below and used within this chapter.

Box 39.2 Disadvantages and advantages of the physicochemical approach to determination of acid–base balance

Disadvantages

- Requires accurate measurement of many variables including plasma P_{CO_2}, $[Na^+]$, $[K^+]$, $[Cl^-]$, [lactate$^-$], [plasma protein] and, in muscle, additionally $[A_{tot}]$.[40]
- Requires advanced calculator or computer to perform calculations.
- Requires consideration of physical chemistry, biochemistry and physiology – it is truly an integrative approach.

Advantages

- Provides for detailed analysis of why changes in $[H^+]$ and $[HCO_3^-]$ occurred, giving insight into the pathophysiology of any type of acid–base disorder.
- Allows for the determination of the individual independent variables, i.e. $[Na^+]$, [lactate$^-$], [plasma protein] . . . that is, the origin of the acid–base disturbance.
- Identification of the origins of the acid–base disturbance allows one to determine the physiological or biochemical mechanism(s) responsible for the alteration(s) in independent variables.
- Knowledge of the physicochemical origins and physiological/biochemical mechanism(s) behind the acid–base disturbance allows for the development and administration of effective treatment strategies for correcting the acid–base disturbance with minimal untoward side-effects.

Physicochemical characteristics refer to those properties and reactions that are physical and chemical in nature; they proceed in the absence of enzymes and life and occur as a result of the physical and chemical properties of the solvent and solute molecules. Also, biochemical reactions, those catalyzed by enzymes, may alter the physicochemical properties of a solution. However, for the purposes of discussing acid–base balance biochemical reactions may be considered distinct from physicochemical reactions. The main physicochemical reactions are detailed below.

The advantages and disadvantages of the physicochemical approach are listed in Box 39.2. The development and widespread use of ion-selective electrodes and combination blood gas–electrolyte analyzers has greatly simplified the process of obtaining the necessary measurements with the accuracy needed to perform detailed assessments of acid–base balance.[9,11,40–43] The advantages of this approach lie in the ability to quantitatively determine the physical and chemical origins of acid–base disturbances. This is therefore a very powerful approach and an important step towards understanding acid–base physiology and pathophysiology. This approach provides an essential foundation for the effective treatment of pathological acid–base disorders.

Physicochemical determinants of acid–base balance

Prior to detailing the physicochemical reactions that increase $[H^+]$ within contracting skeletal muscle, it is necessary to provide an introduction to the physicochemical system of acid–base balance. This approach is founded on three underlying physical premises:

1. A dissociated proton molecule (H^+) is only in physical existence for a fleeting instant of time, approximately 10^{-5} s. The proton is highly reactive, associating briefly with negative charges on proteins, $^-$OH molecules, HCO_3^- molecules and amino acids to name a few. The proton is therefore very unlike inorganic electrolytes such as $Na,^+$ K^+ and $Cl,^-$ which are relatively unreactive.
2. Protons are a main constituent of water, the most prevalent molecule within the body. Water thus provides an almost limitless source of H^+ for biochemical and physicochemical reactions. Protons are part of the solvent that comprises the milieu of the body. It is because of the ability of water to so rapidly dissociate and reassociate H^+ and $^-$OH water is the 'universal' solute.
3. Because of these physical attributes of protons and water, it is physically impossible to add protons to a physiological solution without adding water. Take hydrochloric acid (HCl) as an example. HCl exists in aqueous form and is characterized by very high concentrations of Cl^- and H^+ in solution. The H^+ is an integral part of the aqueous system. As described below, it is the strong acid anion Cl^- that makes this solution so acidic. The strong acid anion Cl^- can be neutralized by the addition of an equivalent amount of the strong base cation Na^+ to the solution, but without an accompanying acid anion such as $Cl,^-$ $HCO_3,^-$ or $H_2PO_4.^-$ Thus NaOH would be added – the strong anions Cl^- and Na^+ remain fully dissociated in solution while there occurs a rapid reaction between H^+ and $^-$OH that decreases $[H^+]$. The resultant solution is saline at neutral pH.

The physicochemical approach to acid–base balance recognizes that three groups of independent variable determine the concentrations of the traditional acid–base variables pH and $[HCO_3^-]$: (i) the strong ion difference (SID), which represents the sum (charge considered) of the strong acid anions and strong base cations; (ii) the total weak acid concentration (A_{tot}), which represents the sum (charge considered) of the weak acids and bases; and (iii) the carbon dioxide (CO_2) concentration, which is usually measured and used as the partial pressure of CO_2 (P_{CO_2}) (Fig. 39.2).

Strong ions and strong ion difference

The terms 'strong acid anion' and 'strong base cation' were introduced in the preceding section and they will be defined here. The term 'strong' refers to the fact that the ion will be fully, or nearly so, dissociated in aqueous solutions (Fig. 39.2). Most of the inorganic ions are 'strong' and hence nearly fully dissociated within the body fluids (Box 39.3). Some organic ions are also strong, such as lactate$^-$ (acid dissociation constant of 3.9) and phosphocreatine^{2-} (PCr^{2-}, acid dissociation constant of 4.5). Anions possess negative charge whereas cations possess positive charge. An anion is an acid by definition because the addition of that strong anion, in the absence of an accompanying strong base, will result in acidification of the solution. Using the example of HCl above, the addition of HCl to plasma will result in acidification. Similarly, the addition of Hlactate will

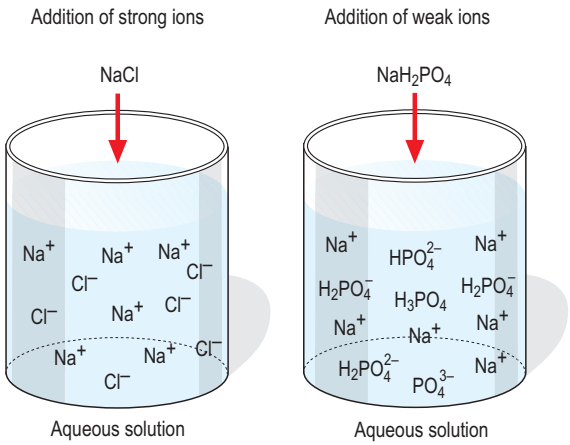

Fig. 39.2
Representation of strong ions and weak ions in an aqueous solution. The addition of NaCl to an aqueous solution results in the complete dissociation into the strong ions Na^+ and Cl^-. In contrast, the addition of sodium phosphate results in the complete dissociation of all of the sodium into Na^+, but the phosphate is capable of reacting with H^+ in solution to form the following weak ions: H_3PO_4, $H_2PO_4^-$, HPO_4^{2-} and PO_4^{3-}.

Box 39.3 A summary of acid–base terminology

The following definitions are placed in order of functional similarities, as opposed to alphabetical order:
Base: any cation in biological fluids[22]
Buffer base: base equivalent to the sum of buffer anion concentrations (including $[HCO_3^-]$) in mEq/L[22]
Base excess/deficit: represents the accumulation of non-volatile base/acid in the blood (excludes plasma $[HCO_3^-]$ and blood hemoglobin concentration)[172]
Alkali (alkaline) reserve: the proton-buffering ability of plasma bicarbonate when bases or non-volatile acids are added to or taken from the body fluids[22]
$[A_{tot}]$: a physicochemical term that defines the *total* concentration of weak anions in solution[23]
[SID]: a physicochemical assessment term that refers to the sum of all strong base cations minus the sum of all strong acid anions:[23]

$$[SID] = \Sigma[\text{strong base cations}] - \Sigma[\text{strong acid anions}]$$

Strong ion: those ions that are fully, or nearly so, dissociated in physiological solutions. In general, if the dissociation constant is ≤ 4.5, then the molecule is considered to be a strong anion; if the dissociation constant is greater than 9, then the molecule is considered to be a strong cation.
Anion gap: a traditional term that is defined as:

$$\text{anion gap} = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$$

Strong ion gap: a term coined by Constable et al[173] as an alternative way of determining the concentration of unmeasured strong ions in plasma:

$$\text{Strong ion gap} = 2.24 \times \text{total [protein] (g/dl)}/(1 + 10^{(6.65\text{-pH})}) - \text{AG},$$
where AG is the anion gap

Unmeasured anions: unmeasured anions contribute to the anion gap, strong ion difference and strong ion gap. The unmeasured anions include both strong (SO_4^{2-}, some amino acids, pyruvate) and weak (inorganic phosphate, carbonate, carbamates, some amino acids) anions. The negative charges on plasma protein contribute to the anion gap, and strong ion gap, but this is usually a 'measured' anion.

also result in acidification. In contrast, the addition of the strong base Na^+ in the absence of accompanying strong anion (as $NaHCO_3^-$) will result in alkalinization. The values for the key variables used in the physicochemical assessment of acid–base balance, for resting horses, are provided in Table 39.1.

The concentrations of strong acid anions and strong base cations within a fluid compartment are summed, with consideration of the charge, to yield the strong ion difference [SID].

Within plasma and the extracellular fluid compartment the [SID] can be calculated as:

$$[SID]\ (mEq/L) = ([Na^+] + [K^+] + [Mg^{2+}] + [Ca^{2+}]) - ([Cl^-] + [lactate^-] + [SO_4^{2-}])$$

Note that it is the free or ionized concentrations of the divalent ions that must be used, and not the total concentration; considerable amounts of the divalent ions are bound to plasma proteins or to each other. The concentrations measured using ion-selective electrodes are those of the free or ionized or dissociated ion in the aqueous portion of the solution (i.e. mEq/L of plasma water), so long as the instrument does not use a calculation to modify the 'concentration' to total (not free) concentration in units of mEq/L of plasma. Thus, while these divalent ions are 'strong', the interactions with charged moieties on protein molecules remove some of the ion from solution. In practice, the free concentrations of the divalent cations and anions are approximately equivalent and can be ignored, leaving:

$$[SID]_{plasma}\ (mEq/L) = ([Na^+] + [K^+]) - ([Cl^-] + [lactate^-])$$

In some treatments of acid–base balance using the physicochemical approach, $[lactate^-]$ is also ignored. However, $[lactate^-]$ cannot be ignored in the exercising and recovering animal.

Within skeletal muscle, PCr^{2-} and Mg^{2+} must be used within the equation because their free concentrations are large and change substantially during exercise:

$$[SID]_{muscle}\ (mEq/L) = ([Na^+] + [K^+] + [Mg^{2+}]) - ([Cl^-] + [lactate^-] + [PCr^{2-}])$$

The strong ions are important determinants of the concentrations of $[H^+]$ and $[HCO_3^-]$ because they directly affect the associated state of H_2O, and thereby determine the concentrations of H^+ and ^-OH.

A decrease in the SID (without concurrent change in pCO_2 or A_{tot}), due to either a decrease in strong cation concentration or an increase in strong anion concentration, will increase $[H^+]$ and decrease $[HCO_3^-]$ – an acidification occurs. Conversely, an increase in SID has an alkalinizing effect and decreases $[H^+]$ and increases $[HCO_3^-]$.

Weak acids and bases, and $[A_{tot}]$

The term 'weak' refers to those anion acids and cation bases that are not fully dissociated in solution. Thus when sodium phosphate (Na_2HPO_4) is added to an aqueous solution two Na^+ are added and fully dissociate and a weak anion HPO_4^{2-} is added. In contrast to Na^+, the HPO_4^{2-} cannot achieve full dissociation due to reactions of the molecule with H^+ within

Table 39.1 Physiologically important acid–base variables, and their concentrations, in arterial plasma and skeletal muscle of horses at rest

	Plasma		Skeletal muscle	
	'Normal' value	Normal range	'Normal' value	Normal range
Dependent variables				
$[H^+]$ nanoEq/L	40	33–45	100	71–126
pH	7.40	7.35–7.48	7.0	6.90–7.15
$[HCO_3^-]$ mEq/L	28	22–34	10[a]	8–12[a]
Independent variables				
pCO_2 mmHg	40	35–45		
[total CO_2] mmol/L	30	23–36	10[a]	8–12[a]
Strong ions				
[SID] mEq/L	40	37–43		
$[Na^+]$ mEq/L	140	132–146		
$[K^+]$ mEq/L	3.7	2.7–4.7		
$[Ca^{2+}]$ mEq/L	2.5	2–3		
$[Mg^{2+}]$ mEq/L	1.0	0.5–2.0		
$[Cl^-]$ mEq/L	105	99–109		
$[lactate^-]$ mEq/L	1.0	0.5–1.5	1.5	1.0–2.0
$[PCr^{2-}]$ mEq/L	na	na	15	12–18
$[SO_4^{2-}]$ mEq/L	0.5	0.3–0.7		
Weak ions				
$[A_{tot}]$ mEq/L	12	11–13		
[plasma protein] g/dL	5.5	5.0–6.0		
[albumin] g/dL			na	na
[globulins] g/dL			na	na
$[HPO_4^{2-}] + [H_2PO_4^-]$ mmol/L	2.7	2.0–3.5	8[b]	7–9[b]
carnosine mmol/L			6[b]	–
Protein histidine concentration mmol/L			46[b]	–

[a] Sahlin et al[174] – human muscle.
[b] Hultman & Sahlin[5] – human muscle.

the solution. Thus the HPO_4^{2-} is also partially and instantaneously transformed into H_3PO_4, $H_2PO_4^-$ and PO_4^{3-} (see Fig. 39.2). This physical attribute of phosphate is what makes phosphates, and many other weak acid anions such as bicarbonate and albumin, good proton 'buffers'. The predominant weak acid anion in plasma and extracellular fluid (ECF) is albumin, while the predominant weak acid anions within skeletal muscle cells are the histidine residues on proteins.

The main weak acids and bases within the extracellular fluid compartment are albumin, globulin, phosphate, and bicarbonate. Bicarbonate, however, is part of the CO_2 system and thus is not used in the calculation, or estimation, of $[A_{tot}]$. As with the strong ions, the weak ions also directly affect the concentrations of H^+ and HCO_3^- in solution. Within skeletal muscle it is primarily the histidine moieties on proteins that contribute to $[A_{tot}]$, with creatine, Pi, ATP and other molecules also contributing.[6] While it is theoretically possible to measure the concentration of weak acids and bases in both extracellular and intracellular fluid compartments, this tends to be prohibitive and appears not to be necessary to be able to effectively estimate acid–base state. Rather, an effective $[A_{tot}]$ and apparent dissociation constant K´a have been determined in equine plasma and rat skeletal muscle (Table 39.2). A value for $[A_{tot}]$ has not been determined in equine or human skeletal muscle. Muscle $[A_{tot}]$ is equivalent to the non-bicarbonate proton-buffering capacity of adult rat plantaris muscle,[7,8] and is similar to that of human vastus lateralis.[5] When rat plantaris values for $[A_{tot}]$

Table 39.2 Values of the constants used within the acid–base equations

Parameter	Constant	Reference
K_A – plasma	2.11 or 2.12×10^{-7} Eq/L	9,43
K_A – resting muscle	1.64×10^{-7} Eq/L	7,8
K_A – exercised muscle	1.98×10^{-7} Eq/L	7,8
K_3	6.0×10^{-11} Eq/L	23
K_C	2.46×10^{-11} $(Eq/L)^2/mmHg$	23
K'_w	4.4×10^{-14} $(Eq/L)^2$	23

and K´a were applied to human muscle, reasonable data were generated.[6] Equine muscle, compared to human muscle, has a much greater non-bicarbonate proton-buffering capacity: 43 mEq/kg dry muscle^{-1}.pH^{-1} in trained humans, versus 58 and 93 mEq/kg^{-1}.pH^{-1} in untrained and trained equine skeletal muscle.[44] Assuming proportionality with rat hindlimb skeletal muscle (buffer capacity of ~40 mEq/kg.pH^{-1} = [A_{tot}] of ~140 mmol/L,[6] this translates to an [A_{tot}] of ~315 mmol/L in trained equine muscle.

The carbon dioxide system

The concentration of CO_2 is the third independent variable of acid–base balance. Carbon dioxide is effectively a strong acid, and because it is a major end-product of cellular respiration is often referred to as a respiratory acid. Also, the primary means for eliminating excess CO_2 from the body is through the respiratory system.[13,28]

Carbon dioxide is a strong acid by virtue of its ability to combine with water to increase the concentration of H^+ while at the same time increasing the weak acid [HCO_3^-]. This reaction effectively acidifies the solution to which CO_2 has been added. The majority (about 95%) of the total CO_2 within the body is in the form of HCO_3^-, with much smaller amounts of H_2CO_3, CO_3^{2-}, dissolved CO_2 ($CO_{2(d)}$), and some that is bound to amino groups on protein to form carbamino compounds. The chemical reactions involved in the hydration and dehydration of CO_2 are:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^- \rightleftharpoons 2H^+ + CO_3^{2-}$$

Solving equations to determine acid–base balance

With this background, the following five mass action equations and one equation expressing electrical neutrality of solutions describe the physicochemical characteristics of any aqueous, physiological solution:[23,24]
Water dissociation:

$$K'_w = [H^+] \cdot [^-OH]$$

Weak electrolyte system:

$$K_A \cdot [HA] = [H^+] \cdot [A^-]$$
$$[A_{tot}] = [HA] + [A^-]$$

Carbon dioxide system:

$$K_c \cdot P_{CO_2} = [H^+] \cdot [HCO_3^-]$$
$$K_3 \cdot [HCO_3^-] = [H^+] \cdot [CO_3^{2-}]$$

Electrical neutrality:

$$[SID] + [H^+] - [HCO_3^-] - [A^-] - [CO_3^{2-}] - [^-OH] = 0$$

It is noteworthy that $[H^+]$ appears in each of these equations and its dependence on the concentrations of strong and weak acids/base and CO_2 is evident. These six equations can be combined into a single equation that may then be solved for $[H^+]$ when the three independent variables and the constants are known:[23,24]

$$[H^+]^4 [\{K_A = [SID]\}] [H^+]^3 = \{K_A ([SID] - [A_{tot}]) - (K_C P_{CO_2} + K'_w)\} [H^+]^2 - \{K_A (K_C P_{CO_2} + K'_w) + K_3 K_C P_{CO_2}\} [H^+] - K_A K_3 K_C P_{CO_2} = 0$$

Contracting skeletal muscle: proton-generating and removing reactions

When considering the acid–base changes that occur in blood during exercise, it is important to have an understanding of the changes that occur within skeletal muscle because that tissue forms 40–60% of the mass of the horse.[45] Contracting skeletal muscle generates the disturbance[11,41] and non-contracting cells are capable of ameliorating the disturbance.[42,46] The role of non-contracting muscle may be small to negligible in horses performing moderate- to high-intensity exercise because most skeletal muscles are used for locomotion and maintenance of posture. That is in contrast to bipedal humans, where many activities require leg muscles and leave many other muscles relatively inactive. This section will thus focus on the time course and magnitude of changes that occur within contracting skeletal muscle, primarily gluteus medius, during moderate- to high-intensity exercise.

Exercise is a consequence of muscular contraction, and muscular contraction results in an increase in cellular energy demand compared to the resting state. The increased energy demand is due to activation of myosin ATPase needed for release of actin–myosin cross-bridge interaction, increased activity of SR Ca^{2+}-ATPase activity resulting from increased cytosolic [Ca^{2+}] and increased rates of Na,K-ATPase activity needed to maintain transmembrane Na^+ and K^+ gradients and repolarization of the muscle membrane potential.

The acid–base changes that occur within contracting skeletal muscle and in blood during exercise are the results of the biochemical (metabolic) and physicochemical reactions that occur within contracting muscle cells. The onset of muscular contraction sets into motion a series of biochemical events that result in stimulation and inhibition of numerous metabolic pathways. Those pathways within the aerobic energy systems are relatively slow to increase, whereas those of the anaerobic pathways (ATP utilization, phosphocreatine degradation, glycolysis) increase rapidly.[47] Thus the onset of exercise (rest to work transition) may be associated with muscular acidification for reasons described below. Similarly, transitions from low to high work rates, as well as exercise at moderate to high intensities, result in increased rates of anaerobic metabolism. Full activation of aerobic pathways may be achieved within minutes of the onset of exercise, but until this is achieved anaerobic pathways continue to supply ATP. Activation of aerobic metabolism results in increased mitochondrial respiration with CO_2 production – while this CO_2 is acidic, its rate of production and removal from the cell can easily be matched by CO_2 elimination rates at the lung.[13,28] Therefore aerobic CO_2 production can be ignored in most discussions of the acid–base changes of exercise.

Muscle characteristics and acid–base

Skeletal muscle is composed of different fiber types, some of which produce acid equivalents at high rates (the anaerobic, fast twitch, glycolytic fibers) and others that do not (the aerobic, slow twitch, oxidative fibers). Fiber types continue to be classified on the basis of their twitch characteristics, oxidative/glycolytic capacities and on their myosin heavy chain composition[48] (and see Chapter 5). The acid–base changes that occur reflect the fiber type composition of the contracting muscles, and thus reflect breed differences and type of activity performed.

Within individual muscle groups, such as the well-studied gluteus medius of equids, skeletal muscle fibers of different composition are in close proximity and form integrated functional units that are selectively recruited by appropriate motor units depending on the locomotory requirements of the animal. Muscle fibers with high oxidative capacity that have low glycoytic capacity, slow contractile properties with low myosin ATPase activity, are fatigue resistant and primarily function in the maintenance of posture (Table 39.3). These slow-twitch oxidative fibers have the ability to oxidize all the pyruvate generated from glycolysis and, during exercise, they have the ability to take up and oxidize lactate released into the interstitium from nearby glycolytic muscle fibers – the intramuscular lactate shuttle.[49] At the other extreme, fibers of high glycolytic capacity with low oxidative capacity have fast contractile properties with high myosin ATPase activity. These fibers function to generate power at high rates for high intensity sprinting, jumping, and pulling activities. The majority of the acid–base disturbance that occurs during high-intensity exercise is generated within the fast-twitch glycolytic (type IIB or type IID/X) that are endowed with a high glycogen content, high activities of glycogen phosphorylase and lactate dehydrogenase, and a high content of carnosine to buffer metabolically generated H^+. These fibers also fatigue rapidly due to the loss of membrane excitability, as well as their high rate of intracellular acidification[8] that effectively downregulate muscle fiber function at multiple membrane and intracellular sites.[4]

It is noteworthy that Quarter Horses and Thoroughbreds, the two fastest horse breeds, have the lowest proportion of slow oxidative (type I) fibers and high proportions of both fast-twitch oxidative glycolytic (type IIA) and fast-twitch glycolytic (type IIB, also known as type IIX) fibers. These fast-twitch fibers are also known to have high activities for glycogen phosphorylase,[50] catalyzing the initial reaction in glycogenolysis, and lactate dehydrogenase[51,52] for converting pyruvate to lactate. Indeed, in racing Thoroughbreds and Standardbreds there is a high degree of correlation between type IIB fiber proportion and lactate accumulation:[51] fiber-type-specific lactate content 6 min *after* the end of 1200–2700 m races was greater in gluteus medius type IIB fibers (97.3 ± 2.1) than in type I (82.6 ± 3.8 μmol/kg dry muscle; $n = 8$), with type IIA fibers intermediate (93.6 ± 2.1). This is consistent with observations that type IIB fiber proportion is positively correlated with elevated plasma [$lactate^-$] during submaximal and maximal exercise in Standardbred trotters.[52–54] Of interest and importance to muscle acid–base regulation is the observation that in type I fibers [$lactate^-$] was only 15 mEq/kg dry muscle (equivalent to about 3 mEq/L) less than in type IIB fibers. This supports the idea that lactate produced in type IIB fibers diffuses out of these fibers into the interstitium where the lactate can be taken up by oxidative fibers[49,54,55] to be used as a fuel source both during and following exercise.

The fast-twitch fibers are also endowed with an important physicochemical feature that aids in the regulation of intracellular acid–base balance: there is an increasing content of the histidine dipeptide, carnosine, with increasing glycolytic capacity. Carnosine has a pKa ~6.9 and, as such, is an effective H^+ buffer and contributes substantively to the non-bicarbonate H^+ buffer capacity of muscle, particularly in fast-twitch glycolytic fibers.[56] Indeed, if the contribution of carnosine to non-bicarbonate buffering is removed, then each of the different fiber types have similar non-bicarbonate

Table 39.3 Skeletal muscle fiber types in horses and relationship to acid–base balance

	Fiber type		
	SO – type I	**FOG – type IIA**	**FG – type IIB**
% of total fibers[a,b]	15	45	40
Total H^+ buffer capacity[a]	88	98	130
Carnosine H^+ buffer capacity[a]	18	58	60
Carnosine % of total[a]	20	29	45
Carnosine content[a]	54 ± 15	85 ± 15	180 ± 15
Glycogen phosphorylase activity[b]	122 ± 20	71 ± 20	172 ± 20
Citrate synthase activity[b]	168 ± 15	167 ± 15	37 ± 15
Glycogen content[c]	+	++	++

SO, slow oxidative; FOG, fast-twitch oxidative glycolytic; FG, fast-twitch glycolytic.

[a,b] Averaged data from Sewell et al[57] (n = 20 2–3-year-old racing Thoroughbreds); Sewell et al[50] (n = 50 2–3-year-old racing Thoroughbreds).

[a] Data from Sewell et al[57]

[b] Data from Sewell et al[50]

[c] Data from Quiroz-Rothe and Rivero[175]

H^+ buffering capacities; thus carnosine confers all of the fiber type difference in non-bicarbonate H^+ buffering capacity.[50,57] Quarter Horses have a higher carnosine content (39.2 ± 1.8 mmol/kg wet muscle; $n = 6$) than Thoroughbreds (31.3 ± 2.9 mmol/kg wet muscle; $n = 6$) and Standardbreds (27.6 mmol/kg wet muscle; $n = 5$).[58] The high H^+ buffering capacity of glycolytic fibers is important given the high rates of metabolic H^+ production resulting from ATP hydrolysis, glycogenolysis, and glycolysis (described above). Without the ability to buffer this rapidly produced H^+ during exercise, cellular $[H^+]$ would rapidly increase to concentrations inhibitory for actin–myosin cross-bridge cycling[4,59] and for many metabolic reactions.[4,60,61] Buffering of H^+ within the cells in which it is produced also reduces the extent of extracellular acidification that occurs. Cessation of activity and resynthesis of ATP and glycogen results in a lowering of intracellular $[H^+]$ and a decrease in the quantity of H^+ buffered by histidine groups within the cell.

Biochemical origins of H^+ changes: anaerobic metabolism and muscle acidification/alkalinization

Muscular acidification occurs as a necessary consequence of providing ATP at high rates, using anaerobic metabolic pathways.[62,63] Rapid increases in anaerobic metabolism are needed during rest-to-work transitions and during transitions from work of lower intensity to higher intensity work, such as occurs during cutting and jumping. The rate-limiting enzymes of anaerobic metabolic pathways are rapidly activated compared to the duration required for peak activation of key rate-limiting enzymes of the aerobic metabolic pathways.

ATP hydrolysis by myosin ATPase, Ca^{2+}-ATPase and the $Na,^+K^+$-ATPase results in the net production of H^+:[62]

$$ATP + H_2O \rightarrow ADP + Pi + 0.425H^+$$

The anaerobic reactions of glycogenolysis and glycolysis are also rapidly activated, resulting in the production of 3 ATP for each lactate$^-$ produced; lactate$^-$ is produced because of an accumulation of pyruvate at the end of the glycolytic pathway, resulting in conversion of pyruvate to lactate by the enzyme lactate dehydrogenase:

$$\text{Glycogen} \xrightarrow{\textit{glycogenolysis}} \text{glucose-1-phosphate} \xrightarrow{\textit{glycolysis}} \text{pyruvate} \xrightarrow{\textit{lactate dehydrogenase}} \text{lactate}^-$$

For each mole of lactate$^-$ produced from glycolysis, 0.36 moles of H^+ are produced, while for each mole of lactate$^-$ produced from glucose-6-phosphate (arising from glucose transport into the cell, with the production of 2 ATP), 0.575 moles of H^+ are produced.[62]

The ATP produced from these anaerobic reactions is rapidly hydrolyzed, resulting in the production of 0.425 H^+ for each ATP hydrolyzed (see above). This reaction, combined with those that produce lactate$^-$, results in a nearly 1:1 stoichiometry for lactate$^-$:H^+.[62]

When ATP utilization rates are high, phosphocreatine (PCr^{2-}) is hydrolyzed, resulting in the consumption of H^+:[62]

$$PCr^{2-} + MgADP^- + H^+ \rightarrow MgATP^{2-} + H_2O + \text{creatine}$$

The rates of hydrolysis of ATP and PCr^{2-} are closely coupled and occur simultaneously as long as there is PCr^{2-} to hydrolyze; in simplified form, the combined ATP hydrolysis reaction and the PCr^{2-} hydrolysis reaction is:[62]

$$1\ PCr^{2-} + 1\ MgADP^- + 0.85\ H^+ \rightarrow 1\ MgATP^{2-} + \text{creatine}$$

Thus, for each mole of PCr^{2-} hydrolyzed to regenerate a mole of $MgATP^{2-}$, 0.85 moles of H^+ is generated.

Examination of this sequence of biochemical reactions shows that the H^+ produced by ATP hydrolysis is more than counteracted by the H^+ consumed by PCr^{2-} hydrolysis, resulting in the well-known increase in intracellular $[H^+]$ at the onset of exercise. Within the first few minutes of exercise there occurs a decreased reliance on PCr^{2-} hydrolysis to regenerate ATP, as ATP is increasingly produced from glycogenolysis/glycolysis as well as from aerobic sources. When exercise is continued above the lactate threshold, the combined reaction of ATP hydrolysis and lactate$^-$ production produce nearly equivalent amounts of lactate$^-$ and H^+ within skeletal muscle.

Most of the H^+ produced does not remain free in solution but binds to negatively charged sites, primarily histidine residues, on weak acids and bases such as intracellular proteins and is thus buffered.[5] Therefore, despite micromolar and millimolar changes in the concentrations of intracellular metabolites and strong ions, proton buffering by intracellular proteins limits $[H^+]$ changes to the nanomolar range.

In addition to reacting with intracellular proteins, H^+ also readily reacts with HCO_3^- (bicarbonate buffer system):

$$H^+ + HCO_3^- \xrightarrow{\textit{carbonic anhydrase}} CO_2 + H_2O$$

When intracellular $[H^+]$ increases as a result of increased anaerobic metabolism, this reversible reaction catalyzed by carbonic anhydrases produces CO_2 and water. The CO_2 itself is acidic and is removed from the cell by carbonic anhydrases and possibly by diffusion. As may be appreciated, during high-intensity exercise, when proton generation rates are very high, the bicarbonate buffer system is very limited with respect to its ability to remove H^+ from solution.

Because increased intracellular $[H^+]$ contributes to skeletal muscle fatigue, prevention or delayed onset of fatigue can only occur if H^+ is removed. Both the bicarbonate and non-bicarbonate (protein) buffer systems are limited. However, the cell can transport $Na,^+$ a strong base cation, into the cell (in exchange for H^+) using the Na^+–H^+ exchanger, and possibly augment intracellular HCO_3^- using a Cl^-–HCO_3^- exchanger.[64] In addition to these mechanisms, the outward transport of lactate$^-$ also contributes to an alkalinizing effect, as detailed below.

In summary, H^+ is produced from the hydrolysis of ATP and from the production of lactate$^-$. In contrast, the hydrolysis of PCr^{2-} at the onset of muscle contraction consumes H^+ to a greater extent than the H^+ produced through ATP

hydrolysis, resulting in intracellular alkalinization. With continuation of moderate- to high-intensity muscle contraction, H^+ and lactate$^-$ continue to be produced, resulting in intracellular acidification. Much of the H^+ is buffered by intracellular proteins or reacts with HCO_3^- to produce CO_2 and H_2O. CO_2 is removed from the cell by diffusion across the plasma membrane and by carbonic anhydrases.

Physicochemical origins of [H^+] changes in skeletal muscle during exercise

In addition to the biochemical reactions summarized above, physicochemical changes within the intracellular compartment of contraction muscle also contribute to the acid–base changes of exercise. There is involvement of each of the three independent physicochemical variables, although the changes in the concentrations of strong ions predominates, as will be exemplified below. The physicochemical descriptions complement the biochemical descriptions provided above.

Muscle [SID] during exercise

The time course and magnitude of changes in muscle [SID], and of the factors contributing to it, have not been well studied in horses. This is due in large part to the fact that muscle biopsies cannot truly be taken during exercise – the exercise must be stopped and the horse restrained to safely obtain a useful piece of muscle. Also, most studies have taken postexercise muscle biopsies between 2 and 20 min after cessation of exercise, during which time there are substantial changes in organic and inorganic strong ions. Accordingly, studies that measured muscle [K^+] showed no change[65] or a small increase[66] after brief periods of high-intensity exercise and this may be attributed to rapid recovery processes. The limited equine data will be used with what is known from human experiments to profile the changes occurring within muscle during exercise and recovery. The focus will be on high-intensity exercise because the changes are more pronounced and hence somewhat easier to follow. Changes with moderate-intensity exercise are attenuated compared to those occurring with high-intensity exercise.[54,67,68] Muscle acid–base responses to low intensity exercise have not been specifically studied and, indeed, changes in metabolites that affect acid–base state are minimal.[69,70] With prolonged endurance exercise it is expected that the major players would be [SID] changes resulting from net K^+ loss, with Na^+ and Cl^- gain, water loss or gain[71] and changes in [A_{tot}] primarily resulting from changes in intracellular water content.

The main variables changing within muscle during exercise that affect [SID] are [PCr^{2-}], [lactate$^-$], [K^+][6] and water content.[72] The osmotic shift of water from plasma and noncontracting tissues into contracting muscle at the onset of exercise is very large and rapid and can be attributed to the accumulation of osmolytes such as creatine, inorganic phosphate, lactate$^-$.[73] This fluid shift produces a large decrease in plasma volume (see below) and the 10% increase in intracellular volume at the end of 2 min of high-intensity exercise in horses[72] effectively dilutes intracellular metabolites and electrolytes and reduces [A_{tot}]. It is the actual concentrations of these variables that determine the acid–base state of the cell at any given point in time.

When working from metabolite or electrolyte data expressed in mmol/kg dry muscle or mmol/kg wet muscle it is necessary to convert to units of mmol/L or mEq/L of intracellular water. The water content of resting, non-exercised skeletal muscle is 0.75 L/kg wet muscle[74] and increases by about 10% with high-intensity exercise;[72] resting muscle thus has a wet:dry weight ratio of ~4, which increases to ~4.5 with high-intensity exercise. Therefore, a resting PCr^{2-} content of 85 mmol/kg dry muscle equates to 21 mmol/kg wet muscle (85/4) and 28 mmol/L (21/0.75) or 56 mEq/L. The doubling from 28 mmol/L to 56 mEq/L recognizes the divalent negative charge on PCr^{2-}.

With the onset of exercise, the initial few seconds of contraction results in the rapid hydrolysis of PCr^{2-} to regenerate ATP being used by myosin-, Ca- and Na,K-ATPases. The hydrolysis of PCr^{2-} effectively removes a strong acid anion from solution, which increases intracellular [SID] and has an alkalinizing effect (Fig. 39.3). The alkalizing effect resulting from PCr^{2-} hydrolysis is short lived. With high-intensity exercise, the high rates of H^+ and lactate$^-$ (a strong acid anion that decreases [SID]) production rapidly acidify the intracellular environment. Concurrent increases in [lactate$^-$][41,61,67] and decreases in [K^+][75] effectively decrease [SID], which accounts for the majority of intracellular acidification during high intensity exercise.[8] As may be expected, the accumulation of muscle lactate$^-$ contributes substantially to the exercise-induced acidosis because lactate$^-$ is a strong acid anion that increases [H^+]. Intracellular lactate$^-$ concentrations greater than 60 mEq/L (234 mmol/kg dry weight) have been reported in the gluteus medius of trained Standardbreds after trotting 1600 m at a high speed of 11 m/s.[76] With lower intensity exercise, PCr^{2-} is resynthesized during the subsequent period of steady-state exercise, thus contributing to decreases in [SID] and increased intracellular acidification.

The physicochemical factors contributing to intracellular acidification will now be examined in more detail.

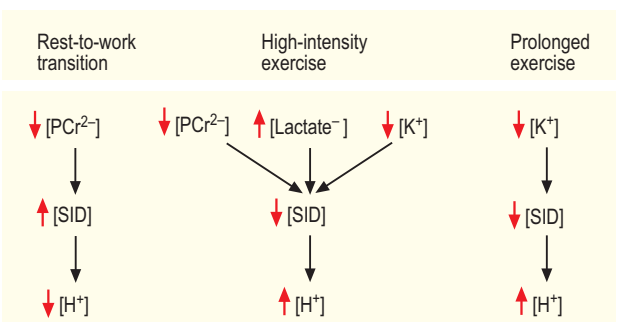

Fig. 39.3 Factors that affect muscle [SID], and the impact on muscle [H^+], during exercise.

Thoroughbreds exercising at high intensity hydrolyzed 32% of PCr^{2-} in 40 s (600 m sprint),[61] and 42% after 5 min at 100% of peak Vo_2.[68] In these studies, muscle biopsies were obtained within 60 s of stopping exercise and thus the amount of postexercise PCr^{2-} resynthesis was low at the time of muscle sampling. In resting equine muscle, $[PCr^{2-}]$ of 21 mmol/kg wet muscle[61,67,74] equates to 56 mEq/L (21 mmol/kg wet muscle/0.75 L/kg intracellular water).[74] Thus, after 40 s of sprinting, muscle $[PCr^{2-}]$ was reduced by 18 mEq/L, which effectively raises [SID] by 18 mEq/L; by virtue of this increase in [SID] it is evident that PCr^{2-} hydrolysis has an alkalinizing effect. This effect, however, is completely offset by the accumulation of $lactate^-$, with muscle $[lactate^-]$ reaching 45 mEq/L.[61] Very similar results for PCr^{2-} degradation were reported by Lindholm and Saltin[67] in five racing Standardbreds completing 2100 m in 178 s; however, these trained race horses experienced considerably less muscle $lactate^-$ accumulation (~ 20 mEq/L), a likely training adaptation.

Combining the effects of changes in $[PCr^{2-}]$ and $[lactate^-]$ decreases [SID], which has a net acidifying effect. This effect alone, however, only accounts for about 50% of the observed decrease in muscle intracellular pH from 7.01 to 6.86;[61] this is equivalent to an increase in $[H^+]$ from 98 to 138 mEq/L. The other contributor to the decrease in [SID] is the rapid and pronounced decrease in $[K^+]$ during high-intensity exercise.[71,75] In the gluteus medius of Standardbreds at rest, intracellular $[K^+]$ is 122 + 7 mEq/L (92 + 5 mEq/kg wet weight, with a water content of 75%).[74] There are no reports of equine muscle $[K^+]$ during exercise[65,66] and, on the basis of the large increases in plasma $[K^+]$ seen during exercise in horses,[77] it is expected that horses experience similar rates and magnitudes of muscle K^+ loss as do humans. In humans, 30 s of high-intensity exercise decreased muscle $[K^+]$ by 20 mEq/L and, with increases in muscle $[Na^+]$ and $[Cl^-]$ balancing each other, the decrease in [SID] is thus approximately 20 + 11 = 31 mEq/L. Based on titrimetric studies conducted on rat fast-twitch skeletal muscle, the 31 mEq/L decrease in [SID] is sufficient to account for about 75% of the increase in $[H^+]$.[6] In summary, using this example of muscle after 40 s of high-intensity exercise, the decrease in [SID] can account fully for the increase in $[H^+]$. Coincidently, the decrease in [SID] approximates the increase in $[lactate^-]$, and the decrease in $[PCr^{2-}]$ was similar to the decrease in $[K^+]$. Further study is needed to determine if this relationship holds during high-intensity exercise. If it does, it means that decreases in [SID] during high-intensity exercise may be estimated from the increase in $[lactate^-]$ alone. Changes in muscle [SID] account for the majority of the change in muscle $[H^+]$ (Fig. 39.4).

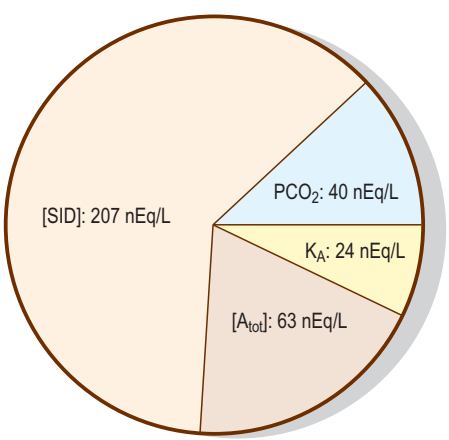

Fig. 39.4
Effects of changes in independent physicochemical variables on muscle $[H^+]$ after high-intensity exercise. The example provided is a brief period of very high-intensity exercise resulting in a decrease in muscle pH from 7.00 to 6.48, equal to an increase in $[H^+]$ from 100 to 334 nEq/L. Data from Lindinger.[6]

Muscle $[A_{tot}]$ during exercise

Exercise affects the intracellular protein portion of $[A_{tot}]$ (which has units of concentration) primarily through changes in cell volume or intracellular water content.[72] These volume changes are pronounced during the first several minutes of exercise[73] and also much later during prolonged exercise resulting in intracellular dehydration. The impact of cell volume changes on skeletal muscle $[A_{tot}]$ and acid–base state has not been studied, although it appears that the total capacity to buffer protons may not be appreciably affected because the content of carnosine remains constant.[78]

With high-intensity exercise, a number of the minor variables contribute to changes in $[A_{tot}]$, including an increase in [creatine] resulting from PCr^{2-} hydrolysis, a decrease in [ATP] and an increase in [Pi]. The increases in [creatine] results from PCr^{2-} hydrolysis, while increases in Pi are due to ATP hydrolysis, increases in glycolytic phosphates, and decreases in ATP.[46] Taken together, the increases in [creatine] and [Pi] account for all of the increase in $[A_{tot}]$ during high-intensity contractions in rat skeletal muscle.[46] The production of H^+ with increase in $[H^+]$ does not affect $[A_{tot}]$ but does decrease $[A^-]$ and increase [HA], as H^+ is buffered by this nonbicarbonate buffer system. Because the concentrations of the constituents comprising $[A_{tot}]$ changes during exercise, the K_A also changes. The increases in $[A_{tot}]$ and K_A accounted for 19% and 7%, respectively, of the increase in $[H^+]$ during 5 min of high-intensity exercise in rat muscle;[6] these have yet to be determined in equine muscle.

Muscle CO_2 during exercise

During high-intensity exercise CO_2 is produced primarily as a result of H^+ buffering by HCO_3^-, with a minor although increasing amount from tricarboxylic acid (TCA) cycle activity. Within the TCA cycle, the dehydrogenation of oxalosuccinate to α-ketoglutarate and of α-ketoglutarate to succinyl CoA produces one molecule of CO_2 for each carbon entering the cycle.

Muscle $[H^+]$ responds in near linear manner to increases in intracellular Pco_2, with a 90 mmHg increase in Pco_2 (40 to

130 mmHg) increasing [H^+] from 100 to 140 nEq/L.[6] Therefore, increases in CO_2 contribute relatively little to contraction-induced changes in intracellular [H^+], compared to the relatively large effect of CO_2 on plasma [H^+] (see Fig. 39.4). The contribution of CO_2 to intracellular acid–base state during exercise can only be estimated using venous plasma P_{CO_2} in blood draining intensely contracting muscles; this estimate assumes that intracellular muscle P_{CO_2} is similar to muscle venous P_{CO_2}.[79] This is reasonable given that CO_2 is highly diffusible and that there is substantial carbonic anhydrase within the interstitium, cells and on the sarcolemma to catalyze the conversion of HCO_3^- to CO_2. It is likely that the majority of the increase in P_{CO_2} results from the reaction of metabolically and physicochemically produced H^+ with HCO_3^- to produce CO_2 and water.

Draught exercise

While the responses described above are typical of racing horses, very similar responses appear to occur in horses pulling heavy loads. As occurs with racing, increasing exercise intensity results in increasing recruitment of fast motor units and fast glycolytic fiber types. Standardbreds performing incremental draught-loading exercise while trotting slowly (4.8 m/s) showed a similar muscle metabolic profile[80] to that seen during racing.[61] Indeed, after 10–12 min of incremental draught loading, muscle [PCr^{2-}] decreased by 15 mEq/L and [$lactate^-$] increased by 20 mEq/L, with one horse achieving a muscle [$lactate^-$] of 57 mEq/L.[80] This study is noteworthy in that the muscle biopsies were obtained 10 s after cessation of the exercise.

Changes in plasma during exercise and recovery

As noted previously, the acid–base disturbance within the plasma during exercise is generated within contracting skeletal muscle. It must therefore be appreciated that the venous plasma draining contracting muscles display the greatest and most rapid changes in metabolite, electrolyte, and gas concentrations compared to mixed venous or arterial plasma. The changes in mixed venous plasma will be greater than those in arterial plasma, and those in arterial plasma will be greater than those seen in venous plasma draining non-contracting tissues (i.e. jugular vein).[81–83]

These differences in blood sampling site are important considerations when evaluating the acid–base and electrolyte profile of exercised horses. In laboratory conditions, acid–base determinations are best performed on arterial and on venous plasma draining contracting skeletal muscle. While blood samples have been collected from the iliac vein in resting horses,[84] the technique does not yet appear to have been applied to exercising horses. The only real difference in acid–base composition between mixed venous and arterial plasma is due to CO_2 loss at the lung but this, together with associated measures of P_{O_2}, provides valuable information on the respiratory system during exercise and recovery.[13] When an acid–base assessment is performed on jugular venous plasma (as it often must be due to ethical or field considerations) then it must be kept in mind that a less severe and somewhat erroneous picture of whole body acid–base status will be the result.

As with muscle, it must also be appreciated that the rapid loss of water and some electrolytes from the plasma compartment with the onset of exercise is among the factors that produces changes in measured concentrations of electrolytes, metabolites protein and red cells (hematocrit or packed cell volume; PCV).[85,86] Indeed, about 50% of the increase in plasma [K^+], all of the increase in [plasma protein] and 50% of the increase in PCV is due to loss of water from the plasma compartment.[85,86] The remainder of the increase in plasma [K^+] is due to net loss of K^+ from contracting skeletal muscle and the remaining increase in PCV is due to splenic contraction resulting in discharge of red cells into the circulation.

Assessment of acid–base status in the blood is performed on constituents measured within the plasma compartment. Therefore concentrations of metabolites measured on samples of lysed whole blood cannot be used because the concentrations of these substances within red cells differs from that measured in plasma. The differences between plasma and red cell intracellular concentrations diminish within the syringe after blood sampling.[87] It is therefore important to separate red cells from plasma immediately after sampling the blood from exercising horses so that the plasma sample is as close to a true reflection of what was in the plasma of the horse at the exact time of blood sampling. As noted above, the P_{CO_2} at different blood sampling sites varies considerably and is an important consideration when determining whole-animal acid–base status, and some of this can be due to marked temperature differences. Determination of the actual pH, P_{CO_2} and P_{O_2} (as opposed to that measured by an instrument at 37°C), and hence [HCO_3^-], requires a non-linear correction of the blood gas and pH values to the temperature within each blood sampling site.[82,88] Increases in temperature results in increases in P_{CO_2}, P_{O_2} and [H^+] (decreased pH).

As in contracting muscle, the main changes that affect plasma [SID] during moderate- to high-intensity exercise are increases in [K^+], [$lactate^-$][77] and [Na^+] but not [Cl^-][81,82] due to the greater rate of loss of water (than of Na^+) from plasma into contracting muscle. Examples of these types of exercise include incremental exercise to fatigue, maximal intensity sprints, and constant rate submaximal exercise tests.

The arterial P_{CO_2} responses to exercise are highly dependent on running velocity and, during incremental exercise tests, on the duration of time spent at each running velocity. Arterial P_{CO_2} remains unchanged during low to mild intensity exercise. During incremental exercise to fatigue, arterial P_{CO_2} decreased slightly but mixed venous P_{CO_2} increased markedly from 50 mmHg at rest to 80–95 mmHg at the highest work load, corresponding to 100%$\dot{V}O_{2peak}$.[81] In Fenger et al's study[81] running velocity was increased in small increments (0.5 to 1 m/s) and each velocity sustained for 90 s to achieve near steady-state of cardiovascular and

respiratory responses.[89] When velocity was consistently increased at 0.5 m/s increments with 4 min at each speed, increasing exercise duration was associated with a marked and progressive hypocapnia[82] indicative of increasing alveolar ventilation.[90] In contrast, when velocity is increased in large (2 m/s) increments with only 1 min at each speed[91,92] or when single high-intensity (running at > 10 m/s) exercise bouts are performed the increase in P_{CO_2} is similar to that achieved during high-intensity sprint exercise.[91,93] In horses sprinting at 115% of peak $\dot{V}O_2$, arterial P_{CO_2} increased from 42 mmHg at the walk to 48 and 59 mmHg at 45 and 75 s of the sprint, comparable to the 58 mmHg P_{CO_2} seen with rapid, non-steady-state incremental exercise test.[91] From these and other similar results it can be concluded that sprinting or rapid increases in exercise intensity result in elevations in arterial P_{CO_2}, indicating that the respiratory system cannot keep the pace of metabolic and physicochemical CO_2 production. However, if sufficient time (90 s) is allowed at each running velocity, the rate of CO_2 elimination by the respiratory system meets or exceeds the rate of CO_2 production.

Incremental steady-state exercise

With this overview, let us now conduct an acid–base evaluation during the incremental 'steady-state' exercise test of Fenger et al.[81] The reason for choosing this type of a test is because it is a very good design for the controlled, clinical assessment of respiratory and metabolic systems during and following exercise. Although the $[A_{tot}]$ data are incomplete, this particular study provides a reasonably good assessment of acid–base state using arterial plasma.

In arterial plasma, the dependent variable $[H^+]$ increased by 21 nEq/L at maximal exercise, and $[HCO_3^-]$ decreased from 32.8 to 16.2 mEq/L. The independent variable [SID] remained unchanged (36.8 at rest and 35.5 mEq/L at maximal exercise) and thus had no effect on the changes in $[H^+]$ or $[HCO_3^-]$. Arterial P_{CO_2} decreased from 44 at rest to 35.5 mmHg at maximal exercise; this reduction appeared to be due to an increase in alveolar ventilation during the progressive exercise test and effectively reduced the mixed venous P_{CO_2} of 83 mmHg to below resting values. By solving for $[H^+]$ with this decrease in P_{CO_2}, but holding [SID] and $[A_{tot}]$ constant at resting values, the decrease in P_{CO_2} alone (independent of any other changes) contributed to a 7.7 nEq/L decrease in $[H^+]$, indicative of considerable sensitivity of $[H^+]$ to changes in P_{CO_2}. Because this decrease in P_{CO_2} caused a decrease in $[H^+]$, it means that increases in either or both of $[A_{tot}]$ and [SID] had to contribute to the increased $[H^+]$ (acidosis). The numerical (although not statistically significant) 1.3 mEq/L decrease in [SID] accounts for only 5.3 nEq/L of the 21 nEq/L increase in $[H^+]$. Therefore, the increase in $[A_{tot}]$ accounts for the difference between measured change in $[H^+]$ and the decrease in $[H^+]$ due to decreased P_{CO_2}, as well as the difference between change in measured $[H^+]$ and the increase in $[H^+]$ due to the increase in $[A_{tot}]$ (Table 39.4). It may appear unusual that [SID] was unchanged at maximal exercise, compared to rest, so we will examine this in more detail. As expected, the main contributor to a decrease in [SID] during exercise is an increase in $[lactate^-]$, and indeed lactate increased to 17 mEq/L at maximal exercise; the 16 mEq/L increase in $[lactate^-]$ thus contributed to a 16 mEq/L decrease in [SID]. This effect of increased $[lactate^-]$ (from 1 to 17 mEq/L), however, was offset by a simultaneous 11 mEq/L increase in $[Na^+]$ and a 3 mEq/L increase in $[K^+]$, with no change in $[Cl^-]$.

The important points about arterial acid–base balance during this type of exercise is that the increases in plasma total weak acids (primarily albumin) and inorganic phosphate are the primary contributors to the acidosis. While the 16 mEq/L increase in the strong acid anion $[lactate^-]$ did have a pronounced acidifying effect (the increase in $[lactate^-]$ alone effectively increased $[H^+]$ by ~55 nEq/L) this effect is offset by the increases in plasma strong base cations $[Na^+]$ and $[K^+]$. The increase in $[Na^+]$ results from the net movement of a low $[Na^+]$ plasma filtrate into skeletal muscle while the increase in $[K^+]$ arises from net K^+ loss by contracting skeletal muscle.[73,75] Finally, within mixed venous plasma the increases in $[A_{tot}]$ and P_{CO_2} both contribute substantially to the acidosis, and this P_{CO_2} effect is abolished upon transit of the blood through the lungs.

Table 39.4 Contributions to increases in arterial plasma dependent variables $[H^+]$ and $[HCO_3^-]$ by each of the independent variables [SID], P_{CO_2} and $[A_{tot}]$ during incremental 'steady-state' exercise in horses, using data from[80]

Variable	Resting	Maximal exercise	Change from rest	Contribution to change in $[H^+]$ (mEq/L)
$[H^+]$ mEq/L (pH)	33 (7.47)	54 (7.26)	+21	–
$[HCO_3^-]$ mEq/L	32.8	16.2	–16.6	–
[SID] mEq/L	36.8	35.5	–1.3	+5.3
PCO_2 mmHg	44.0	35.5	8.5	–7.7
$[A_{tot}]$ mmol/L	Not given	Not given		+23.4*

* calculated as $[H^+]$ change from rest (21) – ([SID] and P_{CO_2} effects)

High intensity sprint exercise

The second example to be illustrated is using high-intensity sprint exercise. We will specifically examine the second and ninth sprints of a series of nine sprints performed by trained Arabian horses, as described by Kronfeld and colleagues (1999).[93] Each sprint lasted for 60 s, with a 4-min active recovery between sprints. After a warm-up, the first sprint was performed at 7 m/s (6% incline) and the remaining eight sprints at 10 m/s. Another noteworthy feature of this study is that jugular venous plasma was used, and this raises some points of interest that will be addressed as we work through the data.

At the end of sprint 2, as in Fenger's et al's study,[81] there was only a small, 1 mEq/L decrease in [SID] that theoretically contributed 1 nEq/L to the 5 nEq/L increase in $[H^+]$ (Tables 39.5 and 39.6). In these tables, this is reported as –0.6 nEq/L because this more accurately represents the

Table 39.5 Contributions to increases in jugular venous plasma dependent variables [H^+] and [HCO_3^-] by the independent variables [SID], P_{CO_2} and [A_{tot}] at the end of the second sprint, using data from Kronfeld et al[93]

Variable	Resting	Second sprint	Change from rest	Contribution to change in [H^+] (nEq/L)
[H^+] nEq/L	38.7	43.7	5.0	–
[SID] mEq/L	48.6	47.6	–1.0	–0.6
P_{CO_2} mmHg	51.6	57.5	+5.9	4.1
[A_{tot}] mmol/L	18.5	19.5	+1.0	1.5

Table 39.6 Contributions to increases in jugular venous plasma dependent variables [H^+] and [HCO_3^-] by the independent variables [SID], P_{CO_2}, and [A_{tot}] at the end of the ninth sprint, using data from Kronfeld et al[93]

Variable	Resting	Ninth sprint	Change from rest	Contribution to change in [H^+] (nEq/L)
[H^+] nEq/L	38.7	42.1	+3.8	–
[SID] mEq/L	48.6	45	–3.6	+4.4
P_{CO_2} mmHg	51.6	48.2	–3.4	–2.4
[A_{tot}] mmol/L	18.5	20	+1.5	+2.0

mean of the individual calculations for eight horses. The point is that changes in [SID] are small and do not play a major role in acid–base balance during this type of exercise. Although a 4.3 mEq/L increase in plasma [lactate$^-$] contributed to an acidifying effect, this was offset by increases in plasma [Na^+] (1.7 mEq/L) and [K^+] (1.4 mEq/L). As the number of sequential sprints increased, plasma [lactate$^-$] continued to increase to 9.5 mEq/L at the end of sprint 9; this now offset the increases in [Na^+] and [K^+], resulting in a 3.6 mEq/L decrease in [SID] that could alone account for all of the increase (3.8 nEq/L) increase in [H^+].

P_{CO_2} peaked at the end of the second sprint and then decreased progressively to below resting by the end of sprint 6. This indicates both a lowering of glycolytic metabolism and resultant decrease in metabolic H^+ production[60,68] that reduces the generation of P_{CO_2} (from H^+ combining with HCO_3^-) and an improvement in alveolar ventilation as the exercise progresses. Nonetheless, the decrease in P_{CO_2} to below resting values contributed to alkalinizing effect equivalent to reducing [H^+] by 2.4 nEq/L. A further small increase in [A_{tot}] also contributed to an acidifying affect that offset most of the alkalinizing effect of lowered P_{CO_2}.

In summary, comparing the results of sprints 2 and 9, we see a marked difference in the origins of the acid–base disturbance. The primary acidifying influence at the end of sprint 2 was the increase in P_{CO_2}, whereas at the end of sprint 9 P_{CO_2} had decreased and contributed to an alkalinizing effect. This is an important regulatory aspect, for this later alkalinizing effect of lowered P_{CO_2} markedly reduced the acidifying effects of decreased [SID] (which account for two-thirds of the acidification) and increased [A_{tot}] (one-third of the acidification at the end of sprint 9). In sprint 2, there was negligible effect of [SID] as [lactate$^-$] continued to increase in plasma with repeated sprints and a progressively decreasing [SID] played an increasing role in systemic acidification. In classical acid–base physiology, one can refer to this acidosis at the end of sprint 2 as a primary respiratory acidosis that progresses to a primary metabolic acidosis with respiratory compensation by the end of sprint 9.

It should be noted that repeated sprints result in a sequential lowering of P_{aCO_2} with each successive sprint[93] and that this is attributed to a significant increase in alveolar ventilation and not to increased breathing frequency, which is tightly coupled to stride frequency.[90] After 5 sprints, an increasing arterial hypocapnia was observed with each successive sprint.[93] In a similar vein, when a low-intensity exercise warm-up precedes a bout of high-intensity exercise, there is an increase in $\dot{V}_{CO_2}$ during the first minute of exercise compared to when no warm-up preceded the high intensity exercise.[94,95] Rather than evoking an increase in alveolar ventilation to explain this result, however, these authors suggested that the warm-up resulted in increased tissue CO_2 storage, which then reduced the amount of CO_2 during the subsequent bout of high-intensity exercise – this does not preclude an increase in alveolar ventilation after a warm-up. Furthermore, since the increase in $\dot{V}_{CO_2}$ occurred within seconds of starting the high-intensity exercise,[94] it is unlikely that the rapidity of the augmented $\dot{V}_{CO_2}$ response could be explained by a reduced ability to store CO_2. It can be concluded that the augmented $\dot{V}_{CO_2}$ during high-intensity exercise after warm-up is primarily due to increased alveolar ventilation, similar to that seen with high intensity steady-state exercise. In further support, during heavy exercise (4.5 m/s at a 10% grade = 60% of peak $\dot{V}_{O_2}$) of 30 min duration, a progressive decrease in P_{aCO_2} was primarily due to a progressive increase in alveolar ventilation secondary to increases in both respiratory frequency and tidal volume.[96]

Steady-state submaximal exercise

The final example exemplifies the changes and contributions seen during steady-state, submaximal exercise in well trained horses. A time point of 15 min into exercise was selected because this is well past the rapid changes that occur with the onset of exercise and was at least 10 min prior to the onset of fatigue for this intensity with this group of horses (Lindinger MI et al, unpublished data). One of the most noteworthy features of submaximal steady-state exercise in trained horses is the alkalosis that occurs during the steady-state period (Table 39.7). Plasma pH rose in both arterial (carotid artery) and mixed venous (pulmonary artery). In arterial plasma, the alkalosis was completely due to the decrease in P_{aCO_2}, since there was negligible change in [SID] (2 mEq/L increase in [lactate$^-$] balanced by 1 mEq/L decrease in [Cl^-] and 1.3 mEq/L increase in [K^+]) and a 1.3 mEq/L increase in [A_{tot}] had an acidifying

Table 39.7 Contribution to increases in arterial and mixed venous dependent variables [H^+] and [HCO_3^-] by the independent variables [SID], PCO_2 and [A_{tot}] at 15 min of steady-state exercise prior to onset of fatigue. Data represent averages obtained from four trained Standardbreds (from Lindinger MI et al, unpublished)

Variable	Resting	Exercise	Change from rest	Contribution to change in [H^+]	Contribution to change in [HCO_3^-]
Arterial plasma					
[H^+] nEq/L (pH)	37 (7.43)	26 (7.58)	–10	–	–
[HCO_3^-] mEq/L	28.3	26.3	–2.0	–	–
[SID] mEq/L	39.9	39.6	–0.3	+0.4	–0.3
PCO_2 mmHg	42.7	28.3	14.4	–12.0	–0.6
[A_{tot}] mmol/L	13.5	14.8	+1.3	+1.4	–1.0
Mixed venous plasma					
[H^+] nEq/L (pH)	43 (7.37)	38 (7.42)	–5	–	–
[HCO_3^-] mEq/L	28.4	31.0	+2.6	–	–
[SID] mEq/L	39.9	43.8	+3.9	–4.8	+3.7
PCO_2 mmHg	49.2	48.1	–1.1	–0.9	0.0
[A_{tot}] mmol/L	13.6	14.9	+1.3	+1.6	–1.0

effect. The decrease in arterial plasma [HCO_3^-] is a hallmark of 'metabolic acidosis' in the clinical acid–base sense and, indeed, that is what one would expect to see with exercise. Importantly, however, this decrease is primarily due to the increase in total *weak* acid concentration (primarily plasma proteins) and secondarily to the decrease in $Paco_2$ (despite the marked 14.4 mmHg decrease). It must be emphasized that such modest increases in [K^+] and [lactate$^-$], with the alveolar hyperventilation, are features of well-trained horses.

In mixed venous plasma, there was a small decrease in $Pmvco_2$, indicating that the influence of alveolar hypoventilation persisted within the peripheral circulation and that the rates of metabolic H^+ production were low; metabolism was primarily aerobic, as evidenced by the low plasma [lactate$^-$] of 3.25 mEq/L. The sole contributor to an acidifying effect was the increase in plasma [proteins] ([PP]), resulting from the fluid shift into contracting muscle. The 4 mEq/L increase in [SID] thus accounted for all of the alkalinizing effect. Plasma [SID] increased due to a 2 mEq/L increase in [Na^+], a 1.4 mEq/L increase in [K^+] and a 2 mEq/L decrease in [Cl^-] that offset the 1.9 mEq/L rise in [lactate$^-$]. Mixed venous plasma [HCO_3^-] increased during steady-state exercise, in contrast what was seen in arterial plasma and what would also be seen in jugular venous plasma. Again, this is solely due to the increase in [SID], as the increase in [A_{tot}] had the effect of reducing [HCO_3^-] by 1 mEq/L.

It is evident from this analysis, using relatively small changes in both dependent and independent acid–base variables, that [H^+] has similar sensitivities to physiological changes in the independent variables, however [HCO_3^-] is much more sensitive to changes in [SID] and [A_{tot}] than to changes in Pco_2.

Endurance exercise

Low-speed endurance exercise, such as draught horses pulling loads for 8 h per day for five consecutive days[97] produces no significant acid–base disturbances. When the speed of endurance exercise is increased, with ensuing sweat losses of water and electrolytes occurring at elevated rates, then a slowly progressing metabolic alkalosis develops.[98–100] It is important to point out that when the hydration status of the horses is maintained, through the use of effective strategies of electrolyte supplementation, this alkalosis does not develop.

The metabolic alkalosis associated with dehydration during endurance rides, or indeed during prolonged transport of a horse, is a direct result of sweating. Equine sweat has a tonicity similar to that of plasma[101] in contrast to the very dilute sweat produced by humans. The reason for the high tonicity of equine sweat is that the equine sweat gland does not appear to have the ability to resorb ions from within the lumen of the sweat glands. Rather, some ions, such as K^+ and Cl^- appear to be secreted for their concentrations in sweat are much greater than in plasma and extracellular fluid.[101] Although the electrolyte composition of equine sweat changes over time, in general, sweat [Na^+] ranges from 65 to 170, [K^+] ranges from 25 to 55 and charge balance is made up by [Cl^-] in the range 100–180 mEq/L.[101] The total amount of electrolyte loss during a 100-mile endurance ride can be in excess of 1 mole for Na^+ and Cl^- representing substantial depletion of body stores,[102] so it is instructive to determine the origins of the electrolyte losses. Because the tonicity and [Na^+] of equine plasma and sweat are similar, there is little if any change in plasma osmolality and [Na^+] during prolonged endurance exercise.[70,102,103] Additionally, when plasma [K^+] is measured, after allowing sufficient time after exercise has stopped for re-equilibration of plasma and muscle K^+ pools, there is little change in plasma [K^+] and clearly the K^+ losses are not borne by the extracellular compartment. Therefore, the K^+ appearing in the sweat originates largely from cells, and likely contracting muscle cells that are known to lose K^+ during the period of exercise.[104] It is important to recall that the bulk of the body's Na^+ and Cl^- stores are extracellular, and it is Cl^- that balances

the positive charge on Na^+ and K^+ lost in sweat. Therefore sweat $[Cl^-] = [Na^+] + [K^+]$. Because the extracellular losses of Cl^- exceeds those of Na^+ by a factor ranging between 1.3 and 1.8, extracellular and plasma $[Cl^-]$ must decrease, and indeed does by 10 to 15 mEq/L.[70,98,102,103] It is this large decrease in plasma $[Cl^-]$ that is responsible for the alkalosis, for this results in a large increase in plasma [SID].

A detailed assessment of acid–base status in horses during the time course of an endurance ride has not yet been performed. Using the principles of acid–base assessment provided above, an extreme case of plasma $[Cl^-]$ depletion (–15 mEq/L[103]) will be used to exemplify the effect on acid–base status:

$$[SID] = ([Na^+] + [K^+]) - ([Cl^-] + [lactate^-])$$

Before endurance exercise:

$$38\ mEq/L = (135 + 4) - (100 + 1)$$

After endurance exercise:

$$53\ mEq/L = (135 + 4) - (85 + 1)$$

The increase in [SID] alone has a large alkalinizing effect and can be calculated to decrease plasma $[H^+]$ from 36.6 to 23.9 nEq/L (pH increase from 7.436 to 7.622), with $[HCO_3^-]$ increasing from 26.9 to 41.2 mEq/L. The fact that such large changes do not occur is primarily attributed to the simultaneous increase in plasma $[A_{tot}]$ resulting from the loss of extracellular water which raises [PP]. An increase in [PP] from 60 to 75 g/L, typical of endurance rides, increases $[A_{tot}]$ from 13 to 16.25 mmol/L, and this change alone (independent of change in [SID] or Pco_2) has the effect of raising $[H^+]$ from 36.6 to 40.5 nEq/L. The combined effect of increased $[A_{tot}]$ and decreased [SID] results in an $[H^+]$ of 25.6 nEq/L (pH 7.591) and $[HCO_3^-]$ of 38.4 mEq/L. There is negligible change in Pco_2 during endurance exercise and the small changes that occur can be neglected for the purposes of assessing acid–base status. Therefore, the acidification resulting from the increase in plasma $[A_{tot}]$ only partially offsets the alkalinization caused by the increase in [SID], resulting in the observed alkalosis.

It is very important to note that, in the dehydrated horse, there is little change in plasma $[Na^+]$ and osmolality. Horses can lose 30 L or more of fluid as sweat with minimal alteration of plasma osmolality and $[Na^+]$. This is solely because sweat osmolality and $[Na^+]$ differs little from that of sweat. To complicate the interpretation, the decrease in plasma $[Cl^-]$ is seemingly inconsistent with dehydration. The key hematological variables for diagnosis of dehydration in the horse are a decrease in plasma $[Cl^-]$ coupled with increases in [PP] and PCV.

Other types of exercise

It is worth noting some interesting features of acid–base balance reported in the literature in horses performing different types of activities, ranging from draught work to show jumping. Show jumping competition resulted in a decrease in jugular venous Pco_2, once again illustrating the degree of alveolar ventilation and an ability of lowered Pco_2 to offset the acidifying effects due to increases in $[A_{tot}]$.[105] In these horses [SID] increased by 2 mEq/L, which also had an alkalinizing effect; a 2 mEq/L decrease in $[Cl^-]$ and 3 mEq/L increase in $[Na^+]$ more than offset the 3.8 mEq/L increase in $[lactate^-]$.

The second day of three-day eventing consists of a steeplechase, a roads and tracks phase and a cross-country phase, with each separated by a rest/cool-down period. Rose and colleagues[106,107] assessed the acid–base changes occurring within jugular venous blood during this period. As with the other forms of exercise described above, plasma $[H^+]$ decreased from 42 to 37 nEq/L at the end of the roads and tracks phase, and was subsequently 41 nEq/L at the end of the cross-country phase. The main reasons for the decrease in $[H^+]$ at the end of roads and tracks was a 6 mmHg decrease in Pco_2 with a 2.3 mEq/L increase in [SID]. The increase in [SID] resulted from increases in $[Na^+]$ and $[K^+]$ and decreases in $[Cl^-]$ that offset the 1.5 mEq/L increase in $[lactate^-]$. Together, the combined effects of lowered Pco_2 and increased [SID] more than offset the acidifying effects of the 1.2 mmol/L increase in $[A_{tot}]$, producing the mild alkalosis. At the end of the cross-country, plasma $[lactate^-]$ had risen to 8.2 mEq/L, negating the effects of increased $[Na^+]$ and lowered $[Cl^-]$ and leaving [SID] at resting values (40 mEq/L). The sole contributor to an acidifying effect was thus the 3 mmol/L increase in $[A_{tot}]$ (resulting from dehydration (57%) and exercise-induced fluid shift (43%)) and this was completely offset by a further decrease in Pco_2 to 31.5 mmHg resulting in a normal $[H^+]$ (41.3 nEq/L). As expected, the combined effects of increased $[A_{tot}]$ and reduced Pco_2 lowered $[HCO_3^-]$ from 28 mEq/L at rest and at the end of roads and tracks to 18 mEq/L at the end of the cross-country. Within 30 min of the cross-country both $[H^+]$ and $[HCO_3^-]$ had normalized to pre-exercise values despite an elevated $[A_{tot}]$ (at this point due solely to dehydration), whose acidifying effects were offset by a continued depression of Pco_2.

Polo consists of periods of low to moderate activity interspersed with brief periods of burst activity while carrying the rider. The total duration of activity for individual horses ranges from 1 to 2 h, allowing time for dehydration to occur as a result of sweating (see endurance exercise section below). Polo exercise results in a modest acidosis of metabolic origin (increases in plasma $[lactate^-]$) that lasts during the period of activity.[108] After cessation of exercise a mild alkalosis may develop, concomitant with decreased plasma $[Cl^-]$ resulting from sweat losses (see the 'Endurance exercise section').

Clinical notes

In a clinical vein, the nature of the generation of the acid–base disturbance, and its subsequent regulation during and following the period of exercise, results in its eventual amelioration over a period of minutes to hours depending on the intensity

and duration. Very high-intensity exercise is capable of lowering arterial plasma pH to 7.1.[77] Therefore caution may be required with repeated sprints of very high intensity due to the cumulative effects of increasing [lactate$^-$] and [PP] that may be capable of decreasing arterial pH below 7.1. It must be understood that the severity of the mixed venous acidosis would be measurably greater than the arterial acidosis. At somewhat lower intensity, horses are capable of several repeated sprints without incurring a severe acid–base disturbance.[93] The final caution pertains to dehydration that results from prolonged endurance exercise or prolonged transport without adequate intake of fluids and electrolytes. Dehydrated horses typically have an alkalosis that results in large part from the decrease in plasma [Cl^-] (loss of strong acid anion). The decrease in plasma [Cl^-] is primarily due to the very large losses of Cl^- in the sweat that serves to physicochemically balance the positive charge of Na^+ and K^+ lost in sweat. At the same time, [PP] may be in excess of 8 g/dL (normal is 5–6 g/dL in a euhydrated horse) and this will have a pronounced acidifying effect that also lowers [HCO_3^-]. Proper correction of this combined acid–base disturbance requires oral (preferably) or intravenous (if necessary) administration of a balanced electrolyte solution to replace the water, Na^+, K^+ and Cl^- lost in sweat. Since Cl^- in the administered solution will balance the sum of Na^+ and K^+, as K^+ is taken up by the tissues (and this occurs very rapidly[12]) the Cl^- will be left in the extracellular compartment with Na^+, serving to retain extracellular fluid and thereby lower plasma [protein]. This effectively corrects both the strong ion and weak ion aspects of the acid–base disturbance simultaneously.

Exercise summary

The strength of the physicochemical approach to acid–base balance is that it allows for the determination of each of the known and measured variables that determines the concentrations of H^+, HCO_3^-, and ^-OH in body fluids. Specifically, the method allows us to determine how much of an effect the increase in [PP] has. In most types of exercise, and in many clinical conditions, [PP] is elevated; large increases in [PP] are a hallmark of dehydration in endurance horses and, with other causes of dehydration, has a marked acidifying effect on plasma, and additionally lowers [HCO_3^-]. With high-intensity exercise, increases in plasma [lactate$^-$] play a major role in decreasing [SID], and hence acidifying the plasma and lowering [HCO_3^-]. With submaximal exercise, however, changes in strong ion concentrations are small and their effects on acid–base balance may be less than those exerted by increases in [A_{tot}]. Finally, the very large increases in mixed venous P_{CO_2} that occur with high-intensity exercise have a major acidifying effect, but raise [HCO_3^-]. When this blood is treated by the lungs, the P_{CO_2} is markedly lowered, often to below resting values for P_{aCO_2}. Thus the acidifying effect of P_{CO_2} within the venous plasma may be reversed to an alkalinizing effect within the arterial plasma. The main strong ion changes contributing to the decrease in [SID], and hence acidification and lowering of [HCO_3^-], are increases in plasma [lactate$^-$] and decreases in plasma [Cl^-].

Responses to training

The impact of training, or exercise conditioning, on acid–base balance has not been well studied. It is known, however, that the responses to exercise conditioning for low to moderate-intensity exercise (endurance training) differ from those for high-intensity exercise (sprint training), both at the whole-body metabolic level (see Chapter 34) and within skeletal muscle (see Chapter 5). Perhaps because of relative ease of implementation, endurance-type training studies are more prevalent than sprint training studies.

Endurance training

Endurance training results in a decrease in anaerobic muscle metabolism[109] and an increased oxidative capacity of muscles[110] that results in an increased reliance and capacity for fatty-acid oxidation during exercise. There is a reduced conversion of pyruvate to lactate$^-$ accompanied by improved matching of glycolytic flux with entry of pyruvate into the TCA cycle.[111] Notably, these adaptations result in a reduced rate of lactate$^-$ and H^+ accumulation within contracting muscle and blood, and these responses may be detectable within the first week of training. This is associated with increases in the activities of enzymes of oxidative metabolism that favor an increase in free-fatty acid oxidation. In highly trained, elite human endurance athletes the adaptations for fat oxidation are very pronounced, with fat serving as the main energy source at exercise intensities as high as 85% of peak $\dot{V}O_2$[112] with concomitant decrease in muscle glycogen utilization at submaximal exercise intensities. At present, it is not known if the elite equine endurance athlete can achieve a similarly high capacity to utilize blood-borne fatty acids.

These intramuscular biochemical adaptations are associated with improvements in the cardiovascular function (increased stroke volume and cardiac output)[89] but there appears to be little change in functional parameters of the respiratory system.[89,92,113] With low-intensity exercise, endurance training appears to have no effect on measured acid–base variables,[114] probably because the metabolic and cardiorespiratory systems are not sufficiently taxed by low work rates.

Sprint training

The effects of sprint training on the ability of skeletal muscle or the whole body to regulate acid–base state have not been studied. None the less, a number of inferences may be made from the limited results available. Within skeletal muscle, sprint training results in a large increase in non-bicarbonate buffering capacity[44] that appears to be due primarily to increases in muscle carnosine content.[56]

Seven weeks of race training in Thoroughbreds increased skeletal muscle non-bicarbonate buffering capacity by 60%, from 58 ± 7 to 93 ± 7 μmol/kg.pH^{-1}.[44] Similar increases have been reported in humans[5,115] but sometimes not in other equine studies.[116,117] In the latter studies, however, the untrained horses were likely somewhat active, making difficult the detection of significant differences. Buffering capacity, even in untrained equine muscle, is substantially greater than in trained humans, and is 43 μmol/kg.pH^{-1}.[115,118] The increased buffering capacity with sprint training is very important in view of the fact that sprint training (in humans) results in increased activities of the glycogenolytic and glycolytic enzymes phosphorylase, phosphofructokinase, glyceraldehyde phosphate dehydrogenase, and lactate dehydrogenase.[119] Indeed, a high degree of correlation between carnosine content and glycogen phosphorylase activity has been shown.[50] Increased activities of these enzymes would be associated with a capacity to increase the rates of lactate$^-$ and H^+ production within contracting muscle. Despite increased rates of production, there was actually a decrease in lactate accumulation within muscle after training compared to before training both in horses[117] and in humans,[115] suggesting decreased reduction of pyruvate to lactate and enhanced pyruvate conversion to acetyl CoA. Additionally, increased amounts of lactate$^-$ could be transferred out of contracting muscle cells by training-induced increases in the monocarboxylate transporter MCT,[120] to be taken up rapidly by other tissues,[49] keeping plasma [lactate$^-$] relatively low.[117]

Thoroughbred race training resulted in no effects on pH_a, P_{ACO_2}, P_{mvCO_2} and $\dot{V}_{CO_2}$ after 7 weeks[89] or 16 weeks,[92] although arterial[89] and mixed venous pH[92] decreased significantly less than before training during incremental exercise tests.

In summary, from the limited number of sprint training studies, it appears likely that an improved ability to regulate acid–base state with moderate- to high-intensity exercise is primarily due to increases in non-bicarbonate proton buffering capacity and an improved ability to utilize pyruvate.

High altitude

The transition to high altitude results in a number of hematological adjustments that affect acid–base status.[121,122] The decreased atmospheric partial pressure of O_2 results in an alveolar hyperventilation that persists for at least 6 days. During the initial 3 days of transition to 3800 m elevation, P_{CO_2} decreased from 40 to 20 mmHg and [SID] from 44 to 26 mEq/L that, together, accounted for increases in pH (7.43 to 7.48) and decreases in [HCO_3^-] (from 23 to 15 mEq/L).[122] After the third day of altitude, acid–base parameters were normalized over a 3–7-day period.[122] Since [PP] was not measured, the influence of [A_{tot}] on acid–base balance is unknown at this time. From these studies it appears that a minimum of 10 days is needed to complete the adjustments affecting plasma acid–base status. This is an important consideration when horses are brought from low- to high-altitude locations for competition.

Diet and acid–base

Nutrition plays an important role in equine health, performance, and acid–base balance, both at rest and during exercise. Large-animal diets are often characterized on the basis of their dietary cation anion difference (DCAD), defined as the balance between strong base cations (K^+ and Na^+) and strong acid anions (Cl^- and SO_4^{2-}). The reason that dietary DCAD affects acid–base balance in the body is because diets high in cations but low in anions (high DCAD) result in an increased cation content of the extracellular fluids as these cations are absorbed within the small intestine. When a high DCAD diet is sustained, much of the excess cation is excreted by the kidneys, but the cations are accompanied by the weak acid HCO_3^- and the strong acid Cl^-, typically producing a mild systemic alkalosis.[123] In contrast, low DCAD diets produce a systemic acidosis[123–125] with increased renal calcium excretion that could lead to negative calcium balance and weakening of the skeletal system.[126] A DCAD of between 250 and 300 mEq/kg is considered neutral – this will not result in significant alterations of acid–base balance. In contrast, a DCAD > 300 mEq/kg will have an alkalinizing effect, while a DCAD < 250 mEq/kg will have an acidifying effect. High-quality, high-forage diets have a large cation content, primarily K^+, that will often produce a DCAD > 300 mEq/kg. In contrast, unsupplemented grain rations have a high Cl^- and low K^+ content and have a DCAD typically less than 250 mEq/kg.

Resting horses

Plasma pH and [HCO_3^-], and urine pH have been shown to increase in proportion to the DCAD over the range 0 to 407 mEq/kg dry matter.[123,125,126] Diets that have a high protein content are also acidogenic due to the production of SO_4^{2-} (strong acid anion) and inorganic phosphate (weak acid anion), which become elevated in plasma. In Arabian horses, a high protein (HP) diet (DCAD = 182 mEq/kg) significantly decreased [SID] by 7 mEq/L compared to horses fed on a low protein (LP; DCAD = 260 mEq/kg) diet.[127] The decrease in [SID] was due to a 7 mEq/L decrease in plasma [Cl^-] in the HP group. It is likely that the decrease in [Cl^-] was offset by increases in [SO_4^{2-}] and [phosphate], but these were not reported. Plasma P_{CO_2} averaged 3 mmHg higher in the HP group. The resultant changes in dependent acid–base variables was small (increased plasma [H^+] by 2–3 nEq/L), with no effect on [HCO_3^-].

Exercise

Only a few studies have examined the influence of DCAD on exercise performance and on acid–base balance during exercise.[124,125,128,129] Popplewell et al[129] demonstrated that horses fed a high DCAD ran significantly faster and, at the end of exercise, had elevated concentrations of lactate in the blood while plasma [H^+] was unchanged.[129] A similar

response was not seen by Cooper et al where the high DCAD diet was marginal at 306 mEq/kg.[128]

In the study by Graham–Thiers et al[127] horses on the high protein (HP) diet (low DCAD) had a more pronounced lowering of [HCO_3^-] during exercise consisting of 6 sequential 1 min sprints, separated by 4 min rest periods. The lower [SID] and Pco_2 during rest in the HP group persisted during exercise and 30 min of recovery and accounted for the reduced [HCO_3^-]. Of interest, and in contrast to Popplewell et al's study,[129] horses on the HP diet averaged 3 mEq/L higher plasma [$lactate^-$], which was offset by a 3 mEq/L decrease in plasma [Cl^-], than horses on the LP diet.

Dietary protein

The purported effects of dietary protein on acid–base balance in the study by Graham-Thiers et al[127] can at least in part be attributed to the low DCAD of the HP diet. A recent study by the same group[130] maintained the DCAD of the HP diet between 387 and 424 mEq/kg dry matter, whereas the DCAD of the low protein (LP) diet was 345–370 mEq/kg. At rest, horses on the LP diet had a minor lowering of arterial and mixed venous plasma [$lactate^-$] and pH, and increased arterial [HCO_3^-] and [K^+], without change in other variables. With high-intensity sprinting exercise, horses on the LP diet maintained a 0.03 pH-unit higher mixed venous pH than horses on the HP diet, although the physiological significance of such a small, although consistent effect, is questionable. The increased mixed venous pH could be attributed to a 2 mEq/L greater [SID] in LP horses both at rest and during exercise, with no differences in Pco_2 and [A_{tot}] between LP and HP. In contrast, arterial plasma was not influenced by diet during exercise. These limited studies suggest that the LP diet alters the functioning of the contracting muscles sufficiently to produce a modest effect of elevated [SID] and pH in mixed venous blood. The effects are so small to be of questionable physiological significance.

Dietary starch

Dietary starch has been suggested to be the cause of a decrease in plasma pH when DCAD was held constant across diets. However, a recent comprehensive study using three high DCAD (305–333 mEq/kg) and three low DCAD (124–154 mEq/kg) diets, with starch comprising 45–49% of each diet, showed that high-starch diets (from corn, oats or alfalfa) had no effect on plasma acid–base balance.[131] These authors concluded that the potential negative effects of high-grain diets (low DCAD) can be overcome by adjustment of the DCAD with supplemental cations. There was also no effect of alfalfa versus non–alfalfa roughage diets on acid–base status and exercise performance in Thoroughbreds.[132]

Dietary fat

The effect of dietary fat on performance and acid–base balance has received more attention than starch and protein. Graham-Thiers et al found no effect of dietary fat (0 versus 10%) on acid–base balance at rest and during repeated sprint exercise, although there was evidence for an increased reliance of fat as an energy source.[130] In contrast, an earlier study of repeated sprint exercise reported that horses on a 10% fat diet showed an increased plasma acidosis with increased [$lactate^-$][133] and decreased Pco_2 and [SID] than horses on the control diet.[134] Peak effects of the high-fat diet required between 6 and 11 weeks of feeding. When horses were on a high-fat (10%) diet for a relatively short duration of 4 weeks, there was a tendency for the high-fat diet to increase plasma [$lactate^-$] during exercise.[135] This was associated with faster gallop speeds during the third and fourth repeated gallops, which Duren et al[135] attribute to an increased activation of glycolysis and glycogenolysis[136] with associated increases in power output with repeated sprint exercise. It appears that, with high-intensity exercise, horses must be maintained on a high-fat diet for at least 6 weeks and that the chronic high-fat diet results in an increased reliance on glycolysis to produce the ATP needed to generate the high power outputs. The effects of a high-fat diet on acid–base balance during high-intensity exercise appear to be minor. The effects of dietary fat on acid–base balance during prolonged low- and moderate-intensity exercise do not appear to have been studied.

Selected clinically relevant issues for seemingly 'normal' horses

Age

A recent study[137] provided a detailed comparison of plasma acid–base status in young (< 9 years) and old (> 19 years) horses. The only differences were a reduced (by 1.5 mmHg) arterial Pco_2 that resulted in a lower pH (7.428 versus 7.404) and this was associated with a lower Po_2 (90 versus 102 mmHg); there were no differences in measured weak and strong ion concentrations. A similar effect of age on arterial Pco_2 has previously been reported.[138] Aguilera-Tejero et al suggest that the apparent hypoxemia in older horses results in an increased ventilation that would thereby reduce arterial Pco_2.[137]

Idiopathic laryngeal hemiplegia

A number of race horses, both Thoroughbred and Standardbred, may perform poorly[138] due, in part, to a syndrome known as idiopathic laryngeal hemiplegia (ILH).[139] ILH is a peripheral neuropathy characterized by dysfunction of the left recurrent laryngeal nerve innervating most of the left laryngeal muscles.[140] Haynes indicated that about 50% of large breed horses have some degree of laryngeal synchrony and asymmetry at rest.[141]

Impaired regulation of acid–base balance occurs during exercise in horses with grade 4 or 5 laryngeal function,[140] where grade 5 is complete hemiplegia. The primary manifestation during a standard exercise test to fatigue is a marked elevated in arterial P_{CO_2} (grade 4, 69 mmHg; grade 5, 75 mmHg) compared to grade 1 (normal laryngeal function, 58 mmHg) that is associated with a reduced arterial P_{O_2} (by 8 mmHg) and increased (by 5–6 mEq/L) plasma [lactate$^-$].[139,140]

Small airway inflammation and exercise-induced pulmonary hemorrhage (EIPH) also commonly occur in racehorses, leading to decrements in performance.[142] Poorly performing horses with these respiratory diseases manifested a pronounced and sustained hypocapnia with lower arterial P_{O_2}, [HCO_3^-] and pH and higher blood [lactate$^-$] during recovery from high intensity exercise. The more pronounced increase in [lactate$^-$] is consistent with impaired blood oxygenation at the lungs, resulting in a greater reliance on anaerobic mechanisms to produce energy during high-intensity exercise. The authors' conclusion that the hypocapnia was due to the lactic acidosis[142] cannot be supported. While the hypocapnia itself would blunt the arterial chemoreceptor drive to ventilate, this may be offset by the increased [H^+]. The hypocapnia can be explained in terms of alveolar hyperventilation, which would facilitate rapid release of CO_2 at the lungs while maintaining compromised ability to extract oxygen.

Administration of alkalinizing substances and other purported ergogenic aids

Alkalinizing substances

There is an extensive literature on the administration of bicarbonate salts and other alkalinizing agents in both horses and humans, and the interested reader is referred to reviews by Schott and Hinchcliff[143] and Heigenhauser and Jones.[144] There is also evidence that the administration of alkalinizing agents will result in enhanced performance with exercise at moderate to high intensities, and that this is due to increased rates of strong acid (i.e. lactate$^-$) removal from contracting muscle. This section will focus on the physicochemical aspects of inducing and correcting the acid–base disturbance resulting from the administration of bicarbonate-, citrate-, and phosphate-containing compounds.

At the outset it must be explained that the administration of HCO_3^- does not in and of itself result in an increase in plasma [HCO_3^-]. When sodium bicarbonate, or baking soda, is dissolved in water, all of the Na^+ completely dissociates from HCO_3^- by virtue of Na^+ being a strong ion; by definition strong ions are completely dissociated in solution.[23,26] The HCO_3^- in solution readily participates in physicochemical reactions with H^+, CO_2 and H_2O, as described above. In this simple solution consisting of water and added baking soda, the [HCO_3^-] will be determined by the [Na^+] and by the P_{CO_2}. Since this solution will come into equilibrium with the CO_2 in the air, the resulting P_{CO_2} will be very low once equilibrium is achieved. The addition of carbonic anhydrase to this solution would greatly increase the speed of the reaction, establishing equilibrium.

When a freshly mixed baking soda solution is administered nasogastrically into the stomach of a horse, which is an acidic environment, acid within the stomach and upper intestinal tract reacts rapidly with the HCO_3^- in solution. The HCO_3^- that was in solution rapidly dissipates, producing CO_2 and H_2O:

$$HCO_3^- + H^+ \rightarrow CO_2 + H_2O$$

The CO_2 diffuses readily into the blood, where most is transformed by the action of carbonic anhydrase to HCO_3^-, transported to the lungs, reconverted to CO_2 and eliminated in expired air. The ingested water and Na^+ are absorbed within the small intestine, resulting in increased plasma water content and [Na^+] – the excess is ultimately removed from the body through normal renal processes. Since the ingested HCO_3^- becomes part of the open CO_2 system, which is in a dynamic equilibrium with inspired air and the tissues, P_{CO_2} is rapidly normalized through ventilation. Therefore the only changes remaining within the plasma (and extracellular) compartment are increased [Na^+] and decreased concentrations of other plasma ions, both strong and weak. Notably, the concentrations of the predominant weak acid, protein, and strong acid Cl^- are decreased, resulting in decreased [A_{tot}] and [Cl^-]. Both the decrease in [Cl^-] and the increase in [Na^+] contribute to an increase in [SID]. Both the increase in [SID] and the decrease in [A_{tot}] contribute to increased [HCO_3^-] and decreased [H^+]; P_{CO_2} remains unchanged.

Because of the nature of these physicochemical reactions, it does not matter which cation salts of bicarbonate are dissolved in water and administered to the horse – all will result in a very similar extracellular alkalosis, at least initially. If calcium salts are used, these are absorbed slowly and the onset of the alkalosis will be slow. If a sufficient amount of calcium is used to induce an alkalosis, it is likely that this would be toxic. Potassium bicarbonate has also been used. Potassium, in contrast to Na^+, does not remain in the extracellular compartment but is rapidly taken up by the tissues, reducing the extent of the extracellular alkalosis presumably at the expense of alkalinizing the intracellular compartment.[12]

Time course

The administration of an alkalinizing agent results in a lowering of plasma and extracellular [H^+], with a concurrent increase in [HCO_3^-], with peak effects appearing to depend on the volume of water administered with the dose. When 1 L of water was administered with a $NaHCO_3$ dose of 0.4 g/kg body mass, peak effects occurred 2–4 h after administration.[145] In contrast, when 2–4 L of water was used to administer doses ranging from 0.25 to 1.5 g/kg, peak effects occurred only 6–8 h after administration.[146–149] Similar time courses occurred with a range of alkalinizing agents (sodium citrate, sodium acetate, sodium lactate, sodium acetate) administered at a dose of 0.5 g/kg in 2 L of water.[150]

As noted above, the administration of an alkalinizing agent with 4 L of water should result in a transient increase

in plasma volume. The time course of PV change has not been studied, although it is known that any early changes in PV that would occur are corrected 6 h after administration.[151] Therefore, after this 6-h period the sole cause for the acid–base disturbance is the increase in extracellular [Na^+] (or other administered cation).

Mechanism for enhanced lactate efflux

The rate of lactate$^-$ facilitated diffusion across the sarcolemma by the monocarboxylate transporter (MCT1), of which there are at least four isoforms in muscle,[49,120] depends on the chemical gradient and driving force for H^+ and lactate$^-$. Extracellular [lactate$^-$] is very low compared to muscle [lactate$^-$] in horses performing moderate- to high-intensity exercise,[152,153] providing a high driving force for lactate$^-$ diffusion out of contracting muscle cells. Similarly, extracellular [H^+] is low compared to intramuscular [H^+], and this is increased for a prolonged duration (up to 16 h) after administration of alkalinizing agents.[150] This combination of chemical changes results in an enhanced rate of removal of lactate$^-$ from contracting muscle during high-intensity exercise, producing a higher plasma [lactate$^-$] and lower muscle [lactate$^-$] at the end of exercise.[153] In order to be able to detect these changes, the dose administered may be important: Greenhaff et al used an $NaHCO_3$ dose of 0.6 mg/kg,[153] and when a dose of 0.4 mg/kg was used no differences in muscle and blood lactate were found.[152]

Creatine supplementation

The practice of creatine supplementation is used in humans to improve performance associated with short-term, high-intensity exercise.[154] Attempts to replicate similar effects in horses with a dose of 25 g creatine monohydrate twice daily have shown no effect on performance, metabolism, and related acid–base variables.[155]

Furosemide

Furosemide is a loop diuretic that is extensively used to treat race horses exhibiting symptoms of exercise-induced pulmonary hemorrhage (EIPH) in some racing jurisdictions.[156] There is evidence that furosemide administration improves racing performance[157] despite the pronounced diuresis with loss of water and electrolytes.[158] The mechanism by which furosemide induces a long-lasting mild alkalosis is through reductions in plasma [Cl^-] due to marked increases in renal Cl^- excretion without concomitant increases in renal strong cation excretion[158] and movement of plasma, Cl^- into red blood cells.[159] Because furosemide results in a pronounced loss of water, Na^+, and titratable acid from (primarily) the extracellular fluid compartment, this results in increased plasma [Na^+] (by 8 mEq/L) and decreased plasma [Cl^-] (by 8 mEq/L) between 5 and 10 h after intramuscular administration of 1 mg/kg.[160] In this study, it appears that plasma [SID] increased by 13 mEq/L 8 h after administration. More recently, a 7 mEq/L increase in plasma [SID] 4 h after administering 1 mg/kg furosemide has been reported.[161] This large increase in [SID] fully explains the increase in pH (7.383 to 7.445) and increase in [HCO_3^-] (3 mEq/L) in arterial plasma.[161] The effect of increased [SID] alone would have been greater, however, the concomitant increase in [PP] and hence [A_{tot}], due to the extracellular dehydration, results in an acidifying effect. Arterial and mixed venous P_{CO_2} remains unchanged in resting horses.[161] During high-intensity treadmill running exercise (4 h after 0.5 or 1 mg/kg furosemide administration), the elevations in arterial and mixed venous pH and [HCO_3^-] were maintained in furosemide-treated horses through to the last minute of maximal exercise; furosemide did not appear to result in increased lactate accumulation within blood.[161] Similar responses were reported by Hinchcliff and McKeever.[162]

In many ways, the alkalosis resulting from furosemide administration qualitatively resembles that resulting from administration of $NaHCO_3$ and related alkalinizing agents. The main feature in common that produces the increased plasma pH and [HCO_3^-] is the pronounced decrease in plasma [Cl^-]. The main differences are elevations in [PP] and [Na^+] with furosemide, while these variables remain largely unchanged with alkalinizing agents. The alkalosis resulting from even high-dose furosemide (1 mg/kg) is relatively mild compared to the moderate alkalosis resulting from high-dose $NaHCO_3$ (> 0.5 mg/kg), although the effects appear to be similar in duration.

References

1. Needham DM. Machina carnis. The biochemistry of muscular contraction in its historical development. Cambridge: Cambridge University Press, 1971.
2. Furusawa K, Kerridge PMT. The hydrogen ion concentration of the muscles of the cat. J Physiol Lond 1927; 63:33–41.
3. Jones NL, Heigenhauser GJF. Effects of hydrogen ion on metabolism during exercise. In: Lamb DR, Gisolfi CV, eds. Perspectives in exercise science and sports medicine, vol 5. Energy metabolism in exercise and sport. Dubuque, IA: Brown & Benchmark, 1992; 107–148.
4. Fitts RH. Cellular mechanisms of muscle fatigue. Physiol Rev 1994; 74:49–94.
5. Hultman E, Sahlin K. Acid–base balance during exercise. Exerc Sport Sci Rev 1980; 8:41–128.
6. Lindinger MI. Origins of [H^+] changes in exercising skeletal muscle. Can J Appl Physiol 1995; 20:357–368.
7. Lindinger MI, Heigenhauser GJF. Acid–base systems in skeletal muscle and their response to exercise. In: Taylor AW, Gollnick, PD, Green HJ, et al. eds. Biochemistry of exercise VII, International series on sports sciences, vol 21. Champaign IL: Human Kinetics; 1990; 341–374.
8. Lindinger MI, Heigenhauser GJF. The roles of ion fluxes in skeletal muscle fatigue. Can J Physiol Pharmacol 1991; 69:246–253.
9. Constable PD. A simplified strong ion model for acid–base equilibria: application to horse plasma. J Appl Physiol 1997; 83:297–311.
10. Kowalchuk JM, Scheuermann BW. Acid–base balance: origin of plasma [H^+] during exercise. Can J Appl Physiol 1995; 20:341–356.

11. Lindinger MI, Heigenhauser GJF, McKelvie RS, et al. Blood ion regulation during repeated maximal exercise and recovery in humans. Am J Physiol 1992; 262:R126–R136.
12. Lindinger MI, Franklin TW, Lands LC, et al. Role of skeletal muscle in plasma ion and acid–base regulation after $NaHCO_3$ and $KHCO_3$ loading in humans. Am J Physiol 1999; 276:R32–R43.
13. Johnson RL, Heigenhauser GJF, Hsia CC, et al. 1996. Determinants of gas exchange and acid–base balance during exercise. In: Rowell LB, Shepherd JT, eds. Handbook of physiology, section 12: Exercise. Regulation and integration of multiple systems. NewYork: Oxford University Press; 1996; 515–584.
14. Whitehair KJ, Haskins SC, Whitehair JG, et al. Clinical applications of quantitative acid–base chemistry. J Vet Int Med 1995; 9:1–11.
15. Constable PD. Clinical assessment of acid–base status. Strong ion difference theory. Vet Clin N A Food Anim Pract 1999; 15:447–471.
16. Carlson GP. Fluid, electrolyte and acid-base balance. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. San Diego: Academic Press; 1997; 485–516.
17. Corley KTT, Marr CM. Pathophysiology, assessment and treatment of acid–base disturbances in the horse. Equine Vet Educ 1998; 10:255–265.
18. Hyyppä S, Pösö AR. Fluid, electrolyte, and acid–base responses to exercise in racehorses. Vet Clinics N Am: Equine Prac 1998; 14:121–136.
19. Kingston JK, Bayly WM. Effect of exercise on acid–base status of horses. Vet Clin North Am Equine Pract 1998; 14:61–73.
20. Davenport HW. The ABC of acid–base chemistry, 6th edn. Chicago: University of Chicago Press; 1974; 124.
21. Herbst D. Evaluation of clinical disorders of acid–base balance. J Am Vet Med Assoc 1975; 166:359–364.
22. Singer RB, Hastings AB. An improved clinical method for the estimation of disturbances of the acid–base balance of human blood. Medicine 1948; 27:223–242.
23. Stewart PA. How to understand acid–base. New York: Elsevier; 1981.
24. Stewart PA. Modern, quantitative acid–base chemistry. Can J Physiol Pharmacol 1983; 61:1444–1461.
25. Peters JP, Van Slyke DD. Quantitative clinical chemistry, vol 1: interpretations. Baltimore: Williams and Wilkins; 1931.
26. Harned HS, Owen BO. The physical chemistry of electrolyte solutions, 3rd edn. New York: Van Nostrand-Reinhold; 1958
27. Heigenhauser GJ. A quantitative approach to acid–base chemistry. Can J Appl Physiol 1995; 20:333–340.
28. Jones NL, Heigenhauser GJF. Getting rid of carbon dioxide during exercise. Clin Sci 1996; 90:323–335.
29. Watson PD. Acid basics II. The Stewart model of acid–base balance. Columbia, SC: Insight Services; 1996.
30. Chin ER, Allen DG. The contribution of pH-dependent mechanisms to fatigue at different intensities in mammalian single muscle fibres. J Physiol 1998; 512:831–840.
31. Jones NL, Sutton JR, Taylor R, et al. Effect of pH on cardiorespiratory and metabolic responses to exercise. J Appl Physiol 1977; 43:959–964.
32. Spriet LL, Matsos CD Peters SJ, et al. Effects of acidosis on rat muscle metabolism and performance during heavy exercise. Am J Physiol 1985; 248:C337–C347.
33. Hollidge-Horvat MG, Parolin ML, Wong D et al. Effect of induced metabolic acidosis on human skeletal muscle metabolism during exercise. Am J Physiol 1999; 277:E647–E658.
34. Neilsen OB, dePaoli F, Overgaard K. Protective effects of lactic acid on force production in rat skeletal muscle. J Physiol 2001; 536:161–166.
35. Brooks GA. Lactate doesn't necessarily cause fatigue: why are we surprised? J Physiol 2001; 536:1.
36. Westerblad H, Allen DG, Lannergren J. Muscle fatigue: lactic acid or inorganic phosphate the major cause? News Physiol Sci 2002; 17:17–21.
37. Sejersted OM, Sjogaard G. Dynamics and consequences of potassium shifts in skeletal muscle and heart during exercise. Physiol Rev 2000; 80:1411–1481.
38. Renaud JM, Light P. Effects of K+ on the twitch and tetanic contraction in the sartorius muscle of the frog, *Rana pipiens*. Implication for fatigue in vivo. Can J Physiol Pharmacol 1992; 70:1236–1246.
39. Cairns SP, Hing WA, Slack JR, et al. Different effects of raised $[K^+]$ on membrane potential and contraction in mouse fast- and slow-twitch muscle. Am J Physiol 1997; 273:C598–C611.
40. Fedde MR, Pieschl RL. Extreme derangements of acid–base balance in exercise: advantages and limitations of the Stewart analysis. Can J Appl Physiol 1995; 20:369–379.
41. Kowalchuk JM, Heigenhauser GJF, Lindinger MI, et al. Factors influencing hydrogen ion concentration in muscle after intense exercise. J Appl Physiol 1988; 65:2080–2089.
42. Kowalchuk JM, Heigenhauser GJF, Lindinger MI, et al. Role of lungs and inactive tissue in acid–base control after maximal exercise. J Appl Physiol 1988; 65:2090–2096.
43. Stämpfli HR, Misiaszek S, Lumsden JH, et al. Weak acid-concentration A_{tot} and dissociation constant K_a of plasma proteins in racehorses. Equine Vet J 1999; Suppl 30: 438–442.
44. McCutcheon LJ, Kelso TB, Bertocci LA et al. Buffering and aerobic capacity in equine muscle: variation and effect of training. Equine Exerc Physiol 1987; 2:348=n358.
45. Gunn, HM. Muscle, bone and fat proportions and muscle distribution of thoroughbreds and other horses. In: Equine Exerc Physiol 1987; 2:253–264.
46. Lindinger MI, Heigenhauser GJ, McKelvie RS, et al. Role of nonworking muscle on blood metabolites and ions with intense intermittent exercise. Am J Physiol 1990; 258:R1486–1494.
47. Hultman E, Sjüholm H. Energy metabolism and contraction force of human skeletal muscle in situ during electrical stimulation. J Physiol 1983; 345:525–532.
48. Pette D, Staron S. Cellular and molecular diversities of mammalian skeletal muscle fibres. Rev Physiol Biochem Pharmacol 1990; 116:1–76.
49. Brooks GA. Lactate shuttles in nature. Biochem Soc Trans 2002; 30:258–264.
50. Sewell DA, Harris RC, Marlin DJ. Skeletal muscle characteristics in 2-year-old race-trained thoroughbred horses. Comp Biochem Physiol 1994; 108A:87–96.
51. Valberg S, Essén Gustavsson B. Metabolic response to racing determined in pools of type I, IIA and IIB fibres. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987; 290–310.
52. Rivero JLL, Serrano AL, Henckel P. Activities of selected aerobic and anaerobic enzymes in the gluteus medius muscle of endurance horses with different performance records. Vet Rec 1995; 137:187–192.
53. Ronéus N, Essén-Gustavsson B, Lindholm A, et al. Plasma lactate response to submaximal and maximal exercise test with training, and its relationship to performance and muscle characteristics in standardbred trotters. Equine Vet J 1994; 26:117–121.

54. Valberg S, EssÈn Gustavsson B, Lindholm A, et al. Energy metabolism in relation to skeletal muscle fibre properties during treadmill exercise. Equine Vet J 1985; 17:439–444.
55. Essen B, Haggmark T. Lactate concentration in type I and II muscle fibres during muscular contraction in man. Acta Physiol Scand 1975; 95:344–346.
56. Sewell DA, Harris RC, Dunnett M. Carnosine accounts for most of the variation in physicochemical buffering in equine muscle. Equine Exerc Physiol 1991; 3:276–280.
57. Sewell DA, Harris RC, Marlin DJ, et al. Estimation of the carnosine content of different fibre types in the middle gluteal muscle of the thoroughbred horse. J Physiol 1992; 455:447–453.
58. Bump KD, Lawrence LM, Moser LR, et al. Effect of breed type on muscle carnosine. Proc 11th Eq Nutr Physiol Symp 1989; 252–256.
59. Fabiato A, Fabiato F. The effects of pH on the myofilaments and the sarcoplasmic reticulum of skinned cells from cardiac and skeletal muscles. J Physiol 1978; 276:233–255.
60. Spriet LL, Lindinger MI, McKelvie RS, et al. Muscle glycogenolysis and H^+ concentration during maximal intermittent cycling. J Appl Physiol 1989; 66:8–13.
61. Gollnick PD, Bertocci LA, Kelso TB, et al. The effect of high-intensity exercise on the respiratory capacity of skeletal muscle. Pflügers Arch 1990; 415:407–413.
62. Hochachka PW, Mommsen TP. Protons and anaerobiosis. Science. 1983; 219(4591):1391–1397.
63. Pörtner H-O. Contributions of anaerobic metabolism to pH regulation in animal tissues: theory. J Exp Biol 1987; 131:69–87.
64. Roos A, Boron WF. Intracellular PH. Physiol Rev 1981; 61:296–434.
65. Wilson JA, Kronfeld DS, Gay LS, et al. Sarcoplasmic reticulum responses to repeated sprints are affected by conditioning of horses. J Anim Sci 1998; 76:3065–3071.
66. Gottlieb-Vedi M, Dahlborn K, Jansson A, et al. Elemental composition of muscle at rest and potassium levels in muscle, plasma and sweat of horses exercising at 20 degrees C and 35 degrees C. Equine Vet J 1996; 22:35–41.
67. Lindholm A, Saltin B. The physiological and biochemical response of standardbred horses to exercise of varying speed and duration. Acta Vet Scand 1974; 15:310–324.
68. Chen J, Gollnick PD. Effect of exercise on hexokinase distribution and mitochondrial respiration in skeletal muscle. Pflügers Arch 1994; 427:257–263.
69. Essen-Gustavsson B, Karlstrom K, Lindholm A. Fibre types, enzyme activities and substrate utilisation in skeletal muscles of horses competing in endurance rides. Equine Vet J 1984; 16:197–202.
70. Snow DH, Kerr, MG, Nimmo MA, et al. Alterations in blood, sweat, urine and muscle composition during prolonged exercise in the horse. Vet Record 1982; 110:377–384.
71. Lindinger MI, Sjögaard G. Potassium regulation during exercise and recovery. Sports Med 1991; 11:382–401.
72. Harris RC, Harman JC, Marlin DJ, et al. Acute changes in the water content and density of blood and plasma in the thoroughbred horse during maximal exercise: relevance to the calculation of metabolite concentration in these tissues and in muscle. Equine Exerc Physiol 1987; 2:464–475.
73. Lindinger MI, Spriet LL, Hultman E, et al. Plasma volume and ion regulation during exercise after low- and high-carbohydrate diets. Am J Physiol 1994; 266:R1896–R1906.
74. Lindholm A, Piehl K. Fibre composition, enzyme activity and concentration of metabolites and electrolytes in muscles of standardbred horses. Acta Vet Scand 1974; 15:287–309.
75. Lindinger MI, McKelvie RS, Heigenhauser GJF. K^+ and Lac^- distribution in humans during and after high intensity exercise: role in muscle fatigue attenuation? J Appl Physiol 1995; 78:765–777.
76. Roneus N, Essen-Gustavsson B. Skeletal muscle characteristics and metabolic response to exercise in young standardbreds. Am J Vet Res. 1997; 58:167–170.
77. Harris P, Snow DH. Plasma potassium and lactate concentration in thoroughbred horses during exercise of varying intensity. Equine Vet J 1992; 23:220–225.
78. Harris RC, Dunnett M, Snow DH. Muscle carnosine content is unchanged during maximal intermittent exercise. Equine Exerc Physiol 1991; 3:257–261.
79. Hogg RJ, Pucacco LR, Carter NW et al. In situ PCO_2 in the renal cortex, liver, muscle, and brain of the New Zealand white rabbit. Am J Physiol 1984; 47:F491–F498.
80. Gottlieb M, Essen-Gustavsson B, Skoglund-Wallberg H. Blood and muscle metabolic responses to draught work of varying intensity and duration in horses. Res Vet Sci 1989; 47:102–109.
81. Fenger CK, McKeever KH, Hinchcliff KW, et al. Determinants of oxygen delivery and hemoglobin saturation during incremental exercise in horses. Am J Vet Res 2000; 61:1325–1332.
82. Taylor LE, Kronfeld DS, Ferrante PL, et al. Blood-gas measurements adjusted for temperature at three sites during incremental exercise in the horse. J Appl Physiol 1998; 85:1030–1036.
83. Harris P, Snow DH. The effects of high intensity exercise on the plasma concentration of lactate, potassium and other electrolytes. Equine Vet J 1988; 20:109–113.
84. Pethick DW, Rose RJ, Bryden WL, et al. Nutrient utilisation by the hindlimb of thoroughbred horses at rest. Equine Vet J 1993; 25:41–44.
85. Lindinger MI, Geor RL, Ecker GL, et al. Plasma volume and ions during exercise in cool, dry; hot, dry; and hot, humid conditions. Equine Vet J 1995; Suppl 20:133–139.
86. Lindinger MI, McCutcheon LJ, Ecker GL, et al. Heat acclimation improves regulation of plasma volume and plasma Na^+ content during exercise in horses. J Appl Physiol 2000; 88:1006–1013.
87. Vaihkonen LK, Hyyppa S, Reeta Poso A. Factors affecting accumulation of lactate in red blood cells. Equine Vet J 1999; Suppl 30:443–447.
88. Fedde MR. Blood gas analyses on equine blood: required correction factors. Equine Vet J 1991; 23:410–412.
89. Evans DL, Rose RJ. Cardiovascular and respiratory responses to submaximal exercise training in the thoroughbred horse. Pflügers Arch 1988; 411:316–321.
90. Bayly WM, Hodgson DR, Schulz DA, et al. Exercise-induced hypercapnia in the horse. J Appl Physiol 1989; 67:1958–1966.
91. Christley RM, Evans DL, Hodgson DR, et al. Blood gas changes during incremental and sprint exercise. Equine Vet J 1999; Suppl 30:24–26.
92. Roberts CA, Marlin DJ, Lekeux P. The effects of training on ventilation and blood gases in exercising thoroughbreds. Equine Vet J 1999; Suppl 30: 57–61.
93. Kronfeld DS, Ferrante PL, Taylor LE, et al. Partition of plasma hydrogen ion concentration changes during repeated sprints. Equine Vet J 1999; Suppl 30:380–383.
94. Geor RJ, McCutcheon LJ, Hinchcliff KW. Effects of warm-up intensity on kinetics of oxygen consumption and carbon dioxide production during high-intensity exercise in horses. Am J Vet Res. 2000; 61:638–645.

95. Tyler CM, Hodgson DR, Rose RJ. Effect of a warm-up on energy supply during high intensity exercise in horses. Equine Vet J 1996; 28:117–120.
96. Hopkins SR, Bayly WM, Slocombe RF, et al. Effect of prolonged heavy exercise on pulmonary gas exchange in horses. J Appl Physiol 1998; 84:1723–1730.
97. Perez R, Recabarren SE, Valdes P, Hetz E. Biochemical and physiological parameters and estimated work output in draught horses pulling loads for long periods. Vet Res Commun 1992; 16:231–246.
98. Carlson GP. Fluid and electrolyte alteration in endurance trained horses. Proc 1st Int Symp Equine Hematology 1975; 473–480.
99. Gillespie JR, Kauffman A, Steere J, et al. Arterial blood gases and pH during long distance running in the horse. Proc 1st Int Symp Equine Hematology 1975; 450–468.
100. Rose RJ, Ilkiw JE, Martin ICA. Blood-gas, acid–base and haematological values in horses during an endurance ride. Equine Vet J 1979; 11:56–59.
101. McCutcheon LJ, Geor RJ, Hare MJ, et al. Sweating rate and sweat composition during exercise and recovery in ambient heat and humidity. Equine Vet J 1995; Suppl 20: 153–157
102. Ecker G, Lindinger MI. Effects of terrain, speed, temperature and distance on water and ion losses in endurance horses. Equine Vet J 1995; Suppl 18:298–305.
103. Rose, RJ, Arnold KS, Church S, et al. Plasma and sweat electrolyte concentrations in the horse during long distance exercise. Equine Vet J 1980; 12:19–22.
104. Sjogaard G. Water and electrolyte fluxes during exercise and their relation to muscle fatigue. Acta Physiol Scand (Suppl) 1986; 556:129–136.
105. Aguilera-Tejero E, Estepa JC, López I, et al. Quantitative analysis of acid–base balance in show jumpers before and after exercise. Res Vet Sci 2000; 68:103–108.
106. Rose RJ, Ilkiw JE, Arnold KS, et al. Plasma biochemistry in the horse during 3-day event competition. Equine Vet J 1980; 12:132–136.
107. Rose RJ, Ilkiw JE, Sampson D, et al. Changes in blood gas, acid–base and metabolic parameters in horses during three-day event competition. Res Vet Sci 1980; 28:393–396.
108. Craig L, Hintz HF, Soderholm LV, et al. Changes in blood constituents accompanying exercise in polo horses. Cornell Vet 1985; 75:297–302.
109. Geor RJ, McCutcheon LJ, Shen H. Muscular and metabolic responses to moderate-intensity short-term training. Equine Vet J 1999; Suppl 30:311–317.
110. Serrano AL, Quiroz-Rothe E, Rivero JLL. Early and long-term changes of equine skeletal muscle in response to endurance training and detraining. Pflügers Arch 2000; 441:263–274.
111. Putman CT, Jones NL, Hultman E, et al. Effects of short-term submaximal training in humans on muscle metabolism in exercise. Am J Physiol 1998; 275:E132–E139.
112. Romijn JA, Coyle EF, Sidossis LS, et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. Am J Physiol 1993; 265:E380–E391.
113. Art T, Lekeux P. Training-induced modifications in cardiorespiratory and ventilatory measurements in Thoroughbred horses. Equine Vet J 1993; 25:532–536.
114. Rose RJ, Allen JR, Hodgson DR, et al. Responses of submaximal treadmill exercise and training in the horse: changes in haematology, arterial blood gas and acid base measurements, plasma biochemical values and heart rate. Vet Rec 1983; Dec 24/31:612–618.
115. Sahlin K, Henriksson J. Buffer capacity and lactate accumulation in skeletal muscle of trained and untrained men. Acta Physiol Scand 1984; 122:331–339.
116. Marlin DJ, Harris RC, Gash SP, et al. Carnosine content of the middle gluteal muscle in thoroughbred horses with relation to age, sex and training. Comp Biochem Physiol 1989; 93:629–632.
117. Hinchcliff KW, Lauderdale MA, Dutson J, et al. High intensity exercise conditioning increases accumulated oxygen deficit of horses. Equine Vet J 2002; 34:9–16.
118. Harris RC, Marlin DJ, Dunnett M, et al. Muscle buffering capacity and dipeptide content in the thoroughbred horse, greyhound dog and man. Comp Biochem Physiol A 1990; 97:249–251.
119. Roberts AD, Billeter R, Howald H. Anaerobic muscle enzyme changes after interval training. Int J Sports Med 1982; 3:18–21.
120. Bonen A. The expression of lactate transporters (MCT1 and MCT4) in heart and muscle. Eur J Appl Physiol 2001; 86:6–11.
121. Foreman JH, Waldsmith JK, Lalum RB. Environmental stress and 3-day eventing: effects of altitude. Equine Vet J 1999; Suppl 30:394–397.
122. Greene HM, Wickeler SJ, Anderson TP, et al. High-altitude effects on respiratory gases, acid–base balance and pulmonary artery pressures in equids. Equine Vet J 1999; Suppl 30:71–76.
123. Baker LA, Topliff DR, Freeman DW, et al. Effect of dietary cation–anion balance on acid–base status in horses. J Equine Vet Sci 1992; 12:160–163.
124. Baker LA, Wall DL, Topliff DW, et al. Effect of dietary cation–anion balance on mineral balance in anaerobically exercised and sedentary horses. J Equine Vet Sci 1993; 13:557–561.
125. Topliff DR, Kennerly MA, Freeman DW, et al. Changes in urinary and serum calcium and chloride concentrations in exercising horses fed varying cation-anion balances. Proc 11th Equine Nutr Physiol Symp 1989; 1–4.
126. Baker LA, Topliff DR, Freeman RG, et al. the comparison of two forms of sodium and potassium, and chloride versus sulfur in the dietary cation–anion difference equation: Effects on acid–base status and mineral balance in sedentary horses. J Equine Vet Sci 1998; 18:389–396.
127. Graham-Thiers PM, Kronfeld DS, Kline KA. Dietary protein influences acid–base responses to repeated sprints. Equine Vet J 1999; Suppl 30:463–467.
128. Cooper SR, Kline KH, Foreman JH, et al. Effects of dietary cation–anion balance on pH, electrolytes, and lactate in standardbred horses. J Equine Vet Sci 1998; 18:662–666.
129. Popplewell JC, Topliff DR, Freeman DW, et al. The effect of dietary cation-anion balance on acid–base balance and blood parameters in anaerobically exercised horses. Proc 13th Equine Nutr Physiol Symp 1993; 191–195.
130. Graham-Thiers PM, Kronfeld DS, Kline KA, et al. Dietary protein restriction and fat supplementation diminish the acidogenic effect of exercise during repeated sprints in horses. J Nutr 2001; 131:1959–1964.
131. Mueller RK, Topliff DR, Freeman DW, et al. Effect of varying DCAD on the acid–base status of mature sedentary horses with varying starch source and level of intake. 1999 Animal Science Research Report, Department of Animal Science, Oklahoma State University; 1999; 189–193.
132. Southwood, LL, Evans DL, Hodgson DR, et al. The effect of roughage source on exercise performance and metabolism in thoroughbred horses. Cornell Vet 1993; 83:243–255.
133. Custalow SE, Ferrante PL, Taylor LE, et al. Lactate and glucose responses to exercise in the horse are affected by

training and dietary fat. 13th Equine Nutr Physiol Symp 1993; 179–184.
134. Taylor LE, Ferrante PL, Meacham TN, et al. Acid–base responses to exercise in horses trained on a diet containing added fat. 13th Equine Nutr Physiol Symp 1993; 185–190.
135. Duren SE, Pagan JD, Harris PA, et al. Time of feeding and fat supplementation affect plasma concentrations of insulin and metabolites during exercise. Equine Vet J 1999; Suppl 30: 479–484.
136. Oldham SL, Potter GD, Evans JW, et al. Storage and mobilization of muscle glycogen in exercising horses fed a fat-supplemented diet. Equine Nutr Physiol Symp 1990; 10:353–359.
137. Aguilera-Tejero E, Estepa JC, López I, et al. Arterial blood gases and acid–base balance in healthy young and aged horses. Equine Vet J 1998; 30:352–354.
138. Grandy JL, Steffey EP, Miller E. Arterial blood PO_2 and PCO_2 in horses during early halothane–oxygen anaesthesia. Equine Vet J 1987; 19:314–318.
139. King CM, Evans DL, Rose RJ. Cardiorespiratory and metabolic responses to exercise in horses with various abnormalities of the upper respiratory tract. Equine Vet J 1994; 26:220–225.
140. Christley RM, Hodgson DR, Evans DL, et al. Cardiorespiratory responses to exercise in horses with different grades of idiopathic laryngeal hemiplegia. Equine Vet J 1997; 29:6–10.
141. Haynes PF. Examination of the upper and lower respiratory tract relevant to purchase. Vet Clin North Am Equine Pract 1992; 8:347–364.
142. Couëtil LL, Denicola DB. Blood gas, plasma lactate and bronchoalveolar lavage cytology analyses in racehorses with respiratory disease. Equine Vet J 1999; Suppl 30:77–82.
143. Schott HC, Hinchcliff KW. Fluids, electrolytes, and bicarbonate. Vet Clin North Am Equine Pract 1993; 9:577–604.
144. Heigenhauser GJ, Jones NL. Bicarbonate loading. In: Lamb DR, Williams MH, eds. Perspectives in exercise science and sports medicine, vol 4. Ergogenics–enhancement of performance exercise and sport. Dubuque, IA: Brown & Benchmark; 1991; 183–221.
145. Harkins JD, Kamerling SG. Effects of induced alkalosis in performance in thoroughbred during a 1,600-m race. Equine Vet J 1992; 24:94–98.
146. Greenhaff PL, Snow DH, Harris RC, et al. Bicarbonate loading in the thoroughbred: dose, method of administration and acid–base changes. Equine Vet J 1990; Suppl 9:83–85.
147. Kline KH, Foreman JH, Hanson MS, et al. Changes in blood gases and electrolytes of horses given varying doses of sodium bicarbonate. J Equine Vet Sci 1995; 15:487–491.
148. Lloyd DR, Rose RJ. Effects of sodium bicarbonate on fluid, electrolyte and acid–base balance in racehorses. Br Vet J 1995; 151:523–545.
149. Rivas LJ, Hinchcliff KW, Kohn CW et al. Effect of sodium bicarbonate administration on blood constituents of horses. Am J Vet Res 1997; 58:658–663.
150. Lloyd, DR, Rose RJ. Effects of several alkalinising agents on acid base balance in horses. Proc 11th Int Conf Racing Analysts Vet 1996; 104–110.
151. Hanson CM, Line KH, Foreman JH, et al. The effects of sodium bicarbonate administered nasogastrically on plasma volume, electrolytes and blood gases in resting quarter horses. J Equine Vet Sci 1993; 10:593–595.
152. Kelso TB, Hodgson DR, Witt EH, et al. Bicarbonate administration and muscle metabolism during high-intensity exercise. Equine Exerc Physiol 1987; 2:438–447.
153. Greenhaff PL, Harris RC, Snow DH, et al. The influence of metabolic alkalosis upon exercise metabolism in the thoroughbred horse. Eur J Appl Physiol 1991; 63:129–134.
154. Casey A, Greenhaff PL. Does dietary creatine supplementation play a role in skeletal muscle metabolism and performance? Am J Clin Nutr 2000; 72:607S–617S.
155. Schuback K, Essén-Gustavsson, Persson SG. Effect of creatine supplementation on muscle metabolic response to a maximal treadmill exercise test in standardbred horses. Equine Vet J 2000; 32:533–540.
156. Hinchcliff KW, Muir WW. Pharmacology of furosemide in the horse: a review. J Vet Intern Med 1991; 5:211–218.
157. Soma LR, Birks EK, Uboh CE, et al. The effects of frusemide on racing times of standardbred pacers. Equine Vet J 2000; 32:334–340.
158. Freestone JF, Carlson GP, Harrold DR, et al. Influence of furosemide treatment on fluid and electrolyte balance in horses. Am J Vet Res 1988; 49:1899–1902.
159. Weiss DJ, Geor RJ, Burger K. Effects of furosemide on hemorheologic alterations induced by incremental treadmill exercise in thoroughbreds. Am J Vet Res 1996; 57:891–895.
160. Freestone JF, Carlson GP, Harrold DR, et al. Furosemide and sodium bicarbonate-induced alkalosis in the horse and response to oral KCL or NaCl therapy. Am J Vet Res 1989; 50:1334–1339.
161. Carlson GP, Jones JH. Effects of frusemide on electrolyte and acid–base balance during exercise. Equine Vet J 1999; Suppl 30:370–373.
162. Hinchcliff KW, McKeever KH. Frusemide and weight carriage alter the acid–base responses of horses to incremental and to brief intense exertion. Equine Vet J 1999; Suppl 30:375–379.
163. Chasiotis D. The regulation of glycogen phosphorylase and glycogen breakdown in human skeletal muscle. Acta Physiol Scand (Suppl 518) 1983; 1–68.
164. Gevers EW, Dowdle E. The effect of pH on glycolysis in vitro. Clin Sci 1963; 25:343–349.
165. Trivedi B, Danforth WH. Effect of pH on the kinetics of frog muscle phosphofructokinase. J Biol Chem 1966; 241:4110–4112.
166. Nakamaru Y, Schwartz A. The influence of hydrogen ion concentration on calcium binding and release by skeletal muscle sarcoplasmic reticulum. J Gen Physiol 1972; 59:22–32.
167. Fitts RH, Courtright JB, Kim DH, et al. Muscle fatigue with prolonged exercise: contractile and biochemical alterations. Am J Physiol 1982; 242:C65–C73.
168. Cooke R, Pate E. The effects of ADP and phosphate on the contraction of muscle fibers. Biophys J 1985; 48:789–798.
169. Wilkie DR. Muscular fatigue: effects of hydrogen ions and inorganic phosphate. Fed Proc 1986; 45:2921–2923.
170. Williams GJ, Collins S, Muir JR, et al. Observations on the interaction of calcium and hydrogen ions on ATP hydrolysis by the contractile elements of cardiac muscle. In: Fleckenstein A, Dhalla NS, eds. Recent advances in studies on cardiac structure and metabolism, vol. 5. Basic functions of cations in myocardial activity. Baltimore: University Park Press, 1975; 273–280.
171. Donaldson SKB. Effect of acidosis on maximum force generation of peeled mammalian skeletal muscle fibers. In: Knuttgen HG, Vegel JA, Poortmans J, eds. Biochemistry of exercise, vol 13. Champaign, IL: Human Kinetics; 1983; 126–133.

172. Mainwood GW, Worsley-Brown P. The effects of extracellular pH and buffer concentration on the efflux of lactate from frog sartorius muscle. J Physiol 1975; 250:1–22.
173. Siggaard-Andersen O. The acid-base status of the blood. Scan J Clin Lab Invest 1963; 15(Suppl):70:1–63.
174. Constable PD, Hinchcliff KW, Muir WW 3rd. Comparison of anion gap and strong ion gap as predictors of unmeasured strong ion concentration in plasma and serum from horses. Am J Vet Res 1998; 59:881–887.
175. Sahlin K, Alvestrand A, Brandt R, Hultman E. Intracellular pH and bicarbonate concentration in human muscle during recovery from exercise. J Appl Physiol 1978; 45:474–480.
176. Quiroz-Rothe E, Rivero JLL. Co-ordinated expression of contractile and non-contractile features of control equine muscle fibre types characterised by immunostaining of myosin heavy chains. Histochem Cell Biol 2001; 116:299–312.

CHAPTER 40

Abnormalities of body fluids and electrolytes in athletic horses

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The cardiovascular system delivers oxygen and nutrients to all tissues. During exercise the cardiovascular system is also involved in transferring the heat load generated in working skeletal muscles to the skin. Heat is lost by convection (transfer between media of different temperatures), conduction (direct transfer between surfaces in contact), radiation (energy absorbed or emitted at the body surface), and evaporation (conversion of a liquid to vapor and consequent cooling effect at the surface at which the change of state occurs). In equine athletes, the most important route of heat transfer during exercise is the evaporation of sweat,[1] accounting for approximately two-thirds of heat dissipation. Therefore, sweating is an essential mechanism to avoid hyperthermia during exercise. Equine sweat is an isotonic to slightly hypertonic fluid with electrolyte concentrations equal or higher than that of plasma. Consequently, horses performing athletic events of several hours duration, in which thermal balance is maintained by evaporation of sweat, will lose considerable amounts of water and electrolytes. When fluid and electrolyte deficits are not partially or totally replaced during and/or after exercise horses may develop clinical signs of dehydration and exhaustion. Clinical disorders associated with fluid, electrolyte and acid-base imbalances are most commonly observed in horses competing in different modalities of endurance rides and three-day events.

Fluid and electrolyte balance is not only important from a medical perspective but also because it relates to exercise performance. The reduction in plasma volume associated with dehydration can impair the ability to maintain adequate perfusion to the working skeletal muscle, potentially leading to fatigue, and to the skin, which may lead to excessive hyperthermia and fatigue. The relationship between hydration status and/or fluid and electrolyte supplementation and exercise performance has not been formally investigated in horses. It has been established that horses dehydrated prior to exercise will have compromised thermoregulatory function, and fluid and/or electrolyte supplementation during and immediately after exercise will hasten recovery. However, the effects of dehydration prior to exercise or fluid/electrolyte supplementation upon direct measurements of athletic performance in endurance exercise have not been formally addressed. In human athletes it is well established that exercise performance, assessed as an increase in time to exhaustion at a given exercise intensity or as a decrease in time to complete a given distance, is enhanced by ingestion of electrolyte containing solutions during exercise.[2]

Understanding of some concepts related to fluid composition is necessary for discussion of fluid and electrolyte disturbances. Concentrations of electrolytes in plasma or fluids are commonly reported in a variety of forms: weight per volume (mg/dL, g/L or %), or number of mols, osmols or equivalents per volume (mmol/L, mOsm/kg or mEq/L). One mol of any substance is the molecular weight of the substance in grams (Na^+ 23 g/mol, K^+ 39.1 g/mol, Cl^- 35.5 g/mol, Ca^{2+} 40.1 g/mol, Mg^{2+} 24.3 g/mol). Electrolytes in body fluids combine based on their charge, the number of positively charged particles (cations) and negatively charged particles (anions) is always equal, and it is often useful to express electrolyte concentrations as mEq/L. One equivalent is defined as the number of mols times its valence or number of ionic charges (valence is 1 for Na^+, K^+ and Cl^-, and 2 for Ca^{2+} and Mg^{2+}). Osmolality refers to the number of dissociated particles per kg of solvent (e.g. water) and osmolarity refers to the number of dissociated particles per liter of solvent. Those particles in solution that cannot freely diffuse across cellular membranes will exert an osmotic effect, and are referred to as effective osmols. The effective osmolality of a solution is referred to as tonicity. Isotonic fluids are those with a concentration of osmotically active particles similar to that of plasma (osmolality of equine plasma is 270–300 mOsm/kg). Hypotonic and hypertonic fluids are those with an osmolality much lower or much higher than 300 mOsm/kg, respectively.

Exercise-associated dehydration/exhaustion

- Most commonly seen in horses competing in endurance events (e.g. endurance races, competitive trail rides and three-day eventing).
- Exhaustion is due to the compound effects of heat accumulation, alterations in electrolyte, fluid and acid–base, and substrate depletion.
- Therapeutic strategy: stop exercise, cool the horse, and provide access to water and hay in mild cases. In more severe cases administration of oral electrolyte solutions via nasogastric tube and/or intravenous fluids is a must.
- Prevention: acclimatization to environment in the case of extreme heat, humidity, or altitude. Administer electrolytes and offer water to horses during endurance exercise. Avoid competitive endurance exercise with unfit or otherwise unsuitable horses (e.g. overweight Quarter Horses). Provide supplementary electrolytes in the diet to compensate for electrolyte losses in sweating.

Recognition of the disease

History and presenting complaint

Exercise-induced dehydration/exhaustion is most commonly recognized as a condition that requires medical intervention in horses exercising for protracted periods in hot environments. It is most commonly observed in horses competing in endurance rides and less frequently in horses undertaking three-day events or combined training competitions. The presenting complaint is severe depression, and lack of thirst and appetite despite apparent dehydration.

Physical examination

Clinical signs observed in horses suffering exercise-induced dehydration/exhaustion include depression, anorexia, lack of thirst despite persistent dehydration, persistently elevated rectal temperature, heart rate and respiratory rate.[3,4] Other clinical signs related to dehydration and poor cardiovascular function include dryness of mucous membranes (gums, conjunctiva), delayed capillary refill time, decreased pulse pressure, and persistent skin-fold test. Dry feces, minimal urine production, poor gastrointestinal motility, poor anal tone, ileus, and colic may also be observed. Other less common signs associated with dehydration and exhaustion include cardiac arrhythmia, muscle cramps, and/or synchronous diaphragmatic flutter.

The severity of dehydration can be subjectively assessed based on the clinical signs observed (Table 40.1). Dehydration below 5% is not detectable clinically, whereas acute dehydration above 10–12% is considered incompatible with life.

In endurance competitions, horses are evaluated at regular intervals in an attempt to assure that only those capable of safely continuing to exercise remain in the competition. At each mandatory rest period ('vet gates'), fitness to continue is assessed based on examination of general appearance, attitude, gait, pulse and respiratory rates, and evaluation of dehydration, capillary refill time, color of mucous membranes, and gastrointestinal motility. The cardiac recovery index is performed routinely in some countries during the veterinary examination at a mandatory stop. The cardiac recovery index involves taking a resting heart rate, the horse is then trotted 30 m (33 yards) out and back and the heart rate is taken again 1 min later. Generally, if the resting heart rate is low (50 bpm or less) and the heart rate taken after trotting is equal or lower than the resting heart rate the horse is considered fit to continue.[5,6] Close examination of horses at the mandatory stop and use of the cardiac recovery index may help to identify those horses with early stages of significant dehydration/exhaustion.

Table 40.1 Clinical signs observed depending on severity of dehydration

	% of body weight	Volume deficit (L) in 450 kg horse	Clinical signs
Mild	5–6	≈ 20–30	Tacky mucous membranes, decreased skin turgor
Moderate	7–9	≈ 30–40	Dry mucous membranes, depression, sunken eyes
Severe	> 9	> 40	Cold extremities, recumbency, moribund

Laboratory examination

Routine hematology reveals alterations related to dehydration and stress, which include increased plasma total protein, packed cell volume, red blood cell count, and hemoglobin; and the total white blood cell count and differential generally show neutrophilia and lymphopenia.[7–9]

Plasma electrolyte concentrations in dehydrated/exhausted horses are variable. Moderate hypochloremia is most commonly observed after endurance exercise in exhausted and non-affected horses. However, the degree of dehydration and hypochloremia, with consequent metabolic alkalosis, is generally more pronounced in affected horses. Although the characteristic acid–base abnormality is hypochloremic metabolic alkalosis, it is also reported that the fastest horses in an endurance race may develop mild metabolic acidosis due to lactate production,[8,10] which probably results in a mixed acid–base disorder with concurrent lactic acidosis and hypochloremic metabolic alkalosis. Other abnormalities can include hypokalemia, hypocalcemia, hypomagnesemia and hypo- or hypernatremia. Substantial decreases in total body electrolyte content due to sweating will be poorly reflected by changes in plasma electrolyte concentrations, because fluid and electrolyte losses are isotonic and of similar composition to plasma. Plasma electrolyte concentrations observed in horses performing endurance rides and three-day events are shown in Tables 40.2 and 40.3.

Table 40.2 Plasma electrolytes concentrations (from jugular venous blood unless specified otherwise) observed in horses competing in endurance rides (average ± SD, except Lindinger[14] average ± SE)

	Before ride	32–50 km	80–100 km	160 km	Reference
Na^+ mEq/L	138.6 ± 0.5	136.4 ± 1.0	133.7 ± 1.8	–	Rose 1980[84]
	139.6 ± 2.5	–	138.5 ± 2.6	136.6 ± 4	Carlson 1974[85]
	139.1 ± 2.5	–	134.9 ± 3.0	–	Carlson 1976[7]
	139.7 ± 0.4	137.7 ± 1.2	141.8 ± 2.6	138.6 ± 0.5	Lindinger 1995[14]
K^+ mEq/L	3.8 ± 0.1	3.4 ± 0.1	3.2 ± 0.2	–	Rose 1980[84]
	3.6 ± 1.8	–	3.5 ± 0.6	3.2 ± 0.5	Carlson 1974[85]
	3.6 ± 0.4	–	2.7 ± 0.3	–	Carlson 1976[7]
	3.6 ± 0.04	2.8 ± 0.11	2.7 ± 0.08	3.2 ± 0.27	Lindinger 1995[14]
Cl^- mEq/L	99.8 ± 0.8	90.1 ± 1.1	84.5 ± 1.2	–	Rose 1980[84]
	101.1 ± 2.4	–	93.3 ± 4.3	93.9 ± 6.8	Carlson 1974[85]
	101.1 ± 2.4	–	90.8 ± 4.8	–	Carlson 1976[7]
	104.8 ± 0.6	100.9 ± 1.1	105.2 ± 1.6	101.6 ± 3.0	Lindinger 1995[14]
iCa^{2+} mmol/L	1.8 ± 0.01	1.6 ± 0.05	1.6 ± 0.03	1.6 ± 0.03	Lindinger 1995[14]
	1.8	1.7 ± 0.04			Schott II 2001[86]
tCa^{2+} mmol/L	3.1 ± 0.2	–	2.6 ± 0.2	2.7 ± 0.2	Carlson 1974[85]
	3.1 ± 0.2	–	2.9 ± 0.4	–	Carlson 1976[7]
tMg^{2+} mmol/L	0.78 ± 0.04	–	0.70 ± 0.08	0.74 ± 0.12	Carlson 1974[85]
	0.80 ± 0.08	–	0.86 ± 0.20	–	Carlson 1976[7]
HCO_3^- mEq/L	25.4 ± 1.7	26.5 ± 3	25.8 ± 4.2	–	Rose 1979[8]
	24.4 ± 0.4	26.4 ± 1	25.3 ± 1.4	–	Rose 1980[84]
	29.5 ± 2.4	–	32.7 ± 2.3	–	Carlson 1976[7]
Total protein g/L	65 ± 7	76 ± 7	89 ± 11	–	Rose 1979[8]
	67 ± 3	–	72 ± 6	67 ± 4	Carlson 1974[85]
	70 ± 4	–	–	79 ± 7	Carlson 1976[7]
	65.5 ± 1.6	73.2 ± 1.3	72.4 ± 1.8	69.4 ± 2.8	Lindinger 1995[14]

iCa^{2+}, ionized calcium; tCa^{2+}, total calcium; tMg^{2+}, total magnesium.

Plasma glucose concentrations in dehydrated/exhausted horses are quite variable. Hyperglycemia can occur in exhausted horses and those with heat-stroke due to high concentrations of stress hormones, such as the catecholamines and cortisol. Hypoglycemia can also occur during protracted exercise because of depletion of liver glycogen, which will lead to fatigue and altered mentation due to lack of glucose availability to neurons.

Dehydration and possibly renal disease may be apparent by elevation in blood urea nitrogen and creatinine concentrations in horses performing protracted exercise. If urine can be obtained, it may be highly concentrated due to severe dehydration, or may be poorly concentrated despite severe dehydration in cases of ischemic renal tubular damage. The use of urinary specific gravity, urinary to plasma creatinine ratios and fractional excretion ratios of electrolytes in the diagnosis and management of acute renal failure is discussed below under the heading 'Acute renal failure' (page 914).

Plasma concentrations of creatine kinase (CK) and aspartate aminotransferase (AST or GOT) may be elevated as a consequence of recent muscular activity, and in case of exertional rhabdomyolysis these enzymes are elevated 20–100-fold or more.

Treatment and prognosis

Prognosis varies from favorable to very grave depending upon severity of clinical signs, promptness of medical therapy, and potential complications. Exercise-induced dehydration and exhaustion is responsive to medical therapy if fluid therapy is aggressive. Unfortunately, loss of horses competing in endurance events still occurs, and the importance of close veterinary supervision and diligent therapeutic intervention cannot be overemphasized.

Immediate care should include stopping exercise and, if possible, moving the horse into the shade. If available, fans should be placed close to the horse to promote cooling. The horse should be cooled by repeated rinsing/bathing with abundant volume of cold water over the entire body. In studies performed under field and laboratory conditions, repeated application of cold water over the entire body surface decreases rectal temperature more quickly than no bathing or bathing with water at ambient temperature.[11,12] These treatments do not cause muscle cramps or myopathies. Wet sheets or towels left in place over the horse's neck or trunk should be avoided, unless cold water is sprayed repeatedly because wet towels will only serve to provide unneeded insulation in a heat-compromised patient.[4]

Table 40.3 Plasma electrolytes concentrations observed in horses competing in three-day event competitions (average ± SD, except Ecker 1995[18] average ± SE)

	Before ride	End Phase B	End Phase C	End Phase D	Reference
Na^+ mEq/L	139.0 ± 1.6	143.5 ± 2.7	141.5 ± 1.6	143.7 ± 2.9	Williamson 1996[87]
	137.6 ± 4.1	–	–	143.5 ± 7.3	Andrews 1995[88]
	139 ± 2	–	–	142 ± 2	Marlin 1995[19]
	135 ± 1.2	–	–	134 ± 2.3	Hinchcliff 1995[89]
	140.2 ± 0.3	–	144.0 ± 0.5	–	Ecker 1995[18]
K^+ mEq/L	3.5 ± 0.5	5.2 ± 0.7	4.2 ± 0.5	4.5 ± 0.7	Williamson 1996[87]
	3.6 ± 0.3	–	–	4.2 ± 0.3	Andrews 1995[88]
	3.6 ± 0.4	–	–	3.8 ± 0.3	Marlin 1995[19]
	4.0 ± 0.3	–	–	3.9 ± 0.2	Hinchcliff 1995[89]
	3.7 ± 0.1	–	3.7 ± 0.1	–	Ecker 1995[18]
Cl^- mEq/L	104.5 ± 1.2	104.4 ± 1.7	102.3 ± 1.7	102.4 ± 2.8	Williamson 1996[87]
	103 ± 5.3	–	–	97.7 ± 5.5	Andrews 1995[88]
	99 ± 2	–	–	96 ± 1	Marlin 1995[19]
	101 ± 1.9	–	–	97 ± 1.8	Hinchcliff 1995[89]
	102.2 ± 0.6	–	102.7 ± 0.5	–	Ecker 1995[18]
tCa^{2+} mmol/L	3.1 ± 0.1	3.0 ± 0.1	3.0 ± 0.1	3.1 ± 0.2	Williamson 1996[87]
	3.2 ± 0.2	–	–	3.3 ± 0.2	Andrews 1995[88]
	3.0 ± 0.1	–	–	3.0 ± 0.2	Marlin 1995[19]
	3.0 ± 0.1	–	–	2.9 ± 0.1	Hinchcliff 1995[89]
iCa^{2+} mmol/L	1.7 ± 0.07	1.5 ± 0.07	1.5 ± 0.07	1.4 ± 0.1	Williamson 1996[87]
	1.7 ± 0.1	–	–	1.4 ± 0.1	Andrews 1995[88]
	1.9 ± 0.05	–	–	1.6 ± 0.1	Hinchcliff 1995[89]
	1.6 ± 0.02	–	1.2 ± 0.05	–	Ecker 1995[18]
tMg^{2+} mmol/L	0.75 ± 0.05	–	–	0.72 ± 0.08	Marlin 1995[19]
HCO_3^- mmol/L	29.5 ± 0.7	–	–	23.7 ± 3.1	Hinchcliff 1995[89]
pH	7.37 ± 0.02	7.30 ± 0.06	7.42 ± 0.03	7.30 ± 0.09	Williamson 1996[87]
	7.40 ± 0.02	–	–	7.31 ± 0.1	Andrews 1995[88]
	7.41 ± 0.03	–	–	7.38 ± 0.05	Hinchcliff 1995[89]
Total protein g/L	66.6 ± 5.6	75.9 ± 4.1	69.8 ± 4.0	77.6 ± 5.0	Williamson 1996[87]
	65 ± 4	–	–	77 ± 5	Andrews 1995[88]
	65.7 ± 2.6	–	–	74.9 ± 3.0	Marlin 1995[19]
	61.8 ± 2.6	–	–	71.8 ± 3.3	Hinchcliff 1995[89]
	75.2 ± 1.3	–	79 ± 1.3	–	Ecker 1995[18]

iCa^{2+}, ionized calcium; tCa^{2+}, total calcium; tMg^{2+}, total magnesium.

The choice of oral versus intravenous fluid administration or a combination of both should be based mostly on severity of the clinical signs, but cost and manpower may be other considerations. Oral fluid therapy may be considered in mildly affected horses that may not drink sufficiently on their own. It is generally recommended to administer isotonic electrolyte

Table 40.4 Composition and tonicity of homemade recipes for electrolyte solutions for nasogastric administration

	1 liter	1 gallon (3.8 liters)	Electrolyte composition (mEq/L)	Tonicity
0.45% NaCl	4.5 g (0.16 oz)	17 g (0.6 oz, 1 tbsp)	Na^+ 77, Cl^- 77	Hypotonic
0.9% NaCl	9 g (0.32 oz)	34 g (1.2 oz, 2 tbsp)	Na^+ 154, Cl^- 154	Isotonic
Dr Carlson's formula[3]	–	1 tbsp table salt + 1 tbsp Lite salt in 4 liters	Na^+ 107, K^+ 28, Cl^- 135	Isotonic
Dr Smith's formula[90]	–	1 part $CaCO_3$ (ground limestone) + 3 parts Lite salt; 2 oz per gallon	Na^+ 96, K^+ 75, Cl^- 154, Ca^{2+} 75, HCO_3^- 25	Slightly hypertonic

Lite salt: mixture of KCl:NaCl at 50:50, Morton Lite salt mixture, Morton International, Rohm and Haas, Philadelphia, PA, USA; tsp, teaspoon (5 ml); tbsp, tablespoon (15 ml); oz, ounce (28.35 g); 1 US gallon = 3.8 L.

solutions at a rate of 6–8 L every 30–60 min via nasogastric tube. Contraindications for oral fluid therapy are nasogastric reflux and signs of colic. If the patient's clinical condition does not improve within the following 2–4 h, intravenous fluids should be administered as soon as possible. Table 40.4 lists some recipes for homemade isotonic solutions.

A balanced polyionic solution that is approximately isotonic is recommended. To that effect, Carlson[3] described the following formula, which is similar in composition to electrolytes lost in sweat and is close to isotonic:

> Mix 1 level tablespoon of table salt (16.6 g NaCl) and 1 level tablespoon of Lite salt (16.9 g of 50:50 mixture of NaCl:KCl) in 4 L (≈ 1 gallon) of water (Na^+ 107 mEq/l, K^+ 28 mEq/l and Cl^- 135 mEq/l, 270 mOsm/l).

The effect of tonicity, glucose supplementation and temperature of oral electrolyte solutions is discussed below under the heading 'Rehydration after exercise'.

Intravenous fluid therapy

Intravenous fluids are classified as crystalloids or colloids. Crystalloid fluids are solutions containing electrolyte and non-electrolyte solutes capable of distributing among the body compartments. Colloid fluids contain large-molecular-weight particles, which do not normally pass through capillary membranes, and some smaller more diffusible particles. Colloid fluids include dextrans, glucose polymer mixtures of low (dextran 40) or high-molecular-weight (dextran 70 and dextran 75), gelatins, modified bovine collagens (oxypolygelatin), and hydroxyethyl starch preparations (hetastarch and pentastarch). Colloid fluids are indicated in those patients suffering increased capillary permeability and hypoproteinemia. Exhausted and dehydrated athletic horses will not generally require colloid fluids. Therefore, the following discusses the administration of crystalloid fluids that are used commonly in field situations for treatment of athletic horses.

The ionic composition, pH and osmolality of commonly used crystalloid fluids are presented in Table 40.5. The composition of polyionic fluids resembles that of extracellular fluid. Note that Ringer's solution and 0.9% saline solution have a relative excess of sodium and especially chloride when compared to extracellular fluid concentrations. Exhausted/dehydrated horses generally have greater deficits of electrolytes relative to water (i.e. hypotonic dehydration) because fluid loss (sweat) is isotonic to slightly hypertonic and fluid intake (fresh water) is hypotonic. Therefore, the relative excess of sodium and chloride in Ringer's and saline solutions works to our advantage in treating exhausted/dehydrated endurance horses.

Anions used as buffers in some fluids are added as a source of base because their metabolism in the body yields bicarbonate:

$$\text{Lactate: } C_3H_5O^-_3 + 3\ O_2 \rightarrow 2\ CO_2 + 2\ H_2O + HCO^-_3$$

$$\text{Acetate: } C_2H_3O^-_2 + 2\ O_2 \rightarrow CO_2 + H_2O + HCO^-_3$$

Horses involved in endurance rides and those in the cross-country test (speed and endurance test, second day) of a three-day event competition will commonly suffer substantial fluid and electrolyte depletion, and hypochloremic metabolic alkalosis is the characteristic acid–base disorder. On occasion, in an attempt to dissipate heat, some horses have persistently elevated respiratory rate, which may lead to hypocapnia (low CO_2 tension in the blood) and mixed respiratory and metabolic alkalosis. Therefore, the primary goal is to correct the volume deficit with chloride-rich fluids, such as Ringer's solution or 0.9% saline solution supplemented with potassium and calcium. A suggested amount of calcium supplementation is 10–20 mL of 23% calcium gluconate per liter of saline solution (10–20 mEq Ca^{2+}/L or 5–10 mmol Ca^{2+}/L). It is contraindicated to administer potassium at rates higher than 0.5 mEq/kg/h because of potential for cardiotoxicity. Unless cardiovascular function is closely monitored, potassium supplementation in intravenous fluids should not exceed 15–20 mEq/L. Ringer's solution is preferred over lac-

Table 40.5 Electrolyte composition of selected common sterile intravenous fluids

	Na^+ (mEq/l)	K^+ (mEq/l)	Cl^- (mEq/l)	Ca^{2+} (mEq/l)	Mg^{2+} (mEq/l)	Buffer* (mEq/l)	pH	mOsm/L
0.9% NaCl	154	0	154	0	0	0	5.0	308
Dextrose 2.5% in 0.45% NaCl	77	0	77	0	0	0	4.5	280
Ringer's solution[a]	147	4	156	4	0	0	5.5	310
Lactated Ringer's solution[b]	130	4	109	3	0	28 (L)	6.5	274
Plasma-Lyte A[c] and Normosol-R[d]	140	5	98	0	3	27 (A)	7.4	294

* Buffers used: lactate (L), acetate (A).
[a] Ringer's injection, Abbott Laboratories, Abbott Park, IL, USA.
[b] Lactated Ringer's injection, Abbott Laboratories, Abbott Park, IL, USA.
[c] Plasma-Lyte A, Baxter Healthcare Corp, Deerfield, IL, USA.
[d] Normosol-R, Abbott Laboratories, Abbott Park, IL, USA.

tated Ringer's solution because, as mentioned above, lactate is metabolized to bicarbonate and may have an alkalinizing effect, which is contraindicated in an already alkalotic patient. However, in dehydrated horses the volume of fluid administered is more important than the actual acidifying/alkalinizing nature of the fluid, and one should not forego fluid administration if the only available fluids are alkalinizing, such as lactated Ringer's solution.

Volume of intravenous fluids and rate of administration

In general, calculation of the volume of intravenous fluids to administer is based on estimation of daily maintenance requirements, current fluid deficits, and assessment of ongoing losses. However, in practical terms, maintenance requirements and ongoing losses can be ignored in exhausted/dehydrated horses unless the horse develops diarrhea, ileus with abundant nasogastric reflux, or polyuric renal failure. The goal of intravenous fluid therapy in exhausted/dehydrated horses is to replace water and electrolyte deficits to improve cardiovascular function and allow the horse to regain homeostasis, and to stimulate normal food and water intake.

Horses engaged in prolonged strenuous exercise events, like endurance competitions of 80 to 160 km or more, are reported to lose 4–8% of body weight (as much as 10% in a few horses) during the competition.[9,13–15] Horses undertaking the speed and endurance test of a three-day event or a combined test may lose an average of 2–4% of body weight, which increases to up to 6–9% in a few horses in certain competitions.[16–19] However, sweating rates and consequently fluid and electrolyte losses depend upon environmental conditions, and horses exercising in hot or hot and humid conditions develop greater deficits when compared to more temperate conditions.[20] If 90% of the body weight loss is fluid loss, then an estimated 20–40 L of fluids are lost in a 450-kg horse (≈ 1000 lb) (Table 40.6). A simple estimation of the fluid deficit can be calculated as:

$$\text{Fluid deficit (L)} = \%\ \text{dehydration} \times \text{body weight (kg)}$$

The rate of administration will be calculated as the fluid deficit divided by the duration of i.v. infusion. If one is to replace the volume deficit in 6–12 h the infusion rates will be 0.5–2.5 mL/s, depending on fluid deficit and duration of infusion. For example, if we intend to replace fluid deficits in a 450-kg horse with 7% dehydration over 6 h:

$$\text{Fluid deficit (L)} = 7\% \times 450\ \text{kg} = 32\ \text{L}$$

Table 40.6 Fluid deficits (L) depending on body weight (kg) and estimation of dehydration (%)

% dehydration	350 kg	400 kg	450 kg	500 kg	550 kg
5%	18 L	20 L	23 L	25 L	28 L
7%	25 L	28 L	32 L	35 L	39 L
9%	32 L	36 L	41 L	45 L	50 L

$$\text{Infusion rate (mL/s)} = \frac{32\ \text{L}}{6\ \text{hours}} \times \frac{1000\ \text{mL}}{1\ \text{L}} \times \frac{1\ \text{h}}{60\ \text{min}} \times \frac{1\ \text{min}}{60\ \text{s}} \simeq 1.5\ \text{mL/s}$$

The flow rate can be estimated by counting the number of drops/s in the drip chamber of the administration set. Most fluid administration sets commercially available for large animals deliver 10 drops/mL. In practical terms, to administer 5–10 L/h simply requires full open intravenous administration through a 14-gauge catheter placed in one or both jugular veins. For exhausted horses with hypovolemic shock, large-bore catheters (10–12 gauge) and wide-bore administration sets that allow rapid intravenous fluid administration (up to 30–40 L in 1–2 h) are recommended for resuscitation.

Prevention

Horses competing in endurance exercise events develop substantial body fluid losses, mostly in the form of water and electrolytes lost in sweat, which is manifest as a 3–6% loss in bodyweight by the end of the competition.[13–18] In addition, weight loss persists after an overnight recovery period, which may be detrimental for horses performing multiday events. In an attempt to decrease the risk of thermoregulatory failure consequent to dehydration and to enhance recovery of horses performing endurance-type exercise it has been recommended to supplement electrolytes in drinking water, with concentrate feeds or as hypertonic oral pastes. These and other strategies are discussed below.

Strategies of water and electrolyte replacement/supplementation before, during, and immediately after exercise

Before exercise In horses performing strenuous prolonged exercise, administration of isotonic oral electrolyte fluids via nasogastric tube prior to exercise has been advocated to maintain adequate levels of hydration during exercise and in an attempt to improve cardiovascular and thermoregulatory function during exercise. In man, hyperhydration prior to prolonged exercise results in better cardiovascular function and heat dissipation than if exercise is performed in the euhydrated state.[21] However, the benefits of pre-exercise fluid loading in horses in controlled laboratory conditions have been equivocal. In a recent study of hyperhydration on physiological strain of horses exercised in the heat, administration of 10 L of water or isotonic carbohydrate–electrolyte solution before and between two 45-min bouts of trotting exercise, when compared to no fluid, resulted in maintained cardiovascular function and sweating rate and decreased heat storage.[22] The effect of fluid administration was observed during the second bout of exercise and was attributed to maintenance of euhydration by oral fluid replacement.[22] In a series of laboratory studies, Sosa León et al determined the effect of oral electrolyte fluid administration prior to either a 90-min bout of trotting exercise or a standardized exercise test (SET) intended to simulate the second day of a three-day event.[23–25] Administration of ≈ 26 L of isotonic electrolyte fluid prior to SET, or ≈ 18 L of

hypotonic carbohydrate–electrolyte solution prior to trotting exercise, when compared to no fluid, resulted in maintained plasma volume but cardiovascular (i.e. cardiac output, stroke volume) and thermoregulatory (i.e. core temperature) function were not improved, and fluid administration resulted in arterial hypoxemia. Marlin et al[26] showed that administration via nasogastric tube of 4 L of isotonic fluids to resting horses caused a modest plasma volume expansion when compared to administration of same volume of water. However, administration of the same isotonic electrolyte solution prior to a 40-min low-intensity treadmill exercise bout did not alter the exercise-induced plasma volume expansion.[26] Relevant differences between the study by Geor et al[22] and the rest of the previous studies are that oral fluids were administered not only before but also in between two bouts of exercise and, more importantly (and unlike the rest of the studies), horses exercised in hot environment. Therefore, the purported beneficial effect of hyperhydration before exercise on thermoregulatory and cardiovascular function may be more critical in the heat when heat dissipation is most dependent on sweat evaporation. In summary, the benefits of fluid loading prior to exercise have not been clearly established in horses, and direct measurements of exercise performance have not been performed.

The efficacy of hyperhydration in human subjects is limited when water or hypotonic carbohydrate–electrolyte solutions are ingested due to rapid renal excretion of excess fluid. Administration of solutions containing glycerol is another strategy that has been studied in order to induce a state of hyperhydration before exercise. In resting human subjects and in horses, glycerol administration induces a state of hyperhydration by enhancing fluid retention due to delayed urinary excretion of the excess fluid.[27,28] However, using glycerol, rather than water, as the liquid base to mix sodium chloride and potassium chloride administered during and after exercise is no more effective than electrolytes alone in maintaining euhydration during endurance exercise in horses.[29,30]

Administration of a salt supplement and free access to water prior to exercise may be a practical alternative to intragastric administration of electrolyte solutions. Coenen et al[31] reported greater water intake during and after a 2-h treadmill exercise bout when horses were fed a salt supplement prior to exercise. Similarly, Schott et al[30] reported that administration of salt pastes before and during a 60-km simulated endurance resulted in greater water intake and lower body weight loss.

During exercise Allowing horses to drink salt water during and/or immediately after exercise appears to be beneficial because it enhances total fluid intake during the early recovery period and attenuates the magnitude of weight loss observed during the overnight recovery.[32,33] In a recent laboratory study, horses received furosemide 2 h prior to a 45-km (28-mile) treadmill exercise bout.[32] The combined effect of diuretic administration and endurance exercise resulted in bodyweight losses of 5.2–5.7% (20–22 kg or approximately 18–20 L), which is similar to that observed in competitive endurance rides.[15] When horses were offered water, 0.45% saline, or 0.9% saline immediately after exercise and then given free access to water, total fluid intake during the first hour after exercise was 11.4 L, 16.6 L, and 18.5 L, respectively.[32] However, these interventions did not result in complete replacement of fluid deficits by the next day. Therefore, it appears to be beneficial to offer salt water (0.9% NaCl, 9 g in 1 L water, 1.2 oz [2 level tablespoons] in 1 US gallon), rather than fresh water, immediately after exercise to stimulate a greater water intake during the recovery period.

Electrolytes can be supplemented by mixing them in grain, beet pulp or pelleted feeds, or by direct oral administration instead of offering salt water during or immediately after exercise, which may not be accepted by some horses. Endurance riders commonly supplement their horses with electrolytes as a top dressing on grain or as an oral paste. Electrolyte supplementation as an oral paste before and during a simulated 60-km (37.5-mile) endurance ride on a treadmill resulted in attenuated weight loss after exercise due to greater voluntary water intake during and after the ride. Furthermore, bodyweight loss recovered by 48 h after exercise in supplemented horses, whereas the bodyweight of non-supplemented horses remained decreased.[29,30] In this study, total electrolyte supplementation in horses of mean body weight of 370 kg was 75 g of potassium chloride and 150 g of sodium chloride (≈ 2500 mEq Na^+, ≈ 1000 mEq K^+, and ≈ 3500 mEq Cl^-) given as smaller doses divided before and during treadmill exercise. This supplementation regimen was estimated to replace electrolyte losses in 20–25 L of sweat.[29,30] Similarly, Coenen et al[31] reported greater water intake during and after a 2-h treadmill exercise bout when horses were fed a salt supplement prior to exercise that provided one-half of the sodium and chloride and one-fifth of the potassium administered in the study of Schott et al.[30]

Some field studies have attempted to address the effect of oral electrolyte supplementation during endurance rides. During a 62-km endurance ride, horses were offered either water, water and a salt paste (30 g NaCl), or a 0.9% saline solution at 20-km, 42-km, and the end of the ride.[33] Total fluid intake was highest and body weight loss was lowest when horses were offered 0.9% saline solution during and immediately after the ride. Administration of salt paste had an intermediate effect but the amount of sodium chloride administered in this manner was also half as much as that by the 0.9% saline drink. Ralston et al[34] investigated the effect of oral electrolyte administration during a 96-km endurance race. In this study, a 60-g oral paste (1.6 g NaCl, 3 g K^+, 0.9 g Ca^{2+} per dose; the rest was amino acids and molasses) was given the night before and at 19 and 50 km during the race. The authors reported that supplemented horses recovered slightly faster at the 50-km checkpoint, and serum potassium concentration decreased to a lesser extent in supplemented horses.[34] However, interpretation of this study is complicated by the low number of unsupplemented horses (3 not supplemented versus 14 supplemented) and the relatively low electrolyte content of the product used.

Rehydration after exercise The composition and temperature of oral electrolyte solutions have been shown to

influence fluid absorption in man.[35,36] Similarly, the effectiveness of oral rehydration solutions given to horses via nasogastric tube after exercise or after diuretic-induced isotonic dehydration depends on the nature of the fluid.[37–39] It is generally recommended in horses to administer water with electrolytes with or without carbohydrates as an isotonic solution, rather than water alone.

It has been observed in humans that fluid absorption is optimal if the oral electrolyte solution is hypotonic, contains glucose, and is below room temperature.[36,40] Addition of glucose to electrolyte solutions for oral rehydration in human athletes appears to enhance electrolyte absorption. This effect is argued to be due to the mechanism of sodium absorption in the small intestine. Sodium is absorbed in the small intestine coupled to absorption of glucose. Sodium absorption is an active process mediated by the concentration gradient generated by Na^+, K^+-ATPase pumps that maintain low intracellular sodium and high extracellular sodium concentrations. Sodium in the intestinal lumen is absorbed by facilitated diffusion with a transport protein that cotransports glucose and sodium. Therefore, glucose in the intestinal lumen facilitates intestinal sodium absorption. Absorption of chloride follows sodium due to the electrical gradient generated by sodium absorption. However, addition of glucose to oral electrolyte solutions in horses dehydrated by furosemide administration does not facilitate fluid and electrolyte absorption.[38,39]

Several models of dehydration have been used to study rehydration strategies. These include controlled treadmill exercise, the administration of the loop diuretic furosemide, and a combination of the furosemide administration and exercise. Although it has been argued that the isotonic dehydration induced by furosemide administration mimics exercise-associated fluid and electrolyte disturbances, it should be realized that the overall physiologic perturbations are quite different. Nonetheless, the furosemide model has provided some insight into the effectiveness of different rehydration solutions. For example, in horses dehydrated by administration of furosemide, hypertonic electrolyte solutions (628 mOsm/kg) appear to delay gastric emptying and impair electrolyte absorption, possibly due to the drawing of water into the gut.[39] However, gastric emptying and fluid absorption is not altered when isotonic fluid is administered at temperatures of 5–37°C (41–98.6°F).[39] Concerning exercise studies, Hyyppä et al[41] administered either 8 L of isotonic carbohydrate and electrolyte solution or water to horses after treadmill exercise intended to simulate the second day of a three-day event. Compared to water alone, the carbohydrate–electrolyte solution resulted in better recovery of body weight and lower body weight loss in a subsequent exercise bout the following day.[41] Administration via nasogastric tube of 6 L of isotonic carbohydrate–electrolyte solution immediately after 40-min of low-intensity treadmill exercise resulted in plasma volume expansion when compared to administration of same volume of water.[37] In summary, administration of and oral isotonic rehydration solution after exercise, when compared to water administration or no fluid, results in more effective rehydration and lower weight losses in a subsequent bout of exercise.

Administration of oral electrolyte pastes to horses with free access to water may be an equally effective and more practical form of rehydration after exercise, when compared to the administration of isotonic fluids via nasogastric tube or allowing horses to drink salt water. The effects of electrolyte paste administration on rehydration after furosemide-induced dehydration has been studied.[42,43] Diuretic-induced dehydration caused a body weight loss of 4.1–5.2%. The administration of 0.5 g/kg of NaCl or 0.25 g/kg of NaCl plus 0.25 g/kg of KCl or 0.3 g/kg of NaCl plus 0.1 g/kg of KCl in these horses increased voluntary water intake and improved rehydration when compared to no oral electrolyte administration.[42,43]

Diet, fiber content and the large intestine as a fluid and electrolyte reservoir

It is generally accepted that the large intestine functions as a reservoir of fluid and electrolyte for horses engaged in prolonged exercise. However, there is a paucity of direct measurements or estimations of the volume of fluid and electrolyte content in the large intestine, as well as a quantitative assessment of the contribution of fluid and electrolyte absorption from the large intestine during exercise or in the recovery period. Methodological limitations are probably the main reason for our limited knowledge of fluid and electrolyte contents of the different body compartments. Estimations of the major components of the extracellular fluid are: plasma (4–6% of bodyweight), interstitial and lymph fluid (8–10% of bodyweight) and transcellular fluids (6–10% of bodyweight), the largest component of which is the gastrointestinal fluid.[44] However, only extracellular fluid volume and plasma volume can be measured in the living horse. A limited number of studies have determined the water or gastrointestinal content of ponies and a small number of horses at post-mortem. From these studies one can estimate the water content in the large intestine of the horse to be 8–18% of the bodyweight, depending on diet and the time between feed ingestion and euthanasia. It is also important to note that the large intestine of 150-kg ponies has a higher water content (as a percentage of body weight) compared to 500-kg horses.[45–48] In a recent study, Warren et al[49] obtained direct measurements of extracellular fluid volume (226 mL/kg) and plasma volume (55 mL/kg) and estimated the gastrointestinal fluid volume of 550-kg horses to be 47–54 L (9–10% of bodyweight) assuming that interstitial fluid accounted for 8% of the bodyweight.

The amount of dietary fiber is thought to influence the size of a horse's large intestinal fluid reservoir. In 100–300-kg ponies, Meyer et al[50] demonstrated that feeding a high-fiber diet (hay), when compared to low-fiber diet (complete feed made with grains, bran, and beet pulp), resulted in greater water and electrolyte content in the large intestine (183 and 101 mL water/kg bodyweight, and 398 and 212 mg Na^+/kg bodyweight in high- and low-fiber diets, respectively). However, in the study by Warren et al[49] dietary fiber content did not significantly alter large intestinal water content (99 versus 86 mL water/kg bodyweight in high- versus low-fiber diet, respectively). Meyer et al[46] also described that, when

comparing five paired groups of exercised ponies and rested ponies on the same diet, low intensity exercise (2.8–3.3 m/s for 1–3 h) resulted in absorption from the gastrointestinal tract of 22 ± 7 (mean ± SD) ml of water, 43 ± 30 mg Na^+ and 23 ± 14 mg Cl^- per kg of bodyweight. These averages extrapolated to a 450-kg horse would suggest that during exercise ≈ 10 L of water, ≈ 19 g Na^+ (840 mEq Na^+), ≈ 10 g Cl^- (290 mEq Cl^-) may be absorbed from the ≈ 45 L present in the gastrointestinal tract.

In summary, based on the limited data available at this time, it appears that water and electrolytes absorbed from the gastrointestinal tract of non-supplemented horses may play an important role during exercise but that quantitatively the amounts absorbed are at best modest compared to losses in the form of sweat. As an example, estimated losses in sweat during an exercise bout lasting 2 h are ≈ 20 L of fluid and ≈ 58 g Na^+ [2500 mEq Na^+], ≈ 106 g Cl^- [3000 mEq Cl^-] and ≈ 27 g K^+ [680 mEq K^+], which is two-fold, three-fold and 10-fold higher than the amounts of water, sodium and chloride, respectively, that are potentially available by absorption from the gastrointestinal tract.

Electrolyte requirements in athletic horses

The electrolyte requirements of adult horses vary widely depending upon the level of physical activity. Horses performing protracted exercise bouts may lose large amounts of Na^+ and Cl^- because their sweat has a high NaCl content, similar to that of plasma (Table 40.7). In addition, as the sodium and chloride content of horse feedstuffs is low, salt supplementation is required to offset sodium and chloride losses in sweat. In contrast, potassium losses in sweat are lower and some feedstuffs (i.e. most forages) have a high content of potassium, which makes potassium balance less of a concern.

Electrolyte supplementation is generally provided by giving free access to a salt block. However, it has been shown that there is great individual variation of voluntary sodium intake from a salt block. In a study using Standardbred trotters in racetrack training, total sodium intake of some horses did not even meet the suggested maintenance requirement of 20 mg/kg/day (10 g of sodium or 25.4 g of table salt in a 500-kg horse).[51,52] In contrast, Houpt et al[53] found that salt intake from salt blocks was excessive (over 100 g) in furosemide-treated horses. It appears that salt intake in horses may not be closely regulated to balance losses. Therefore, it has been recommended to provide supplemental loose salt in the diet rather than allow horses to compensate for their electrolyte losses by voluntary intake from salt blocks.

Few studies have addressed the requirement of electrolytes based on dietary intake and direct measurements of electrolyte losses in sweat during training and performance exercise. Although dietary intake can be measured easily, it is more difficult to make a complete assessment of ongoing fecal and urinary losses to account for stimulation of compensatory mechanisms. Some studies have attempted to estimate ion losses based on changes in extracellular fluid volume and plasma electrolyte concentrations, but this approach underestimates ion losses in sweat by over 50% when compared to direct measurement of sweating rates and sweat electrolyte concentrations.[54] Studies that have measured sweat ion losses during training in various environmental conditions and exercise bouts intended to simulate the second day of a three-day event and prolonged low-intensity exercise have demonstrated that a balanced ration and appropriate ion

Table 40.7 Suggested electrolyte requirements (mg/kg bodyweight daily) of adult horses depending on physical activity and sweat losses

	Maintenance	Slight loss (≤ 5 L sweat)	Moderate loss (10–15 L sweat)	Intense loss (≥ 20 L)	Reference
Na^+	20	60	68–75	–	Ott 1989[91]
	20	40	100	250	Meyer 1987[92]
	20	50	80–120	140–170	Jansson 2002*
K^+	50	62	75–100	–	Ott 1989[91]
	50	60	88	150	Meyer 1987[92]
Cl^-	30	–	–	–	Ott 1989[91]
	20	50	140	350	Meyer 1987[92]
	30	75	130–180	210–260	Jansson 2002*
Ca^{2+}	40	50	60	80	Ott 1989[91]
	50	52	58	68	Meyer 1987[92]
Mg^{2+}	15	19	23	30	Ott 1989[91]
	20	22	28	30	Meyer 1987[92]

* A Jansson, personal communication, 2002.
Slight loss (≤ 5 L sweat), e.g. 30 min of trotting in summer.
Moderate loss (10–15 L sweat), e.g. Thoroughbred and Standardbred training and racing in temperate climates.
Intense loss (≥ 20 L), e.g. speed and endurance of three-day event in summer and endurance rides.
Note: horses suffering moderate and intense sweat losses should receive above amounts as salt supplements in days of exercise. Otherwise they should receive maintenance requirements. Fresh water should always be available, especially when salt is supplemented.

supplements can replace sodium and chloride losses in sweat. McCutcheon et al[54] demonstrated that dietary intake of sodium, potassium, and chloride was adequate to replace daily electrolyte losses due to sweating during training in hot and cool conditions when the diet of 450-kg horses was supplemented with a salt supplement that provided 40 g sodium, 26 g of potassium, and 84 g of chloride. However, these same horses, when performing a simulated speed and endurance test of a three-day event in hot environment, had sodium losses more than twice those incurred during more temperate conditions and about 30% higher than the sodium daily intake.

In summary, continued salt supplementation in the form of salt water, oral electrolyte pastes, or electrolytes top-dressed on the ration appears to be necessary in athletic horses because of increased requirements related to loss of electrolytes in sweat.[32,54] A number of commercial electrolyte supplements and homemade recipes are available to supplement the diet of horses that sweat profusely during training and competition. However, the composition of such products is very different and one should carefully examine the composition before choosing any one product (Table 40.8). It is rather common to recommend the addition of 50–75 g (1.8–2.6 oz) of common table salt to the diet of horses exercised heavily in hot environments.

Etiology and pathophysiology

Dehydration will occur during exercise as a consequence of sweating. Sweating allows heat dissipation during exercise, however, protracted fluid losses can result in compromised cardiovascular function, which impairs thermoregulatory function and may eventually lead to fatigue or exhaustion if

Table 40.8 Comparison of the electrolyte content of selected commercially available electrolyte supplements and homemade recipes when administered at the recommended dose

Product	Na^+ g (mEq)	K^+ g (mEq)	Cl^- g (mEq)	Ca^{2+} g (mEq)	Mg^{2+} mg (mEq)	Dose g [oz]
A and C	2.3 (99)	0.4 (9.4)	4.2 (119)	0.2 (11)	10 (0.8)	57 [2]
B	4.7 (205)	2.5 (65)	9.6 (270)	0.7 (36)	46 (3.8)	28.4 [1]
D and E	11 (481)	7.3 (188)	24 (671)	1.5 (75)	153 (13)	57 [2]
F	5.3 (230)	9.4 (241)	20 (556)	1.8 (90)	114 (9.4)	45 [1.6]
G	13 (569)	10 (268)	28 (802)	2.2 (110)	192 (16)	60 [2.1]
H	5.9 (256)	10 (269)	22 (619)	2 (100)	490 (40)	50 [1.8]
I	16 (683)	6.3 (161)	24 (683)	0.3 (14)	228 (19)	57 [2]
J	10 (436)	3 (77)	18 (520)	1.0 (51)	1020 (84)	60 [2.1]
K	7.6 (329)	3.5 (91)	15 (420)	0.3 (15)	15 (1.2)	60 mL [2.1 fl oz]
L	16 (684)	3.7 (94)	28 (778)	1.5 (75)	1500 (123)	60 [2.1]
M	87 (3764)	0 (0)	133 (3764)	0 (0)	0 (0)	220 [7.8]*
Flaminio[a]	5.4 (235)	2.4 (61)	10.5 (296)	0.3 (14)	92 (7.6)	20 [0.7]
Bryant[b]	12 (513)	7.9 (201)	25 (715)	6 (300)	0 (0)	57 [2]
Frazier[c]	5.6 (244)	7.5 (191)	15 (435)	5.7 (285)	8.6 (707)	57 [2]

Note: products included in this table are examples of commercially available electrolyte supplements indicated for athletic horses. The author does not specifically recommend any product listed (or not listed) in this table. The author thanks Dr David Poole (UK), Dr Peter Huntington (Australia), and Dr Anna Jansson (Sweden) for assisting with product information.

A: Electrolyte Supplement, First Priority, Elgin, IL, USA.
B: Endura-Lyte, Life Science Products, Butler, St Joseph, MO, USA.
C: Equi-Phar Equi-Lyte Powder, Vedco, St Joseph, MO, USA.
D: Endura-Max, Kentucky Equine Research Inc, Versailles, KY, USA.
E: Equivit Restore, Kentucky Equine Research Inc (Australasia), Brighton, Victoria, Australia.
F: Humidimix, VetSearch International, Peakhurst, New South Wales, Australia.
G: Electrolyte Replacer, Ranvet Pty Ltd, East Botany, New South Wales, Australia.
H: Humilyte, Troy Laboratories, Smithfield, New South Wales, Australia.
I: Electro-Dex, Horse Health Products Ltd, Pulborough, West Sussex, UK.
J: Surelyte, Dodson and Horrell Ltd, Ringstead, Northamptonshire, UK.
K: Hidrahorse, Esteve Veterinaria, Barcelona, Spain.
L: Rehalyt Basic, Eclipse Biofarmab, Hiskullevägen, Hishult, Sweden.
M: Kraaft salt, Kraaft, Sweden.
* Recommended total amount to be given divided in smaller doses.
[a] Flaminio[93] and personal communication Flaminio 2002. Preparation: 3 parts NaCl, 1 part KCl, 1/4 part of calcium (calcium acetate) and 1/8 part of magnesium (magnesium citrate) dosed as 20 g [0.7 oz] before ride, every 30 km and after ride.
[b] Bryant, 1993, personal communication in Schott.[95] Suggested preparation by author (EJC): 1 part of NaCl, 2 parts of Lyte salt (NaCl:KCl of 50:50), 1 part of calcium carbonate, dosed as 57 g [2 oz] increments.
[c] Frazier.[94] Preparation: 2 parts of Lyte salt (NaCl:KCl of 50:50), 1 part of calcium carbonate and 1 part of magnesium oxide dosed as 57 g [2 oz] at each veterinary checkpoint.

Table 40.9 Electrolyte composition (in mEq/L) of horse plasma, sweat and skeletal muscle

	Na^+ (mEq/L)	K^+ (mEq/L)	Cl^- (mEq/L)	Ca^{2+} (mmol/L)
Plasma	132–146	3.0–5.0	98–110	2.8–3.4
Sweat[20]	117–134	26–42	142–156	2–3
Muscle, horses				
mEq or mmol/kg dw (ww)[60]	40 (10)	305 (76.3)	120 (30)	10 (2.5)
mEq/L[59]		147		
mEq/kg wet weight[61]		91		
mEq/kg dw (ww)[62]		222 (74)		
Muscle, humans mEq/L[63]	10	142	4	2

Gottlieb-Vedi et al[60] and Wilson et al[62] reported as values in dry weight (dw), transformed to wet weight (ww) values by dividing by 4 (water of muscle is ~ 750 mL/kg, therefore 1 kg of dry weight is 4 kg of wet weight).

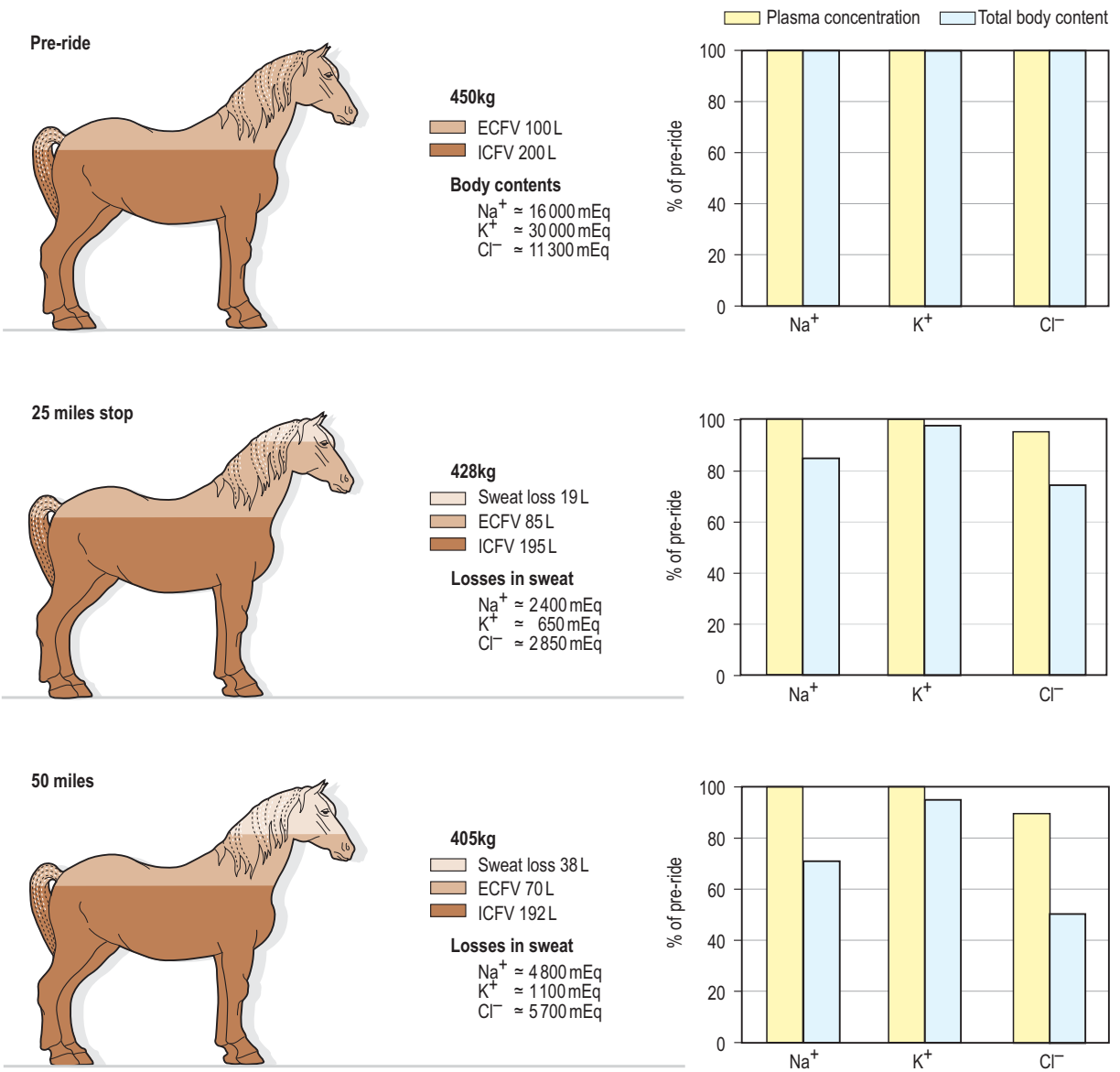


Fig. 40.1
Estimates of fluid and electrolyte losses during an 80-km (50-mile) endurance ride. ECFV, extracellular fluid volume; ICFV, intracellular fluid volume. (Adapted from Schott and Hinchcliff[57] with permission).

fluid and electrolyte losses are not replaced. We should probably keep in mind that evolution has equipped the horse to maintain body temperature during short sprints, although hyperthermia can occur with short bouts of exercise. However, no wild or feral horse will run several hours at high speeds, as we force endurance horses to do.

Rehydration becomes necessary after prolonged exercise or after episodes of water deprivation and intense sweating, as may occur during transportation in summer months. Effective rehydration may improve performance and reduce the risk of illness in subsequent exercise events. It is well established in horses that hypertonic dehydration due to water deprivation and isotonic dehydration due to furosemide administration will impair thermoregulation during a subsequent low-intensity treadmill exercise bout even in favorable ambient temperature and humidity (21–22°C, 25–40%).[55] In both forms of dehydration, the sweating rates were similar to the euhydrated state but heat transfer from the core to the periphery was decreased in horses dehydrated prior to exercise when compared to euhydrated state which was hypothesized to be caused by decreased blood flow to the skin.[55] This hypothesis is supported by the observation of decreased plasma volume during exercise in dehydrated horses compared to the euhydrated state.[56]

Losses of fluid and electrolytes in sweat during prolonged strenuous exercise induce a state of isotonic dehydration because electrolyte concentrations in sweat are similar to those in plasma (Table 40.9). Because an increase in plasma osmolality is a more potent stimulus for thirst than hypovolemia, a thirst response is not triggered until a significant state of dehydration occurs. This concept is referred to as 'involuntary dehydration', a state in which mild to moderate dehydration (2–5%) develops without triggering voluntary water consumption. Although involuntary dehydration has not been well documented in horses, it is commonly observed that endurance horses drink little during the first half of a ride.

Figure 40.1 shows estimates of fluid and electrolytes losses in horses during low-intensity protracted exercise (e.g. 80-km [50-mile] endurance ride). Note that the magnitude of these deficits is poorly reflected by changes in plasma concentrations of electrolytes due to the nature of the losses. The following assumptions were used to calculate total fluid and electrolyte deficits during a 50-mile ride:

- a 450-kg horse has lost 5% of the bodyweight (BW) (22.5 kg) at the 25-mile checkpoint and 10% of BW (45 kg) at the end of the ride
- total body water (TBW) is 666 ml/kg of body weight (BW), extracellular fluid volume is 222 mL/kg BW, intracellular fluid volume is 444 mL/kg BW, and plasma volume is 5 mL/kg BW
- 100% of the bodyweight losses represent body water losses (which includes urinary, fecal, respiratory, and sweat losses)
- after accounting for water and feed consumption, and losses in urine, feces and via the respiratory tract sweat fluid losses were 85% of body water losses, as described by Kingston et al[58]
- similarly to values reported in Table 40.2, plasma sodium and potassium concentrations did not change and plasma chloride concentration decreased from 105 mEq/L to 100 mEq/L by 40 km (25 miles) and to 95 mEq/L by 80-km (50 miles)
- sweat, and intramuscular potassium concentrations are as reported by McCutcheon & Geor[20] and Pickar et al[59] (see Table 40.9)
- intracellular electrolyte concentrations are assumed to be equal to those measured intramuscularly.

Note that intramuscular K^+ concentrations reported by Gottlieb-Vedi et al,[60] Johnson et al,[61] and Wilson et al[62] appear to be excessively low and intramuscular Cl^- concentrations excessively high when compared to well-established values in other species,[63] therefore intramuscular Na^+ and Cl^- concentrations were used from Rose[63] and intramuscular K^+ concentrations were used from Pickar et al[59] (see Table 40.9).

Epidemiology

After lameness, metabolic conditions (dehydration, synchronous diaphragmatic flutter, exhaustion, etc.) are the most common medical reason for elimination of horses from endurance events. As an example, 10–30% of non-finishing

Table 40.10 Completion rates and causes of disqualification in the Tevis Cup

Year/no. horses	% Non-finishers	% Lame	% Metabolic	% Rider	% Over time
2002/216	57	32	30	21	17
2001/225	60	60	15	19	6
2000/259	51	67	21	19	17
1999/224	49	61	10	17	12
1998/219	45	59	22	9	9

From: Tevis Cup Ride Home Page (www.foothill.net/tevis).
Note: Non-finishers, horses that did not complete the race; lame, horses disqualified due to musculoskeletal injury; metabolic, horses disqualified due to dehydration, synchronous diaphragmatic flutter, or other medical condition; rider, horses removed from competitions by rider's decision; over time, horses disqualified at a checkpoint due to being over time.

horses in the Tevis Cup have been disqualified during the last 5 years because of metabolic reasons (Table 40.10). The Tevis Cup is a one-day 160-km (100-mile) endurance race that takes place in the Sierra Nevada mountains of California. The completion rate in the Tevis Cup during the last 20 years has varied between 40–66%. The number of horses starting the race during the last 20 years has varied between 157 and 271.

In a study of the reasons for elimination in endurance competitions that take place in Europe and in Arabic countries (n = 7117 horses) it is reported that, on average, lameness accounts for 63% of the disqualifications and metabolic conditions account for 24%.[64] Endurance competitions of 80–110 km were reported to have the highest percentage of horses disqualified due to metabolic conditions (37%). However, some competitions that take place in Arabic countries may pose a greater metabolic challenge to endurance horses, as reflected by 68% of the disqualified horses suffering some metabolic condition,[64] perhaps a reflection of higher racing speeds and harsher environmental conditions.

Complications associated with exercise-induced dehydration and electrolyte imbalance

Acute renal failure

Due to decreased renal perfusion and ischemia, horses may develop renal tubular damage. This condition is discussed in more detail on page 913.

Cardiac dysrhythmias

Horses subjected to exhaustive endurance exercise may occasionally develop atrial fibrillation or ventricular premature depolarizations.[4,65] It is well described that alteration in electrolyte gradients across cellular membranes may alter membrane resting potential or excitation threshold (see Fig. 40.3 and the rest of the section 'Synchronous diaphragmatic flutter'). The electrolyte and acid–base disturbances associated with exhaustive exercise apparently result in abnormalities of impulse generation in the sinus node or impulse conduction across the atrial myocardium. Cardiac dysrhythmias seen in athletic endurance horses generally respond rapidly to cessation of exercise and intravenous administration of fluids to replace fluid and electrolyte deficits.[4]

Laminitis

Some horses with exercise associated dehydration/exhaustion may initially respond positively to oral and/or intravenous fluid therapy only to develop in the following hours or days mild to severe signs of laminitis. Hypoxic damage, reperfusion injury, endotoxemia and subsequent increased vascular permeability, microvascular thrombosis, administration of corticosteroids, and large intestinal absorption of exotoxins released by *Streptococcus bovis* with consequent activation of matrix metalloproteinases have all been incriminated in the pathogenesis of laminitis. It is likely that a combination of these events plays a role in the cases of laminitis observed after exhaustive exercise. Suggested therapy for horses that develop laminitis after exhaustive endurance exercise include replacement of fluid and electrolyte deficits, keeping the horse in a stall with soft deep bedding, and administration of non-steroidal anti-inflammatory drugs (NSAIDs). Capsaicin ointment applied on the skin overlying the palmar digital nerves has recently been shown to significantly decrease lameness in a reversible model of equine foot soreness.[65b] Judicious use of capsaicin ointment may prove to be an effective adjunctive therapy in laminitic horses after exercise-associated dehydration/exhaustion, which may be at risk of acute renal failure due to dehydration, myoglobinuria and/or administration of NSAIDs. Other medications used in laminitic horses include: (i) aspirin (acetylsalicylic acid), heparin, and warfarin to minimize platelet aggregation; (ii) acepromazine, phenoxybenzamine, isoxuprine, pentoxifylline, and nitroglycerine ointment to vasodilate and improve laminar blood flow; and (iii) dimethylsulfoxide for its anti-inflammatory effects. None of these drugs has been consistently demonstrated to be effective in the treatment of laminitis and the author does not recommend any of them.

Synchronous diaphragmatic flutter (thumps)

- Not a problem in and of itself but is indicative of severe electrolyte disturbances.
- The contraction of the diaphragm and flank coincides with cardiac contraction.
- Typically seen in horses with hypochloremic metabolic alkalosis; hypokalemia and/or ionized hypocalcemia is also commonly observed.
- Responsive to calcium-enriched fluids.

Recognition of the disease

History and presenting complaint

Most commonly seen in endurance horses, (SDF) is associated with dehydration and exhaustion. It has also been described in horses with other clinical disorders associated with ionized hypocalcemia and/or alkalosis, such as impending enteritis, colic, and uterine torsion.[66] There is no apparent breed, age, or sex predilection, but horses known to develop SDF should be watched more closely because there is a tendency for recurrence.

Physical examination

Easily diagnosed by placement of one hand over the flank and simultaneous cardiac auscultation, which will demonstrate that thumping in the flank is synchronous with cardiac contraction, specifically with atrial depolarization. Muscle contractions may be more apparent on one side only, may be continuous or intermittent and the intensity of contraction may vary from barely perceptive to an obvious thumping sound.

Other clinical signs related to dehydration and electrolyte disturbance may be present, such us depression, dry congested mucous membranes, delayed capillary refill time, weak arterial pulse, and persistently elevated heart rate and/or respiratory rate after exercise. Many exhausted endurance horses develop SDF along with the abovementioned signs of dehydration and exhaustion, however other horses develop SDF with few other indications of exhaustion.

Laboratory examination

Consistent abnormalities in horses afflicted of SDF include hypokalemia, hypochloremia, and alkalosis.[66] Hypocalcemia is not as common, however ionized calcium concentrations in horses with SDF have not been reported. Ionized calcium should decrease as a consequence of alkalosis and increased protein binding of calcium.

Treatment and prognosis

Mild cases may recover without specific treatment once the horse is allowed to rest and has free access to water and hay. In horses with clinical signs of dehydration and SDF, oral or intravenous fluids are indicated as discussed in the section on exercise induced dehydration/exhaustion.

Specific therapy for SDF involves intravenous administration of calcium solutions like 23% calcium gluconate. The general recommendation is to slowly administer (over 15–30 min) 250–500 mL of 23% calcium gluconate that has been diluted 1:4 with saline or 5% dextrose. Close monitoring of the cardiovascular response by cardiac auscultation and electrocardiography, if available, is recommended. Dilute calcium infusion should be discontinued if alterations in heart rhythm or rate are observed. Increased alertness of the patient, cessation of SDF, and return of gastrointestinal motility and appetite are evidence of a favorable response to calcium-rich fluids. Bicarbonate administration is contraindicated. In fact, bicarbonate administration in volume and electrolyte depleted horses causes SDF.[67]

Prognosis for SDF is favorable. However, other complications associated with dehydration and electrolyte disturbances can occur, such as laminitis, rhabdomyolysis, or acute renal failure.

Prevention

Development of hypocalcemia and lack of compensatory mechanisms for calcium mobilization from osseous deposits is often argued as the main cause of synchronous diaphragmatic flutter. It is suggested that excessive dietary calcium intake may impair the normal response of the parathyroid gland to hypocalcemia. Therefore, switching from alfalfa hay (1.2–1.4% of calcium in dry matter) to grass hay (0.3–0.45% of calcium in dry matter) has been advocated to decrease dietary calcium intake and possibly to increase the sensitivity of the parathyroid gland to release parathyroid hormone in response to hypocalcemia. However, the effect of ingestion of different hay types or calcium dietary intake on secretion of parathyroid hormone has not been investigated in horses. Another possible dietary manipulation would be to provide anionic diets, which are those with excess of anions over cations. In dairy cattle, it is proven that prevention of parturient paresis ('milk fever', hypocalcemia of lactating dairy

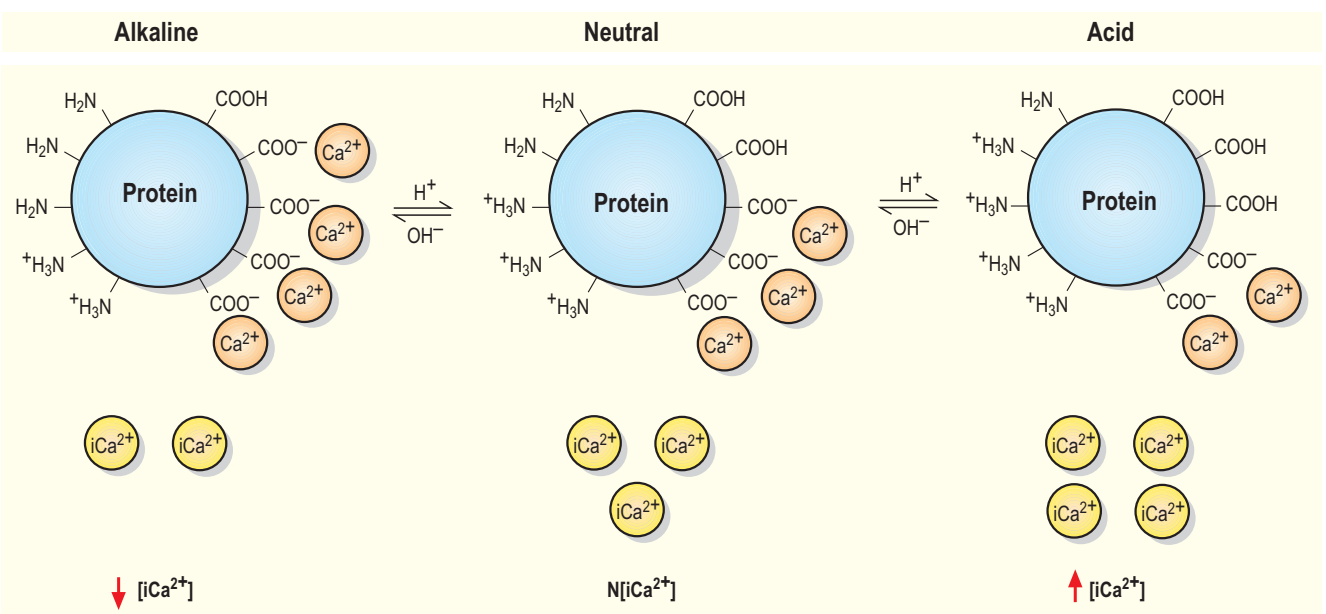


Fig. 40.2
Relationship between pH, protein-bound calcium and plasma ionised calcium. Alkalosis increases protein-bound calcium because of the increased number of negatively charged plasma proteins. (Adapted, with modifications, from Pitts[96].)

cows) is more effective by feeding anionic diets than by lowering dietary calcium intake.[68] Anionic excess apparently enhances calcium absorption from the gastrointestinal tract and resorption of calcium from bone. Whether diets with anionic excess would prove beneficial for the management of SDF in endurance horses is not known.

Provision of supplemental electrolytes before, during and after the athletic event to avoid electrolyte imbalances and development of alkalosis may help prevent development of SDF.[69]

Etiology and pathophysiology

It is suggested that fluid, electrolyte and acid–base derangements alter the normal resting potential and/or action potential of the phrenic nerve, which results in stimulation of the phrenic nerve as it runs over the atria and consequent diaphragm contraction each time the atria depolarize.

Hypochloremic metabolic alkalosis is the most consistent metabolic derangement. It is worth noting that SDF can be reproduced experimentally in horses that are volume and electrolyte depleted by administration of furosemide followed by oral administration of hypertonic sodium bicarbonate.[69]

Alkalosis increases protein-bound calcium due to increased number of negative charges of plasma proteins (Fig. 40.2). Ionized hypocalcemia may be responsible for increased neuromuscular irritability by decreasing the threshold potential (e.g. from –65 mV to –75 mV) (Fig. 40.3), which brings it closer to the membrane resting potential (e.g. –90 mV) and facilitates depolarization and nerve conduction, which in the case of the phrenic nerve stimulates the diaphragm to contract. Conversely, ionized hypercalcemia decreases neuromuscular irritability because it increases the threshold potential. Alterations in the ratio of intracellular:extracellular potassium concentrations may also make cells more or less excitable by altering the membrane resting potential. Hypokalemia (low $K^{+[ECF]/[ICF]}$) hyperpolarizes the cell membrane (makes it more negative), which decreases neuromuscular irritability; and hyperkalemia and/or intracellular potassium depletion (high $K^{+[ECF]/[ICF]}$) increases the resting potential (e.g. from –90 mV to –80 mV), which makes the cells more excitable (Fig. 40.3).[63]

The role of multiple electrolyte alterations in the development of neuromuscular disorders has been described using a formula of neuronal irritability (NI).[70] The formula illustrates how neuronal irritability, and signs of SDF or muscle fasciculations, will develop in hyponatremia, ionized hypocalcemia, hypomagnesemia, alkalosis, or with an increase in the ratio of extracellular to intracellular potassium concentration:

$$N = \frac{Na^{+} + K^{+[ECF]/[ICF]}}{Ca^{2+} + Mg^{2+} + H^{+}}$$

The typical alterations observed in endurance horses are concurrent total body potassium depletion, alkalosis and consequent increase in binding of calcium to albumin, and ionized hypocalcemia. It is likely that multiple electrolyte and metabolic disorders are responsible for development of SDF.

Epidemiology

The incidence of SDF in horses competing in endurance competitions is not well established. It is generally described to be more common in poorly conditioned horses and in competitions that take place in hot climates. In Tevis Cup races between 1962 to 1971, 974 horses started the race, 44% failed to finish, and SDF was observed in 42 of those eliminated.[66]

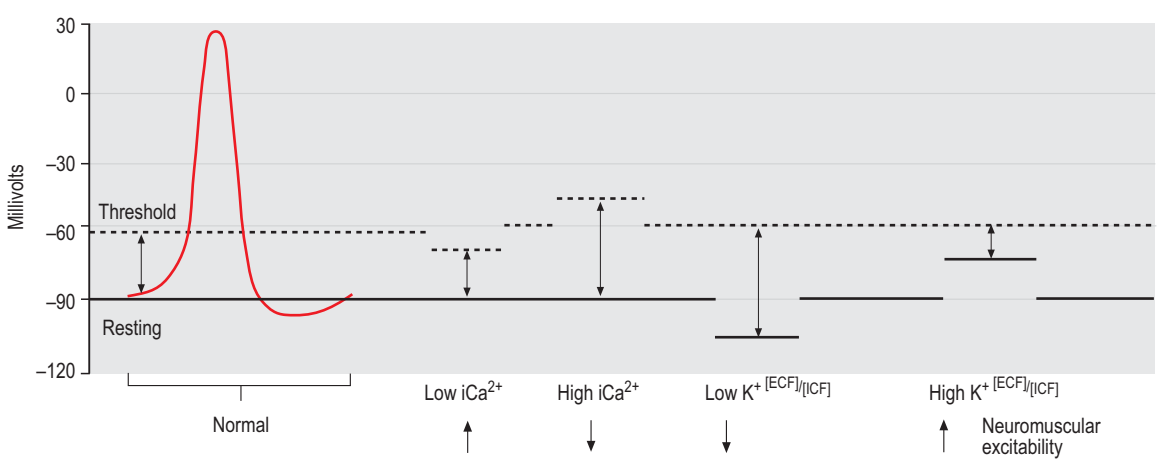


Fig. 40.3
Relationship between resting membrane potential, threshold potential, and plasma ionized calcium concentration; and the ratio of extracellular to intracellular potassium. Ionized hypocalcemia decreases the threshold potential (e.g. from –65 mV to –75 mV), which brings it closer to the membrane resting potential (–90 mV) and facilitates depolarization and nerve conduction. (Adapted, with modifications, from Leaf and Cotran[97].)

Acute renal failure

- Inability to concentrate urine despite clinical signs of dehydration.
- Oliguria in the initial stages of renal failure. Polyuria and/or polydipsia observed as acute renal failure progresses to chronic renal failure.
- Due to decreased blood flow/ischemia or nephrotoxic compounds. Most common nephrotoxins are non-steroidal anti-inflammatory drugs, aminoglycoside antibiotics, vitamin K_3, hemoglobin, and myoglobin.
- Therapy is directed to replacement of fluid, electrolyte and/or acid–base abnormalities. Other drugs indicated for treatment of renal failure (diuretics and renal vasodilators) should only be used after correction of fluid and electrolyte deficits.

Recognition of the disease

History and presenting complaint

Horses afflicted with acute renal failure (ARF) will generally have a history of participating in an athletic event that induced moderate or severe dehydration and frequently concomitant NSAID administration. The presenting complaint may be oliguria (decreased urine production), although urine production may be variable.

Physical examination

Acute renal failure is generally suspected in horses showing marked depression, anorexia, and a lack of urine production within the first 6–12 h of initiation of fluid therapy. Alternatively, affected horses are unable to concentrate urine despite clinical signs of dehydration. However, clinical signs observed are most often those related to the inciting condition.

Renal ultrasonography may be of use in diagnosing acute renal failure. Nephrolithiasis and congenital renal disorders may be ruled out by renal ultrasonography. Ultrasonographic findings described in horses with ARF include perirenal edema, loss of detail of the corticomedullary junction, or dilation of the renal pelvis.[71]

Laboratory examination

Plasma biochemical measurements of horses with acute renal failure will demonstrate increases in plasma urea nitrogen (also referred as BUN) and creatinine concentrations (i.e. azotemia). However, azotemia is only indicative of decreased glomerular filtration and may be solely a consequence of dehydration (prerenal ARF). Determination of the specific gravity of the urine by refractometry is one of the few readily available tests in the field to determine presence of ARF in horses. In cases of oliguria due solely to dehydration, urine specific gravity is usually above 1.025; however, in cases of intrinsic ARF it is generally below 1.020. These cut-off values will only be valid when performed in urine collected before initiation of fluid therapy or administration of diuretics (e.g. furosemide) or α_2-agonist sedatives (e.g. xylazine).

Hyponatremia and hypochloremia are fairly common in horses with renal failure due to increased loss of sodium and chloride in urine because of decreased renal tubular reabsorptive function. Hypocalcemia and hypophosphatemia are often found in horses with acute renal failure.

Urinalysis and urine sediment evaluation

Urine can be collected as a midstream catch during voiding or via urethral catheterization. It is recommended to obtain a urine sample for urinalysis assessment whenever renal failure is suspected in athletic horses.

Horse urine is normally alkaline (pH 7 to 9). However, aciduria may develop as a consequence of exercise-induced fluid and electrolyte losses. In an attempt to maintain plasma volume in the face of dehydration, renal tubular reabsorption of sodium is maximal and sodium is reabsorbed in exchange for potassium. When potassium depletion occurs due to continued losses in sweat, sodium continues to be reabsorbed in the renal tubules in exchange for hydrogen ions. This results in paradoxic aciduria, which describes a state of alkalosis in which the kidneys do not compensate by urinary elimination of an alkaline urine but rather maintain sodium reabsorption at the expense of elimination of inappropriately acidic urine.

Reagent strip analysis is useful to obtain an estimate of pH and the presence or absence of blood, protein, glucose, ketone bodies, and bilirubin. A positive result for blood indicates presence of red blood cells, hemoglobin, or myoglobin. To distinguish between these pigments one can examine the urine sediment for presence of red blood cells, examine plasma to assess if it appears hemolytic (pink or red tinge in normally light yellow plasma) and measure the activities of creatine kinase (CK, normal 145–380 units/L) and aspartate aminotransferase (AST, normal 220–600 units/L) as indicators of rhabdomyolysis and thus the potential for myoglobinuria. A false-positive result for urine protein is common in alkaline urine, and the presence of protein in urine is better assessed with other more specific biochemical assays. Proteinuria and hematuria may transiently follow exercise.[72] Proteinuria is a characteristic finding in glomerulonephritis due to filtration of albumin and other proteins into the urine. A urine protein to urine creatinine ratio above 2:1 is indicative of clinically significant proteinuria in a patient. Glucose should not be detected in normal equine urine and glucosuria may be observed in cases of acute renal failure. Ketones are rarely detected in equine urine, even in cases of catabolic states. Bilirubinuria may be observed in cases of hemolysis and liver disease, however other plasma biochemical data (total and conjugated bilirubin, bile acids, alkaline phosphatase, aspartate aminotransferase, γ-glutamyl transferase and sorbitol dehydrogenase) may be more useful in assessing liver disease.

Sediment examination of equine urine is a simple and very useful technique to evaluate presence and magnitude of renal tubular disease and to determine presence or not of infectious or inflammatory disorders. However, sediment examination should be performed within 1 h of collection,

because casts are unstable in alkaline urine. A normal horse urine sediment should not contain casts, fewer than five red blood cells and fewer than ten white blood cells should be seen per high power field. Briefly, a urine sediment examination is performed by centrifugation of a 6–10 mL urine sample at 1000 rpm for 5 min. The supernatant is discarded and the sediment is resuspended in a couple of drops of sediment staining solution and transferred to a glass slide with a coverslip on top. The sediment is examined first at low power to evaluate for casts (long cylindrical molds of protein and cells shed from the renal tubules; Fig. 40.4). The presence of casts is indicative of renal tubular necrosis. Increased numbers of red blood cells can result from inflammation, infection, and neoplasia, and it is transiently observed after exercise.

Renal tubular function is assessed by clearance rates of electrolytes. However, the clearance rate of a substance in urine requires volumetric urine collection, which is not practical in clinical settings. Fractional creatinine clearance values, more commonly referred to as fractional excretion ratios, allow a similar assessment of renal tubular function by comparing the clearance of an electrolyte to creatinine clearance. Fractional excretion ratios are calculated after measurement of electrolytes in plasma and urine, and obviate the need for volumetric urine collection. Fractional excretion ratio of substance X (i.e. Na^+) is calculated as:

$$\frac{Cl_x}{Cl_{Cr}} = \left(\frac{\text{Urine [X]}}{\text{Plasma [X]}} \Big/ \frac{\text{Urine [Cr]}}{\text{Plasma [Cr]}} \right) \times 100$$

Normal fractional clearance values are less than 1% for sodium, less than 1.6% for chloride, 20–60% for potassium, less than 1% for phosphorus and 2–6% for calcium.[73] However, the results of these calculations must be interpreted taking into consideration fluid therapy and dietary intake.

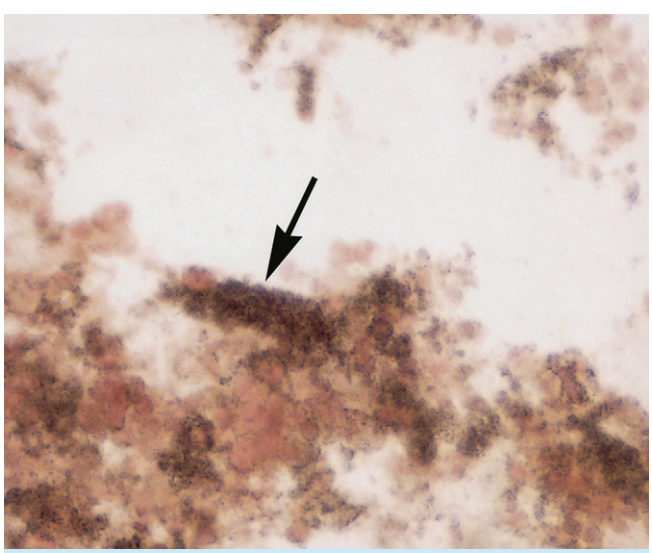


Fig. 40.4
Microscopic evaluation of urine sediment from a horse with acute renal failure. Note the presence of granular casts, one of them in the center of the image (arrow) (×42).

Fractional clearances of potassium, calcium, and phosphorus will vary greatly depending upon dietary intake. Potassium intake is generally adequate and excessive amounts are readily excreted in the urine. The kidneys also play an important role in calcium and phosphorus homeostasis and urinary loss of these electrolytes varies with dietary intake.

Once fluid therapy has been initiated, urine specific gravity and fractional excretion ratios will not be useful because the results are altered by fluid diuresis. However, urine sediment microscopic evaluation will still be useful in assessing ongoing renal damage.

Treatment and prognosis

Therapy for acute renal failure is aimed at removing the primary cause and restoring normal fluid balance by correcting dehydration and electrolyte and acid–base disorders. The prognosis will depend upon the initiating cause and the severity of renal damage. In those cases due to hypoperfusion or ischemia, the prognosis is favorable when the condition is treated promptly. In cases where fluid replacement has been delayed and/or the kidneys suffer multiple simultaneous insults from different nephrotoxins, as in a dehydrated horse that is 'tying-up' (rhabdomyolysis) and is given phenylbutazone, the prognosis is guarded to poor.

Fluid therapy

Regardless of the cause of acute renal failure, initial therapy should include replacement of fluid deficits (preferably by intravenous administration) and correction of any electrolyte or acid–base abnormalities. After these have been corrected, one should attempt to monitor urinary output. Other than subjective assessment of frequency and volume of urination, monitoring of bodyweight will be useful in assessing excessive fluid retention in cases of oliguric renal failure. As described under the heading 'Exercise-induced dehydration/exhaustion', the fluid of choice in horses after prolonged endurance type exercise is Ringer's solution, although other balanced polyionic solutions also are suitable.

Adjunctive medications

When urine output remains reduced after replacement of fluid deficits over the first 6–12 h, administration of drugs that increase renal blood flow, glomerular filtration, and urinary flow may be indicated.

1. Diuretics: Furosemide is a loop diuretic, it blocks the $Na^+/K^+/2Cl^-$ cotransporter in the ascending limb of the loop of Henle, which promotes natriuresis and diuresis. The aim of furosemide administration is to turn oliguric renal failure into non-oliguric renal failure, which facilitates the management of fluid and electrolyte status. The efficacy of furosemide in treating horses with acute renal failure is not documented. In human patients with ARF administration of furosemide does not affect the long-term outcome. The use of

furosemide is contraindicated in horses with suspected urinary tract obstruction or rupture.

Manitol is an osmotic diuretic that increases intravascular osmolality, causing an increase in intravascular volume and as a consequence it increases renal blood flow and glomerular filtration rate. These osmotic effects cause an increase in urinary output and may be effective in the treatment of ARF characterized by tubular obstruction and swelling of the tubular cells.[74]

2. Renal vasodilators: Dopamine activates dopaminergic receptors present in the renal cortex and induces increased renal blood flow and urine output when infused at 5 μg/kg/min, without significant alteration in arterial blood pressure and heart rate. However, some horses develop dysrhythmias with dopamine infusion.[75] Fenoldopam is a selective, α_1-dopaminergic agonist that, in animal models and humans, increases renal blood flow, glomerular filtration rate, and urinary output without unwanted side-effects.[76,77] The effect of fenoldopam on renal hemodynamics in horses is unknown.

Prevention

Acute renal failure in athletic horses will be prevented using those strategies that minimize the risk of development of clinically significant dehydration that may compromise renal perfusion. Avoidance of commonly used nephrotoxic drugs is of the utmost importance in horses that show clinical signs of dehydration/exhaustion. If administration of an NSAID is considered necessary, it is advisable to delay administration until fluid and electrolyte deficits have been at least partially corrected by administration of oral and/or intravenous fluids.

Etiology and pathophysiology

Acute renal failure in the horse results from toxic causes or from ischemic or hemodynamic causes.[74,78] Causes of nephrotoxic acute renal failure include aminoglycoside antibiotics (neomycin being the most nephrotoxic), nonsteroidal anti-inflammatory drugs, vitamin K_3, myoglobin, vitamin D, heavy metals, mycotoxins, and acorns.

Aminoglycoside antibiotics (gentamicin, amikacin, neomycin, streptomycin, kanamycin, and tobramycin) are toxic to the tubular epithelial cells. These antibiotics are reabsorbed from the urine and accumulate in tubular epithelial cells, which causes disruption of the cellular metabolism resulting in tubular swelling and sloughing.[79]

Phenylbutazone and other NSAIDs exert their analgesic and anti-inflammatory effects by inhibition of cyclo-oxygenase, an enzyme responsible for prostaglandin and thromboxane synthesis. However, NSAIDs inhibit also the synthesis of local protective vasodilator prostaglandins in the kidney, thereby reducing blood flow to the renal medulla and inducing renal papillary necrosis.[80,81] Acute renal failure is more likely when NSAIDs are administered in abnormally high doses or when administered to hypovolemic or dehydrated horses. Ketoprofen may be less nephrotoxic when compared to other NSAIDs.[81]

Vitamin K_3 (menadione sodium bisulfite) had been a common cause of acute renal failure in the US before its withdrawal from the market. The development of ARF appears to be an idiosyncratic reaction.[82]

Acute tubular necrosis may occur in cases of moderate or severe myoglobinuria or hemoglobinuria.[74] The pathogenesis for this condition is not completely understood; hemoglobin or myoglobin casts present within the renal tubules may result in ischemic injury, and these pigments also reduce renal blood flow by direct vasoconstrictor effects. In addition, myoglobin deposited in the renal tubules appears to induce oxidative damage of components of tubular cell membranes.[83]

Dehydration and decreased renal blood flow may cause acute renal damage due to hypoxic damage of tubular epithelial cells. Tubular epithelial cells are more susceptible to hypoxia because these cells are involved in solute reabsorption, which demands a high metabolic rate and high demand for oxygen. However, due to unique physiologic and anatomic features of the kidneys, only about 10–20% of the total renal blood flow reaches the medullary portion of the kidney. The low medullary blood flow is required to provide a functional countercurrent mechanism; however, it also renders the medulla relatively hypoxic and more susceptible to ischemic injury.

Epidemiology

Incidence of acute renal failure in the general horse population and specifically in athletic horses is not well documented. The more common causes of acute renal failure are described to be ischemic renal tubular damage due to renal hypoperfusion or NSAIDs (most commonly phenylbutazone and flunixin meglumine), and gentamicin nephrotoxicity.

References

1. Hodgson DR, McCutcheon LJ, Byrd SK, et al. Dissipation of metabolic heat in the horse during exercise. J Appl Physiol 1993; 74(3):1161–1170.
2. Coyle EF, Hamilton M. Fluid replacement during exercise: effects on physiological homeostasis and performance. In: Gisolfi CV, Lamb DR, eds. Perspectives in exercise science and sports medicine, vol 3: Fluid homeostasis during exercise. Carmel, IN: Benchmarck Press Inc; 1990; 281–308.
3. Carlson GP. The exhausted horse syndrome. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: WB Saunders; 1987; 482–485.
4. Foreman JH. The exhausted horses syndrome. Vet Clin North Am: Equine Pract 1998; 14(1):205–219.
5. Ridgeway KJ. Inride veterinary examination, postride examination and judging of best condition. Proceedings 37th Annu Conv Am Assoc Equine Pract; 1991; 815–826.
6. Robert C, Benamou-Smith A, Leclerc J-L. Use of the recovery check in long-distance endurance rides. Equine Vet J 2002; Suppl 34:106–111.
7. Carlson GP, Ocen PO, Harrold D. Clinicopathologic alterations in normal and exhausted endurance horses. Theriogenology 1976; 6(2–3):93–104.

8. Rose RJ, Ilkiw JE, Martin ICA. Blood-gas, acid–base and haematological values in horses during an endurance ride. Equine Vet J 1979; 11(1):56–59.
9. Snow DH, Kerr MG, Nimmo MA, et al. Alterations in blood, sweat, urine and muscle composition during prolonged exercise in the horse. Vet Rec 1982; 110:377–384.
10. Lucke JN, Hall GM. A biochemical study of the Arab Horse Society's marathon race. Vet Rec 1980; 107:523–525.
11. Kohn CW, Hinchcliff KW, McKeever KH. Evaluation of washing with cold water to facilitate heat dissipation in horses exercised in hot, humid conditions. Am J Vet Res 1999; 60(3):299–305
12. Williamson L, White S, Maykuth P, et al. Comparison between post exercise cooling methods. Equine Vet J 1995; Suppl 18: 337–340.
13. Ecker GL, Lindinger MI. Effects of terrain, speed, temperature and distance on water and ion losses. Equine Vet J 1995; Suppl 18:298–305.
14. Lindinger MI, Ecker GL. Ion and water losses from body fluids during a 163 km endurance ride. Equine Vet J 1995; Suppl 18:314–322.
15. Schott II HC, McGlade KS, Molander HA, et al. Bodyweight, fluid, electrolyte, and hormonal changes in horses during and after recovery from 50- and 100-mile endurance rides. Am J Vet Res 1997; 58:303–309.
16. Andrews FM, Ralston SL, Sommardahl CS, et al. Weight, water and cation losses in horses competing in a three-day-event. J Am Vet Med Assoc 1994; 205:721–724.
17. Andrews FM, Ralston SL, Williamson LH, et al. Weight loss, water loss and cation balance during the endurance test of a 3-day event. Equine Vet J 1995; Suppl 18:294–297.
18. Ecker GL, Lindinger MI. Water and ion losses during the cross-country phase of eventing. Equine Vet J 1995; Suppl 20: 111–119.
19. Marlin DJ, Harris PA, Schroter RC, et al. Physiological, metabolic and biochemical responses of horses competing in the speed and endurance phase of a CCI**** 3-day event. Equine Vet J 1995; Suppl 20:37–46.
20. McCutcheon LJ, Geor RJ. Sweating. Vet Clin North Am: Equine Prac 1998; 14(1):75–95.
21. Greenleaf JE, Castle BL. Exercise temperature regulation in man during hypohydration and hyperhydration. J Appl Physiol 1971; 30:847–853.
22. Geor RJ, McCutcheon LJ. Hydration effects on physiological strain of horses during exercise-heat stress. J Appl Physiol 1998; 84(6):2042–2051.
23. Sosa León LA, Davie AJ, Hodgson DR, et al. Effects of oral fluid on cardiorespiratory and metabolic responses to prolonged exercise. Equine Vet J 1995; Suppl 18:274–278.
24. Sosa León LA, Hodgson DR, Evans DL, et al. Effects of hyperhydration on cardiorespiratory and metabolic responses to exercise in horses during a simulated 2nd day of the 3-day-event. Pferdeheilkunde 1996; 12(4):459–462.
25. Sosa León LA, Hodgson DR, Evans DL, et al. Hyperhydration prior to moderate-intensity exercise causes arterial hypoxaemia. Equine Vet J 2002; Suppl 34:425–429.
26. Marlin DJ, Scott CM, Mills PC, et al. Effects of administration of water versus an isotonic oral rehydration solution (ORS) at rest and changes during exercise and recovery. Vet J 1998; 155:69–78.
27. Freund BJ, Montain SJ, Young AJ, et al. Glycerol hyperhydration; hormonal, renal and vascular fluid response. J Appl Physiol 1995; 79:2069–2077.
28. Schott II HC, Patterson KS, Eberhart SW. Glycerol hyperhydration in resting horses. Vet J 2001; 161:194–204.
29. Düsterdieck KF, Schott II HC, Eberhart SW, et al. Electrolyte and glycerol supplementation improve water intake by horses performing a simulated 60 km endurance ride. Equine Vet J 1999; Suppl 30:418–424.
30. Schott II HC, Düsterdieck KJ, Eberhart SW, et al. Effects of electrolyte and glycerol supplementation on recovery from endurance exercise. Equine Vet J, 1999; Suppl 30: 384–393.
31. Coenen M, Meyer H, Steinbrenner B. Effects of NaCl supplementation before exercise on metabolism of water and electrolytes. Equine Vet J 1995; 18:270–273.
32. Butudom P, Schott II HC, Davis MW, et al. Drinking salt water enhances rehydration in horses dehydrated by frusemide administration and endurance exercise. Equine Vet J 2002; Suppl 34:513–518.
33. Nyman S, Jansson A, Dahlborn K, et al. Strategies for voluntary rehydration in horses during endurance exercise. Equine Vet J 1996; Suppl 22:99–106.
34. Ralston SL, Larson K. The effect of oral electrolyte supplementation during a 96 kilometer endurance race for horses. J Equine Vet Sci 1989; 9(1):13–19.
35. Costill DL, Saltin B. Factors limiting gastric emptying during rest and exercise. J Appl Physiol 1974; 37:679–683.
36. Coyle EF, Montain SJ. Benefits of fluid replacement with carbohydrate during exercise. Med Sci Sports Exerc 1992; 24:S324–S330.
37. Marlin DJ, Scott CM, Mills PC, et al. Rehydration following exercise: effects of administration of water versus an isotonic oral rehydration solution (ORS) Vet J 1998; 156:41–49.
38. Monreal L, Garzón N, Espada Y, et al. Electrolyte vs. glucose–electrolyte isotonic solutions for oral rehydration therapy in horses. Equine Vet J 1999; Suppl 30:425–429.
39. Sosa León LA, Davie AJ, Hodgson DR, et al. The effects of tonicity, glucose concentration and temperature of an oral rehydration solution on its absorption and elimination. Equine Vet J 1995; Suppl 20:140–146.
40. Gisolfi CV, Summers RW, Schedl HP, et al. Intestinal water absorption from select carbohydrate solutions in humans. J Appl Physiol 1992; 73:2142–2150.
41. Hyyppä, Saastamoinen M, Pösö AR. Restoration of water and electrolyte balance in horses after repeated exercise in hot and humid conditions. Equine Vet J 1996; Suppl 22: 108–112.
42. Schott II HC, Axiak SM, Woody KA, et al. Effect of oral administration of electrolyte pastes on rehydration of horses. Am J Vet Res 2002; 63(1):19–27.
43. Sosa León LA, Hodgson DR, Carlson GP, et al. Effects of concentrated electrolytes administered via a paste on fluid, electrolyte, and acid base balance in horses. Am J Vet Res 1998; 59(7):898–903.
44. Carlson GP. Thermoregulation, fluid and electrolyte balance. In: Snow DH, Persson SGB, Rose RJ, eds. Proceedings of the first International Conference of equine exercise physiol Cambridge, UK: Granta Editions; 1982; 291–309.
45. Argenzio RA. Function of the equine large intestine and their interrelationship in disease. Cornell Vet 1975; 65:303–330.
46. Meyer H. Influence of feed intake and composition, feed and water restriction, and exercise on gastrointestinal fill in horses, part 1. Equine Pract 1996; 18(7):26–29.
47. Meyer H. Influence of feed intake and composition, feed and water restriction, and exercise on gastrointestinal fill in horses, part 2. Equine Pract 1996; 18(9):20–23.
48. Webb AI, Weaver BM. Body composition of the horse. Equine Vet J 1979; 11(1):39–47.
49. Warren LK, Lawrence LM, Roberts A, et al. The effect of dietary fiber on gastrointestinal fluid volume and the response to dehydration and exercise. Proc 17th Equine Nutr Physiol Symp 2001; 148–149.

50. Meyer H, Coenen H. Influence of exercise on the water and electrolyte content of the alimentary tract. Proc 11th Equine Nutr Physiol Symp 1989; 3–7.
51. Jansson A, Rytthammar Å, Lindberg JE, et al. Voluntary salt (NaCl) intake in standardbred horses. Pferdeheilkunde 1996; 12(4):443–445.
52. Jansson A, Dahlborn K. Effects of feeding frequency and voluntary salt intake on fluid and electrolyte regulation in athletic horses. J Appl Physiol 1999; 86(5):1610–1616.
53. Houpt KA, Northrup A, Wheatley T, et al. Thirst and salt appetite in horses treated with furosemide. J Appl Physiol 1991; 71(6):2380–2386.
54. McCutcheon LJ, Geor RJ. Sweat fluid and ion losses in horses during training and competition in cool vs. hot ambient conditions: implications for ion supplementation. Equine Vet J 1996; Suppl 22:54–62.
55. Naylor JRJ, Bayly WM, Gollnick PD, et al. Effects of dehydration on the thermoregulatory responses of horses during low-intensity exercise. J Appl Physiol 1993; 75(2):994–1001.
56. Naylor JRJ, Bayly WM, Schott II HC, et al. Equine plasma and blood volumes decrease with dehydration but subsequently increase with exercise. J Appl Physiol 1993; 75(2):1002–1008.
57. Schott II HC, Hinchcliff KW. Treatments affecting fluid and electrolyte status during exercise. Vet Clin North Am: Equine Pract 1998; 14(1):175–204.
58. Kingston JK, McCutcheon LJ, Geor RJ. Comparison of three methods for estimation of exercise-related ion losses in sweat of horses. Am J Vet Res 1999; 60(10):1248–1254.
59. Pickar JG, Spier SJ, Snyder JR, et al. Altered ionic permeability in skeletal muscle from horses with hyperkalemic periodic paralysis. Am J Physiol 1991; 260 (Cell Physiol 29): C926–C933.
60. Gottlieb-Vedi M, Dahlborn K, Jansson A, et al. Elemental composition of muscle at rest and potassium levels in muscle, plasma and sweat of horses exercising at 20 degrees C and 35 degrees C. Equine Vet J 1996; Suppl 22:35–41.
61. Johnson PJ, Goetz TE, Foreman JH, et al. Effect of whole-body potassium depletion on plasma, erythrocyte, and middle gluteal muscle potassium concentration of healthy, adult horses. Am J Vet Res 1991; 52(10):1676–83.
62. Wilson JA, Kronfeld DS, Gay LS, et al. Sarcoplasmic reticulum responses to repeated sprints are affected by conditioning of horses. J Anim Sci 1998; 76(12):3065–3071
63. Rose BD. Clinical physiology of acid–base and electrolyte disorders. New York: McGraw-Hill; 1989; 704–706.
64. Burger D, Dollinger S. Raisons d'élimination, état de santé et carrière sportive des chevaus dans les raids d'endurance en Europe et dans les pays arabes: approche statistique. Prat Vet Equine 1998; 30(18):19–25, 91–97.
65. Leroux AJ, Schott II HC, Hines MT. Ventricular tachycardia associated with exhaustive exercise in a horse. J Am Vet Med Assoc 1995; 207(3):335–337.
65b. Seino KK, Foreman JH, Greene SA, et al. Effects of topical perineural capsaicin in a reversible model of equine foot lameness. J Vet Intern Med 2003; 17:563–566.
66. Mansmann RA, Carlson GP, White II NA, et al. Synchronous diaphragmatic flutter in horses. J Am Vet Med Assoc 1974; 165(3):265–270.
67. Freestone JF, Carlson GP, Harrold DR, et al. Furosemide and sodium bicarbonate-induced alkalosis in the horse and response to oral KCl or NaCl therarpy. Am J Vet Res 1989; 50(8):1334–1339.
68. Otzel GR. Meta-analysis of nutritional risk factors for milk fever in dairy cattle. J Dairy Sci 1991; 74:3900–3912.
69. Carlson GP. Medical problems associated with protracted heat and work stress in horses. Compend Contin Educ Pract Vet 1985; 7(10):S542–S550.
70. Coffman JR, Amend JF, Garner HE, et al. A conceptual approach to pathophysiologic evaluation of neuromuscular disorders in the horse. J Equine Med Surg 1978; 2(2): 85–90.
71. Divers TJ, Yeager AE. The value of ultrasonographic examination in the diagnosis and management of renal diseases in horses. Equine Vet Educ 1997; 7:334–341.
72. Schott II HC, Hodgson DR, Bayly WM. Haematuria, pigmenturia and proteinuria in exercising horses. Equine Vet J 1995; 27(1):67–72.
73. Schott II HC. Examination of the urinary system. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders; 1998; 830–845.
74. Bayly WM. Acute renal failure. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders; 1998; 848–856.
75. Trim CM, Moore JN, Clark ES. Effects of dopamine infusion in conscious horses. Equine Vet J 1989; Suppl 7:124–128.
76. Murphy MB, Murray C, Shorten GD. Fenoldopam – a selective peripheral dopamine-receptor agonist for the treatment of severe hypertension. N Engl J Med 2001; 345(21): 1548–1557.
77. Singer I, Epstein M. Potential of dopamine A-1 agonists in the management of acute renal failure. Am J Kidney Dis 1998; 31:743–755.
78. Divers TJ, Whitlock RH, Byars TD, et al. Acute renal failure in six horses resulting from haemodynamic causes. Equine Vet J 1987; 19:178–184.
79. Humes HD, Weinberg JM, Knauss TC. Clinical and pathophysiologic aspects of aminoglycoside nephrotoxicity. Am J Kidney Dis 1982; 2:5–29.
80. Gunson DE. Renal papillary necrosis in horses. J Am Vet Med Assoc 1983; 182:263–266.
81. MacAllister CG, Morgan SJ, Borne AT, et al. Comparison of adverse effects of phenylbutazone, flunixin meglumine, and ketoprofen in horses. J Am Vet Med Assoc 1993; 202:71–77.
82. Rebhun WC, Tennant BC, Dill SG, et al. Vitamin K_3-induced renal toxicosis in the horse. J Am Vet Med Assoc 1984; 184:1237–1239.
83. Moore KP, Holt SG, Patel RP, et al. A causative role for redox cycling of myoglobin and its inhibition by alkalinization in the pathogenesis and treatment of rhabdomyolysis-induced renal failure. J Biol Chem 1998; 273:31731–31737.
84. Rose RJ, Arnold KW, Church S, et al. Plasma and sweat electrolyte concentrations in the horse during long distance exercise. Equine Vet J 1980; 12:19–22.
85. Carlson GP, Mansmann RA. Serum electrolyte and plasma protein alterations in horses used in endurance rides. Am Vet Med Assoc 1974; 165(3):262–264.
86. Schott II HC, Davis MW, Butudom P, et al. Ionized calcium concentration during endurance exercise. 19th Forum American College of Veterinary Medicine. J Vet Intern Med 2001; 15(3):287, abstract 62.
87. Williamson LH, Andrews FM, Maykuth PL, et al. Biochemical changes in three-day-event horses at the beginning, middle and end of phase C and after phase D. Equine Vet J 1996; Suppl 22:92–98.
88. Andrews FM, Geiser DR, White SL, et al. Haematological and biochemical changes in horses competing in a 3 Star horse trial and 3-day event. Equine Vet J 1995; Suppl 20: 57–63.

89. Hinchcliff KW, Kohn CW, Geor R, et al. Acid: base and serum biochemistry changes in horses competing at a modified 1-star 3-day-event. Equine Vet J 1995; Suppl 20: 105–110.
90. Smith CA, Wagner PC. Electrolyte imbalances and metabolic disturbances in endurance horses. Compend Contin Educ Pract Vet 1985; 7(10):S575-S585.
91. Ott EA, (Chairman) and the Subcommittee on horse nutrition. Nutrient Requirements of Horses, 5th edn. Washington DC: National Research Council, National Academy Press; 1989.
92. Meyer H. Nutrition of the equine athlete. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Editions; 1987; 644–673.
93. Flaminio MJBF, Rush BR. Fluid and electrolyte balance in endurance horses. Vet Clin North Am: Equine Pract 1998; 14(1):147–158.
94. Frazier DL. Synchronous diaphragmatic flutter. Proc 37th Ann Conv Am Assoc Equine Pract 1991; 833.
95. Schott II HC, Hinchcliff KW. Fluids, electrolytes, and bicarbonate. Vet Clin North Am: Equine Pract 1993; 9(3):577–604.
96. Pitts, RF. Physiology of the kidney and body fluids, 2nd edn. Chicago: Year Book Medical Publishers; 1968; 169.
97. Leaf A, Cotran R. Renal pathophysiology. New York: Oxford University Press; 1976; 116.

CHAPTER 41

Thermoregulation and exercise-associated heat illnesses

L. Jill McCutcheon and Raymond J. Geor

Body heat is produced by metabolism and is also gained from the environment. In homeotherms, internal temperature is normally maintained within a narrow range (37–40°C) by integrated neurophysiologic mechanisms that balance heat production and heat loss. Thermoregulation is the process by which the internal temperature is regulated to maintain body temperature within this thermoneutral zone. For example, during heat exposure or exercise, when heat gain occurs, the thermoregulatory system will provoke mechanisms for heat loss such that the rise in internal (or core) body temperature is mitigated. It is the most important regulation system in homeothermic animals.[1]

In horses, as in humans and other mammalian species, an excessive elevation in body temperature limits performance capacity. Therefore, a thorough understanding of thermoregulation and means for enhancement of these mechanisms is crucial to management of the athletic horse. The fact that horses often train and compete in hot weather, ambient conditions that substantially increase the risk of thermal injury, further underscores the importance of such understanding.

Heat production and dissipation

Core body temperature is a dynamic equilibrium between factors that add or remove heat. This balance is maintained by integration of mechanisms that vary the body's rate of heat production, alter the transfer of heat to the periphery (e.g. skin), and regulate evaporative cooling. The hypothalamus contains the central coordinating center for the various processes of thermoregulation. Specialized neurons within the hypothalamus act as a thermostat that initiates thermoregulatory adjustments to deviations from normal body temperature. Heat-regulating mechanisms are activated by thermal receptors in the skin that provide input to the hypothalamus, or by direct stimulation of the anterior hypothalamus via changes in the temperature of blood perfusing the area.

The greatest disequilibrium in heat balance occurs during exercise. Conversion of chemical energy (i.e. stored substrates) to mechanical energy (e.g. muscular contraction) is inefficient with approximately 75–80% of the total chemical energy released as heat rather than physical work.[2] As such, the rate of metabolic heat production increases markedly with the onset of exercise and is accompanied by increases in muscle and core body temperatures. The increase in core temperature provokes activation of heat dissipatory mechanisms such that increases in body temperature are mitigated. However, whether balance between heat gain and heat loss can be re-established will depend on the duration and intensity of exercise and the efficiency of heat dissipation. The latter is primarily influenced by ambient conditions but also modified by physiological adaptations (e.g. conditioning, heat acclimatization) in heat dissipatory mechanisms.

Heat production

For living organisms, biologic work is either external, which includes moving the body or other objects through muscular contraction, or internal work that would include all other forms of biologic work, such as smooth muscle contraction, synthesis of molecules and compounds, or active transport within cells. With the exception of periods of growth, ultimately all this work is transformed into heat that is either stored or liberated. Energy expenditure by the body can therefore be expressed by the following equation:

$$\text{Total energy expenditure} = \text{internal heat production + external work performed + energy stored}$$

The body has a basal level of energy expenditure or basal metabolic rate (BMR) that is lowest when environmental temperature range is within a thermoneutral zone. This BMR minimizes energy expenditure required to maintain normal body temperature. The BMR is altered by numerous factors, both internal and within the environment, which increase or decrease energy expenditure. Metabolic rate is normally lowered during sleep and increases with any form of work or stress. Perturbations of BMR such as exercise, fever, catecholamine release, feed consumption (thermic effect of feed), or dealing with a cold environment can therefore affect heat balance. In mammals, there have been extensive investigations of the relationship between bodyweight and heat production,[2,3] which have demonstrated that resting heat production is proportional to body mass to the power of 0.75 in adults but not in growing animals. There are, however, differences between species and it could be expected that within a species such as the horse with extensive variation in size and weight based on breed, lighter breeds may have a significantly lower resting heat production when compared to heavier breeds.

Heat production in horses is influenced by dietary factors, including the quantity and quality of feed and water intake. Replacing hay in the diet with grains has been demonstrated to decrease heat production,[4] with a further reduction in heat production possible with fat supplementation.[5] When exposed to hot or cold environments, water restriction and dehydration can also reduce heat production.

During exercise, the workload or speed is the main determinant of the rate of heat production. Other factors such as the weight of rider and tack, and the nature of the terrain and footing will also contribute to the overall workload.[6,7] Heat production during exercise can be estimated from oxygen consumption data:

$$\text{Metabolic heat} = \dot{V}O_2(\text{liters per min}) \times k \times \text{exercise duration (min)}$$

where $\dot{V}O_2$ = oxygen consumption and k = amount of heat liberated per liter of oxygen consumed. Values for k range from 4.7 kcal to 5.1 kcal depending on the substrate oxidized (lowest value for pure fat oxidation, highest value for pure carbohydrate oxidation).[3]

Metabolic rate in horses is 40- to 60-fold higher during exercise at maximum oxygen uptake ($\dot{V}O_{2max}$) when compared to the resting state. For a 500-kg horse with a $\dot{V}O_{2max}$ of 80 L/min, this equates to metabolic heat production in excess of 400 kcal/min (~ 1.3 MJ/min) of exercise. Production of this quantity of heat without any ability for heat dissipation would result in an increase in body temperature of approximately 1°C per minute during exercise. Although the rate of metabolic heat production is lower during endurance exercise, the overall heat load is substantially higher because of the longer work duration. For example, it has been estimated that the metabolic heat production of an endurance horse running at 8 m/s is about 150–200 kcal/min; if no heat was dissipated, this heat load would result in an increase in core temperature of approximately 21°C per hour. These hypothetical measurements emphasize that effective heat-loss mechanisms are crucial and serve to further underline the additional impact severe ambient conditions will impose on the horse's ability to lose heat to the surrounding environment.

In contrast to most other large domestic species in which skeletal muscle comprises 30–40% of total bodyweight, half the total bodyweight of the Thoroughbred is working muscle. This higher percentage of bodyweight from muscle contributes to the horse's higher mass-specific $\dot{V}O_2$ when compared to other athletic species, including man. Furthermore, a running horse uses a greater proportion of its body mass for locomotion than does a human performing running or leg cycling exercise. Thus, the mass-specific heat load for the exercising horse is as much as two- to three-fold higher compared to that of exercising humans. Despite a substantially higher rate of heat production in the horse, the ratio of surface area to body mass is approximately 50% less than that of humans (man = 1:35–40 m^2/kg; horse = 1:90–100 m^2/kg).[6,7] As a result, the horse has a significantly smaller surface area over which to dissipate a relatively larger metabolic heat load and, at any given workload, must dissipate approximately four times more heat per unit of body surface area during exercise than human athletes. The disadvantage posed by a smaller surface-area:body-mass ratio can be partially offset by higher rates of cutaneous and respiratory heat loss. However, it is apparent that exercise is a considerable thermoregulatory challenge to the horse, with prolonged exercise representing one of the most demanding situations.

Mechanisms of heat transfer

Conductive, convective, radiative, and evaporative heat loss are the four basic mechanisms for heat transfer. Heat loss by *conduction* involves direct transfer of heat through a liquid, solid, or gas from one molecule to another. Although most of the body heat is transferred to the periphery by the circulation, a small amount moves by conduction directly through the deep tissues to the cooler surface. Heat loss by conduction then occurs by the warming of air molecules and cooler surfaces in contact with the skin. The rate of conductive heat loss is directly proportional to the temperature gradient between the skin and surrounding surfaces, and inversely proportional to the thickness of the hair coat. Heat loss by conduction from the surfaces of the head, neck and distal limbs is more effective due to a higher surface area to mass ratio in these regions when compared to proximal limbs, thorax and abdomen.

Convection represents the transfer of heat between two media, such as the skin surface and surrounding air. The effectiveness of heat loss by convection depends on how rapidly the air near the body is exchanged once it is warmed. Conductive heat loss is most effective when the warm air surrounding the body is continually replaced by cooler air, as occurs as a running horse moves through the air and/or wind speed is moderate to high. On the other hand, the trap-

ping of air within a long hair coat will impede convective heat transfer to the environment. Convective heat transfer also occurs in the respiratory tract, the rate of which is dependent on pulmonary ventilation and the temperature difference between inspired and expired air.

Radiative heat transfer occurs when electromagnetic radiated is emitted or absorbed at the skin surface. As body temperature is normally higher than the environment, there is a net loss of radiative heat energy at the skin surface. However, in hot ambient conditions, when the temperature of objects in the environment exceeds skin temperature, radiant heat energy is absorbed from the surroundings. Under these conditions, the only avenue for heat loss is evaporative cooling. A gain of radiant heat energy also occurs via direct (or reflected) sunlight. It has been suggested that solar radiation can contribute up to 15% of the heat gain in horses during exercise in sunny conditions.[8]

For the horse, the most important mechanism for heat loss is *evaporative* cooling including the evaporation of sweat from skin surfaces and water from the respiratory tract. The efficacy of this mechanism is dependent upon the extent of the vapor pressure gradient between body surface and environment. Calculations of the estimated heat loss are based on the latent heat of vaporization of water (from a liquid to a vapor – 598 kcal [2501 kJ] for each gram of water at 0°C).[9] After accounting for possible variations in the thermodynamic properties of sweat when compared to water, it is estimated that the evaporation of 1 L of sweat from the skin surface will dissipate approximately 580 cal (2428 kJ or 2.4 MJ) of body heat.[10] The quantity of heat (~ 2.4 MJ) dissipated in association with the evaporation of 1 L of sweat in thermoneutral conditions is approximately equivalent to the heat generated by 2 min of high-intensity exercise or 6 min of moderate-intensity exercise. In optimum conditions, (i.e. when relative humidity is low) the evaporation of sweat is a very efficient mechanism of heat loss and can account for as much as 65% of total heat loss during exercise. However, several environmental factors will influence the efficacy of evaporative heat loss. These include ambient temperature and relative humidity, the extent of the vapor pressure gradient between the skin surface, and the rate of air movement.[11–13] At high ambient humidity, the vapor pressure gradient between the body surface and the environment narrows thereby constraining evaporative cooling and increasing the rate of heat storage.

The extensive surface area of the respiratory tract also provides a mechanism for heat dissipation. This process relies upon the difference in vapor pressure between the inspired air and that of the epithelial surface of the respiratory tract. The external nares of the horse contribute considerable surface area for heat exchange. Similarly, the extensive surface area of the upper respiratory tract, including the internal nares and nasal turbinates provide an environment in which air entering the nasal passages contacts the highly vascularized epithelium of the upper respiratory tract. Horses also have a unique anatomical arrangement by which their internal carotid arteries are enveloped by a pair of air-filled guttural pouches. Preliminary studies suggest that exercising horses can use their guttural pouches to cool blood en route to the brain.[14] It is surmised that this heat loss from the upper respiratory tract contributes to selective brain cooling, whereby the temperature of blood reaching the brain is lower when compared with that measured in mixed venous (pulmonary artery) blood or within skeletal muscle.[15] Heat loss from the respiratory tract is dependent upon relative humidity and minute ventilation. Under cool, dry conditions, the extent of heat loss via this mechanism is estimated to be between 15 and 25% of total heat loss. In hot, humid conditions, when cutaneous evaporative cooling is compromised, respiratory heat loss may account for a relatively higher proportion of total heat loss and therefore represent 25% or more of total heat loss. While elevations in the respiratory rate increase the proportion of heat loss from the respiratory tract in these conditions, mechanical limitations imposed during exercise (e.g. the coupling of stride to respiration during canter and gallop) may ultimately limit heat loss from the respiratory tract.

Mechanisms of sweat formation

In only a limited number of species, including some bovidae, primates and equidae, is the sweat gland primarily a thermoregulatory organ.[4,16] In the horse, sweat glands are present in both haired and relatively hairless skin with regional variation in the density of glands that is not dependent on the presence of a haircoat. Structurally, the gland is similar to that of many other domestic species, consisting of a fundus and a duct connecting the fundus with the skin surface. Throughout most of its length, the duct lining is composed of two layers, with a single layer of keratinocytes lining the duct at the skin surface. Located within the dermis, the fundus is lined by an inner layer of secretory epithelium interspersed with myoepithelial cells and surrounded by a fenestrated sheath of fibrocytes that encloses a layer of connective tissue. Although sweating appears to be under sympathetic nervous control, there is no evidence of direct sympathetic innervation of the sweat gland. Rather, sweating appears to occur via humoral stimulation of β_2-adrendergic receptors on sweat glands. As a result, sweating can be initiated by epinephrine (adrenaline) release in advance of any stimulus related to an increase in core temperature.

As most studies to date have investigated sweating rate and composition in Thoroughbred horses, the degree to which sweating rate and composition varies between breeds is unknown. To date, it appears that the basic composition of sweat is similar between breeds. Equine sweat, unlike that of humans, is isotonic to slightly hypertonic relative to plasma.[11,15,17] Sweat ion concentrations are largely a reflection of sweating rate and therefore are subject to alteration based on environmental conditions and exercise intensity (Table 41.1). Although there is some variation in sweat ion composition of equine sweat, individual differences in sweat composition do not appear to be as extensive in horses when compared to human athletes. Epinephrine (adrenaline) infusion will produce a more dilute sweat and may account for the less concentrated sweat produced during high intensity exercise when compared to low intensity exercise.[11,15,18]

Table 41.1 Sweating rate, ion concentrations, and osmolality in horses at two exercise intensities and three different ambient conditions after 10 min exercise (data from[11,90])

Variable	CD high	CD low	HD low	HH low
Sodium (mmol/L)	124.0 ± 6.7	116.7 ± 6.1	133.6 ± 2.3	130.6 ± 1.7
Potassium (mmol/L)	25.8 ± 2.1	32.6 ± 1.4	41.5 ± 1.1	28.1 ± 0.9
Chloride (mmol/L)	142.0 ± 5.6	144.3 ± 4.3	155.8 ± 3.2	149.5 ± 2.9
Osmolality (mOsm/kg)	313 ± 18	303 ± 6	339 ± 6	327 ± 5
Sweating rate (mL/m^2/min)	40.4 ± 3.7	21.1 ± 5.2	32.8 ± 5.1	27.0 ± 6.2

CD, cool, dry (room temperature [T] = 20°C, relative humidity [RH] = 45–55%); HD, hot, dry (T = 32–34°C, RH = 45–55%); HH, hot, humid (T = 32–34°C, RH = 80–85%); high, exercise at 90% of maximum oxygen consumption ($\dot{V}O_{2max}$); low, exercise at 50% of $\dot{V}O_{2max}$.

During exercise, an increase in body temperature as a result of metabolic heat production is the primary stimulus for sweating. Normally, sweating is initiated at a specific core temperature and continues in proportion to the increase in core temperature. Hodgson et al[19] demonstrated that increases in sweating rate at three different exercise intensities (40%, 65%, and 90% of $\dot{V}O_{2max}$) were closely related to elevations in carotid artery blood temperature (Fig. 41.1). Rate of rise in body temperature and the concentration of circulating catecholamines associated with different exercise intensities could also contribute to the determination of sweating rate.

Thermoregulation during exercise

During exercise, metabolic heat from working muscles must be transferred to the skin surface to be lost to the environment. Peripheral thermoreceptors in skin, spinal cord, skeletal muscle, abdomen, and hypothalamus detect changes in thermal load and produce a proportional output that is integrated in the hypothalamus to allow adequate thermoregulatory effector activity, particularly by the circulatory system and sweat glands. The primary physiologic mechanisms driving heat loss are an increase in the proportion of cardiac output directed toward the cutaneous circulation and an increase in the rate of sweat secretion. The increase in cardiac output and blood flow to contracting muscles enables a substantial increase in convective heat transfer away from the muscle. The circulation carries the heat to the body core, resulting in an increase in core temperature. Increasing core temperature and, to a lesser extent, increasing skin temperature provides the afferent signal for reflex increases in skin blood flow and sweating, thereby facilitating heat transfer to the skin surface and its dissipation to the environment.

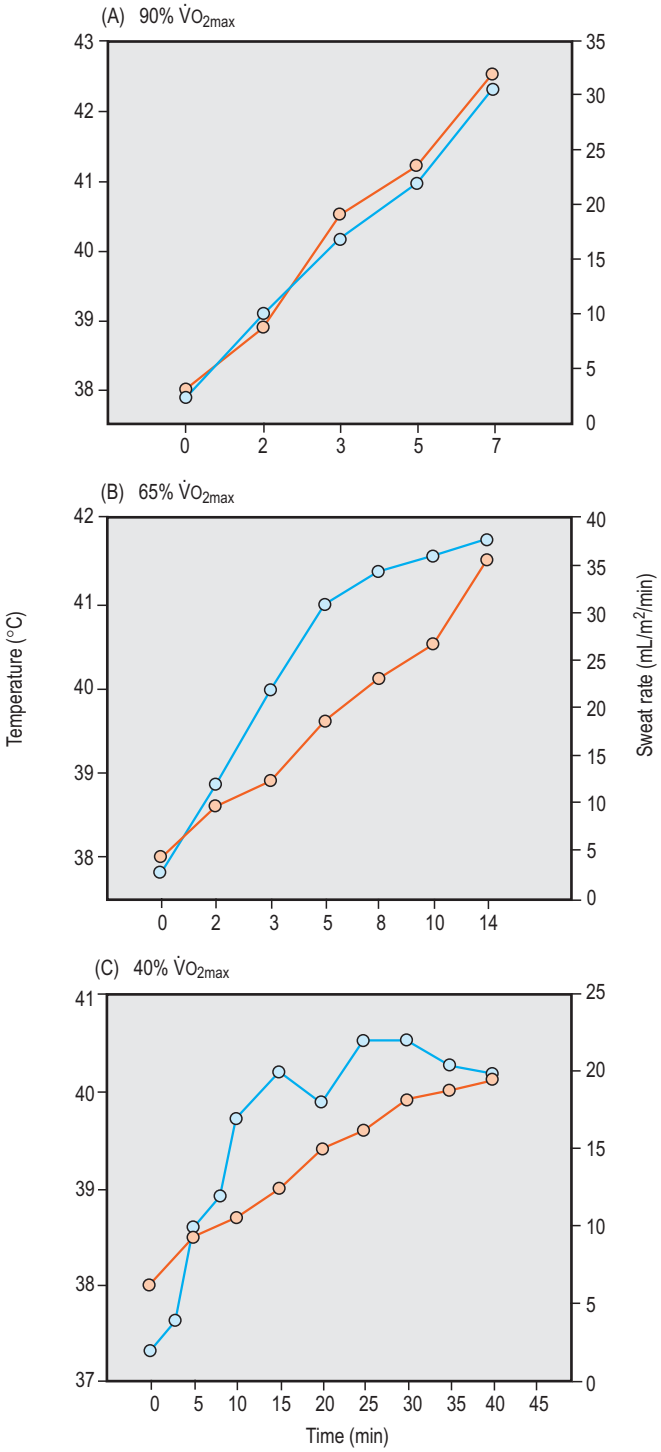


Fig. 41.1
Carotid artery temperature (orange circles) and sweat rate (blue circles) in horses exercising at 90% (A), 65% (B), and 40% (C) of maximal O_2 uptake ($\dot{V}O_{2max}$). Ambient temperature was 21–23.5°C. (Adapted from Hodgson et al.[19])

Skin blood flow is substantially increased by the opening of capillary beds that are normally bypassed by arteriovenous anastamoses that connect arteries directly to veins. The increase in blood flow through the vascular beds of the skin

allows heat to be lost to the environment via convection and direct radiation of heat from the skin surface. The efficacy of transfer of heat by convection and radiation varies according to the rate of air movement across the skin (wind speed) and the gradient of skin temperature to environmental temperature. Increased skin blood flow also provides the latent heat for vaporization of sweat and as well as the fluid required for sweat production. The attempt to maximize blood flow for increased activity and thermoregulation is also reflected in decreased splanchnic and adipose tissue blood flow.[20] Greater oxygen demand increases respiratory rate and respiratory blood flow and both activities will enhance the extent of evaporative cooling by the respiratory system.

Sweating rates of ~ 20 to 55 mL/m^2/min have been measured on the necks and backs of horses exercising on a treadmill in a laboratory.[19,21–23] Assuming a body surface area of 4.5 to 5.0 m^2 for a 500-kg horse, these sweating rates correspond to fluid losses of 6–15 L per hour. This estimate of hourly sweat fluid loss is in agreement with sweat rates calculated on the basis of the decrease in body mass during prolonged exercise under field conditions.[24] When expressed in terms of sweating rate per unit area of skin, these sweating rates are two- to three-fold greater than those reported for human subjects.

At any given point in time during exercise, core body temperature reflects the balance between heat production and dissipation. Soon after the onset of exercise, the rate of heat production greatly exceeds the rate of heat dissipation such that there is a rapid increase in muscle temperature.[25] During short-term, high-intensity exercise (e.g. racing), the rate of heat production will exceed the rate of heat loss throughout exercise and body temperature will continue to increase until the cessation of exercise. In this circumstance, a large proportion of the metabolic heat load will be dissipated during the recovery period. Conversely, during more prolonged low- to moderate-intensity exercise in temperate ambient conditions, activation of heat dissipatory mechanisms progressively attenuates the rate of rise of body temperature. Eventually, the rate of heat loss increases sufficiently to balance metabolic heat production, allowing a near steady-state core temperature to be achieved.[25]

Effects of environmental heat load on exercise responses

Not surprisingly, the thermal response to exercise is affected by the ambient conditions. As environmental temperature increases, the thermal gradient between the skin and the environment is reduced, and sensible heat loss (i.e. convective and radiative heat transfer) is impaired. When ambient temperature exceeds skin temperature (> 35–36°C), the gradient for heat transfer is reversed and the body gains heat from the environment. If humidity is low, a decrease in sensible heat loss can be offset by an increase in sweating rate and evaporative cooling. As humidity rises, the gradient between skin and ambient dew point is reduced and evaporative heat loss is also impaired. The decrease in sweat evaporation is manifested by excessive wetting of the skin surface and drippage of sweat from the body. Sweat that drips from the body only removes 5% to 10% of the heat that can be dissipated by evaporation of sweat. Therefore, during exercise under conditions of high ambient heat and humidity, the rate of heat dissipation may be inadequate to prevent the progressive rise in body temperature. The impact of the environment on the rate of rise of core body temperature in exercising horses is depicted in Fig. 41.2. The rate of heat storage when exercising in hot, humid conditions may be more than twice the rate occurring during exercise at the same intensity in cool, dry conditions.[13,26–28]

Increased demands for respiratory heat loss are reflected by an increase in respiratory rate and during and after exercise. Kohn and Hinchcliff[29] reported a 20% to 25% increase in the respiratory rate of horses during speed and endurance tests in hot when compared to cool conditions. In laboratory experiments, an approximately two-fold increase in post-exercise respiratory rate has been observed in horses under hot, humid when compared to cool, dry environmental conditions.[13,26] When ponies were exposed to heat (41°C dry bulb temperature), there were three-fold increases in respiratory rate and blood flow to tissues of the upper respiratory tract,[30] reflecting the role of the respiratory system in heat dissipation. Similarly, during moderate intensity (~ 30% $\dot{V}O_{2max}$) exercise respiratory rate was five-fold greater in hot than in thermoneutral conditions.[20]

An important consequence of the impairment to heat dissipation during exercise in the heat is a decrease in the time to attainment of a critical upper limit in core body temperature. In humans, it is clearly established that time to exhaustion in trained subjects during exercise in the heat is inversely related to the initial level of body temperature and directly

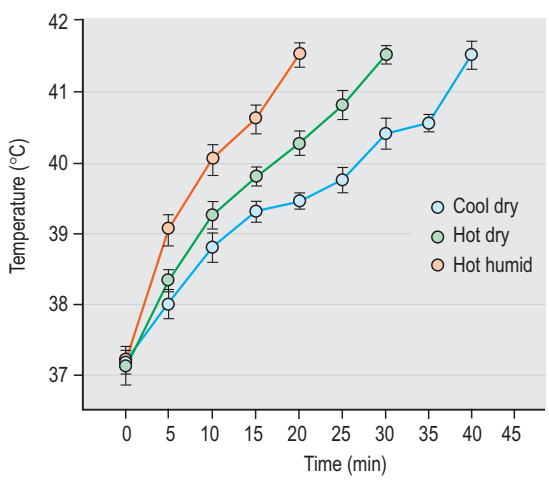


Fig. 41.2
Time course of rise in pulmonary artery blood temperature (T_{pa}) during exercise at 50% of maximal O_2 uptake in cool, dry (room temperature [T] = 20°C; relative humidity [RH] = 45–55%), hot dry (T = 32–34°C, RH = 45–55%), and hot, humid (T = 32–34°C, RH = 80–85%) ambient conditions. Exercise was discontinued when T_{pa} reached 41.5°C. (Adapted from Geor et al.[13])

related to the rate of heat storage.[31] That the lowering of core temperature prior to the start of exercise[32] or cooling the body during the period of exercise[33] will delay attainment of the critically high body temperature and extend exercise duration is further evidence for the relationship between body temperature and exercise performance.

Several factors may contribute to a decrease in performance when exercise is undertaken in hot versus cool conditions. These include the effects of hyperthermia on brain and muscle function, and compromise of cardiovascular and respiratory function. There appears to be a critical body temperature above which mammals will not continue to exercise voluntarily, likely a protective mechanism to protect the human or animal from reaching tissue temperatures that harm cell function.[28] Thus, a more rapid attainment in critical body temperature will translate to a reduction in exercise duration. In trained humans exercising over a range of work intensities in the heat, voluntary fatigue occurs at a core (esophageal) temperature of 39.7–40.0°C.[31,34–36] Furthermore, following heat acclimation procedures that enhance thermoregulatory mechanisms and reduce the rate of heat storage during exercise, the core temperature at the onset of fatigue is unchanged.[35,37] Measurements of central blood (pulmonary artery) temperature in horses during heavy exercise have demonstrated that fatigue occurs as blood temperature approaches 42.5–43°C;[19,38] muscle temperature may reach 44–45°C during such high-intensity exercise. Hypothalamic blood temperature, on the other hand, is approximately 1°C lower than central blood temperature in horses during heavy exercise in moderate ambient conditions.[15] The difference between the temperatures in these two regions provides evidence for the existence of a mechanism for selective brain cooling in the horse. Particularly during exercise in the heat, the onset of fatigue at some critical upper limit in brain temperature may represent a mechanism to avoid heat stroke.

Human studies, dating back to the work of Asmussen and Boje,[39] have indicated that a moderately elevated, but steady-state core body temperature is advantageous to muscle function and to the dissociation of oxygen from red blood cells within muscle tissue. The increase in muscle temperature acts on glycolytic and glycogenolytic enzymes, altering flux rate through these pathways.[40,41] This Q_{10} effect is accentuated during exercise in the heat. However, at high muscle temperature (> 46°C) deleterious structural and functional alterations in skeletal muscle proteins can be induced.[42] These proteins play essential roles in mitochondrial respiration, regulation of calcium by the sarcoplasmic reticulum and the subsequent interactions of myosin and actin, and control of electrolyte movement across the sarcolemma.[31,43] As a consequence, substantial detrimental alterations to skeletal muscle metabolism may occur with elevation of muscle temperature to this critical range.

During exercise heat stress, circulatory adjustments must be regulated to maintain adequate blood flow to contracting muscle and to the thermoregulatory tissues, particularly the skin and the upper respiratory tract.[10] Given a finite cardiac output, the increased demands for blood flow to these thermoregulatory tissues may compromise blood flow to skeletal muscle, thereby limiting oxygen delivery and, possibly, exercise duration. Recent studies in ponies have provided data on the effects of environmental heat load (41°C dry bulb) on the redistribution of cardiac output during exercise.[20] Blood flow to the fore and hind limbs during moderate (~ 30% $\dot{V}o_{2max}$) and high-intensity (~ 65% $\dot{V}o_{2max}$) exercise was reduced by as much as 25–30% when compared to similar exercise in thermoneutral conditions. This reduction in muscle blood flow during exercise heat stress is likely to restrict performance and contribute to an early onset of fatigue.

A reduction in maximal aerobic power is another potential reason for decreased physical performance during exercise in the heat. A reduction in peak oxygen uptake has been demonstrated in human subjects exercising in the heat.[44–46] When non-heat acclimatized horses performed an incremental treadmill exercise test in hot, humid conditions (temperature 30°C, relative humidity 75%), peak expired minute ventilation, oxygen uptake and oxygen pulse were significantly lower and plasma lactate concentrations higher when compared to exercise in temperate conditions (15°C, 55% relative humidity).[47] Although the mechanism of the reduction in peak oxygen uptake in horses exercising in heat and humidity has not been determined, it is possible that alterations in breathing strategy that favor heat loss from the upper respiratory tract (dead space ventilation) and compromise of skeletal muscle blood flow result in decreased oxygen uptake and delivery. Regardless of mechanism, such a reduction in peak oxygen uptake is likely to impair performance relative to exercise performed in temperate conditions.

Physiologic factors affecting thermoregulatory capacity

The term 'exercise heat tolerance' refers to an ability to withstand high internal and external heat loads during exercise. In humans it is well recognized that high aerobic fitness and a period of acclimatization in the heat improves both physiological and psychological responses to the challenge of exercise in the heat.[48] Adaptations in heat dissipatory mechanisms improve cardiovascular stability, decrease the rate of heat storage, and increase the duration of exercise before volitional fatigue. However, highly trained athletes are also able to tolerate higher levels of hyperthermia when compared to untrained individuals, that is, volitional fatigue occurs at a higher core temperature.[49] Conversely, regardless of training or heat acclimatization dehydration decreases exercise heat tolerance, as evidenced by an increase in the rate of heat storage and the development of volitional fatigue at a lower level of hyperthermia. There is now evidence that these physiological factors also modify the thermoregulatory capacity of horses. Specifically, conditioning and heat acclimatization improve tolerance to exercise in the heat,

whereas dehydration adversely affects heat dissipation in horses during exercise.

Other factors that can influence thermoregulation in exercising horses include coat color and the density of the hair coat. Coat color will affect the quantity of solar heat absorbed, while a long hair coat will limit evaporative heat loss.

Conditioning

Physical training in a cool environment is broadly accepted to improve exercise heat tolerance. The extent to which heat dissipatory effector mechanisms are stimulated and the duration of that stimulus will determine the effectiveness of training in improving exercise-heat tolerance. Detectable changes in heat tolerance are evident in human athletes after 1 to 2 weeks of training but are much more substantial if regular training is sustained for 8 to 12 weeks.[50–53] In human subjects, the stimulus must be sufficient to elevate core temperature by approximately 1.5 to 2.0°C for a minimum of 30 min/day.[50,52,53]

At a given percent of maximal oxygen uptake ($\dot{V}O_{2max}$), trained athletes have a higher metabolic rate and, hence, greater heat production at any given relative exercise intensity. Despite this higher metabolic rate, the trained individual is able to maintain a similar core temperature when compared to the untrained subject indicating an enhanced ability to dissipate heat. Improved cutaneous blood flow and whole-body sweating has been measured in trained individuals and are the main contributions to more effective heat dissipation in human subjects.[54] However, highly trained human athletes have been shown to have less extensive sweat fluid losses during exercise[55,56] and there is evidence for similar sweating economy in horses following training.[57] Specifically, 8 weeks of moderate intensity treadmill conditioning resulted in a 1.6-fold increase in sweating sensitivity and an approximately 0.7°C decrease in sweating threshold in horses during exercise in hot, dry conditions (temperature 32–24°C, relative humidity 45–55%). Despite higher sweating rates for a given core temperature during exercise, decreases in recovery sweating rates resulted in an overall reduction in sweat fluid losses (Fig. 41.3).[57] This enhancement in sweating economy as a result of training may assist in minimizing demands placed on the circulatory system by reducing the extent of dehydration associated with fluid losses. Alterations in sweat composition following training in horses appear to reflect changes in the rate of sweat production rather than a modification of the sweat gland itself.[23,57]

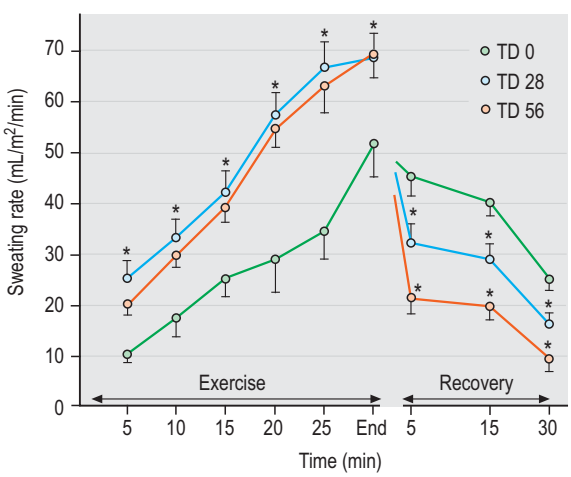


Fig. 41.3
Mean sweating rate for five horses averaged for 5-min intervals during an exercise test in hot, dry conditions (32–34°C and 45–55% relative humidity) at 50% of maximal O_2 uptake ($\dot{V}O_{2max}$) on training days (TD) 0, 28, and 56 of an 8-week training regimen. *Significantly different from TD 0 ($P < 0.05$). (Data from McCutcheon and Geor.[57])

Improvements to cardiovascular function are one of the hallmarks of training. The increase in plasma volume, stroke volume and cardiac output all contribute to increased cardiac stability during exercise and in particular, a lower heart rate at the same work output.[58] Expanded plasma volume in the trained athlete also improves thermoregulatory capacity by reducing the extent to which cutaneous blood flow is compromised. Increased resting plasma volume reduces the risk of a fall in cardiac output during exercise in the face of the decline in plasma volume associated with sweat fluid losses. In studies of human subjects, Roberts et al[59] observed earlier onset of cutaneous vasodilation in trained individuals. Similarly, in more recent work, Fritzsche and Coyle[54] demonstrated that cutaneous blood flow was higher in trained than in untrained individuals at the same relative work load despite similar core (esophageal) body temperatures. In the horse, as in human subjects, enhanced capacity for heat dissipation is, in part, a reflection of an expansion of blood volume[60] and likely a higher proportion of blood flow directed to the skin surface.

The time course of decay in training-induced thermoregulatory adaptations after the onset of detraining has not been determined in horses. In humans there is a strong association between aerobic fitness and exercise-heat tolerance, and the decline in thermoregulatory function with detraining tends to parallel the reduction in aerobic fitness.[49,50]

Heat acclimatization

The term 'acclimatization' is used to describe adaptive changes that occur when a subject undertakes repeated, prolonged exposure to severe environmental conditions (*acclimation* refers to the adaptations produced in controlled laboratory conditions). In the context of the present discussion, hot conditions are normally considered those that will induce the greatest thermoregulatory challenge for horses. As indicated previously, exercise training in a cool environment improves physiological responses when horses exercise in hot conditions. The adaptive responses to training and acclimatization are qualitatively the same. However, the more profound thermal stimulus used during acclimatization will

result in thermoregulatory adaptations of a greater magnitude.[60,61] Furthermore, factors that modify the environment in which acclimatization is undertaken will influence the extent of alterations. These differences are apparent in the higher rate of sweat production during exercise when acclimatization occurs in hot, dry versus hot, humid conditions.[62]

Human studies have demonstrated that the process of heat acclimation begins within a few (3–5) days of regular exposure to and exercise in the heat, with most adaptations complete within a 14-day period.[35,37,50,52,61] The most notable changes are an increase in plasma volume, a decrease in heart rate and core temperature during exercise, an increase in sweating rate and initiation of sweating at a lower body temperature, and redistribution of cardiac output such that there is an increase in blood flow to capillary beds of the skin. In general, the cardiovascular adaptations are complete during the first week of acclimation, whereas alterations in sweating responses require 10 to 14 days of repeated heat exposure.[60,61] Heat acclimation also may result in an improved efficiency of biochemical energy transformation in contracting muscles, thereby attenuating heat production in the acclimated versus unacclimated state.[26]

In horses, there is evidence that regular exercise in the heat results in physiological adaptations that are consistent with thermal acclimation. Marlin and coworkers[38] subjected 5 horses to 15 consecutive days of treadmill exercise in 30°C and 85% relative humidity. Training consisted of a combination of low, medium and high intensity exercise, with a total duration of exercise-heat exposure of 80 min per day. Before and after acclimation, horses undertook a treadmill exercise test designed to simulate the speed and endurance test of a three-day event at 30°C and 85% relative humidity. Following acclimation, four of the five horses were able to complete a significantly greater amount of phase D in the exercise test (pre: 6.3 ± 0.3 min; post: 7.3 ± 0.3 min; target time = 8 min), suggesting an improvement in heat tolerance. Resting body temperatures (rectal, pulmonary artery, tail skin) were lower after acclimation, whereas plasma volume was unchanged.[38]

In another study, six conditioned horses were exposed for 4 h to heat and humidity (temperature 33–35°C, relative humidity 80–85%) for 21 days.[63–66] One hour of low- and moderate-intensity treadmill exercise (30–60% $\dot{V}O_{2max}$) was completed during daily heat exposure. At regular intervals during the 21-day period, horses undertook a standardized submaximal (50% $\dot{V}O_{2max}$) exercise test in the same environmental conditions. In addition, before and after 18 days of acclimation, the horses performed the same exercise test in hot, dry conditions (relative humidity 45–50%). Exercise duration was defined as the time taken for attainment of a pulmonary artery blood temperature of 41.5°C. Similar to the findings of Marlin et al[38] there were significant decreases in resting body temperatures after 5–7 days of heat acclimation. However, in contrast to Marlin's findings, there was a 7–10% increase in plasma volume during the first week of heat acclimation. Thereafter, plasma volume tended to decrease and was not different from preacclimation values at the end of the experimental period.[65] There was a 25% increase in exercise duration when comparing trials performed in the hot, dry conditions before and after acclimation (Fig. 41.4). However, heat acclimation did not increase

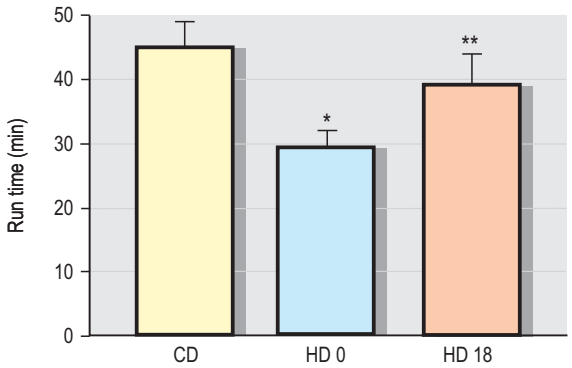


Fig. 41.4
Mean ± SE exercise duration during a standardized exercise test (SET) at 50% maximal O_2 uptake ($\dot{V}O_{2max}$) in cool dry (CD; room temperature [T] = 20°C; relative humidity [RH] = 45–55%) and hot dry conditions (T = 32–34°C, RH = 45–55%) before (HD 0) and after 18 days of heat acclimation (HD 18). *Significantly different from CD and HD 18; **significantly different from HD 0 ($P < 0.05$). (Data from Geor et al.[64])

Table 41.2. Run time during treadmill exercise in hot and humid conditions, pre-exercise body mass and change in body mass on days 0, 3, 7, 14 and 21 of heat acclimation in trained Thoroughbred horses

	Run time (min)	Body mass (kg)	Total sweat fluid loss associated with SET (L)	Sweat loss during exercise (mL)	% of total loss (exercise)	Sweat loss during recovery (ml)	% of total loss (recovery)
Day 0	19.09 ± 1.41	454.1 ± 11.7	11.67 ± 1.23	3844 ± 380	33.8 ± 2	7413 ± 953	66.2 ± 2
Day 3	20.92 ± 1.98	452.0 ± 12.0	12.00 ± 0.86	4179 ± 645	38.0 ± 4	6452 ± 818	62.1 ± 4
Day 7	19.59 ± 1.70	449.5 ± 11.5	11.50 ± 0.99	4324 ± 756	39.8 ± 3	5772 ± 875	59.8 ± 3
Day 14	20.42 ± 1.78	449.7 ± 10.1	10.08 ± 1.31	4451 ± 577	41.7 ± 3*	5323 ± 444	58.0 ± 3*
Day 21	19.61 ± 1.86	445.7 ± 8.7	8.67 ± 0.71*	4452 ± 490	50.7 ± 3*	4193 ± 435*	49.1 ± 3*

Values are mean ± SE for six horses. Run time represents duration of exercise at 50% $\dot{V}O_{2max}$ to attainment of a pulmonary artery temperature of 41.5°C. Total sweat fluid loss includes exercise and 1 h of recovery. Exercise includes exercise at 50% $\dot{V}O_{2max}$ only. Recovery includes 1 h of recovery only.
SET, standardized exercise test. *Significantly different from *day 0*, $P < 0.05$.

exercise duration in the hot, humid environment,[64] further emphasizing the biophysical limitations to heat dissipation in such conditions ('uncompensable heat stress').

Sweating rates greatly exceeded evaporative capacity throughout the 21-day period of humid heat exposure, as evidenced by profuse drippage of sweat from the body. In contrast to the findings of some studies in human subjects, whole-body sweat loss was attenuated with repeated heat exposure. Although sweating rates were slightly higher during exercise after acclimation, a more rapid abatement of sweating during the recovery period after exercise resulted in a significant reduction in overall sweat losses (Table 41.2). Similarly, calculated sweat ion losses were 26% lower after acclimation, for the most part a result of a 10% decrease in mean sweat sodium concentration. The more rapid decline in sweating rate during recovery may represent an adaptive mechanism for conservation of water and ions. An increase in respiratory heat loss as a result of humid heat acclimation, evidenced by an increase in postexercise respiratory rate, may have partially offset the decrease in cutaneous heat loss during the recovery period.[63,64]

In summary, horses undergo a number of physiological adaptations to repeated cycles of exercise heat stress that are consistent with a heat acclimation response. These adaptations are evident after 7–14 days and appear to confer a modest improvement in tolerance for exercise in the heat although, similar to observations in man,[37] this improvement is largely negated when exercise is performed in uncompensable heat stress conditions (high heat and humidity).

The physiologic adaptations associated with acclimatization to heat will diminish in the absence of the thermoregulatory stimulus. In human subjects, the rate of decay is reported to vary from one to several weeks[61,62] In physically fit individuals, there is a slower rate of decay of the thermoregulatory adaptations emphasizing the importance of exercise training in augmenting the benefits of heat acclimatization.[63] The time course of the decay in thermoregulatory adaptations in horses has not been reported.

Hydration state

Prolonged exercise, particularly when it is performed in hot and humid ambient conditions, can result in large fluid deficits that limit thermoregulatory and cardiovascular function. Studies in humans have demonstrated that dehydration of as little as 2–3% of body weight can impair heat transfer from the body core to the periphery, decrease sweating sensitivity (the increase in sweating rate per unit increase in core temperature), and increase the rate of rise in core body temperature during exertion.[67–69] Furthermore, dehydration decreases exercise heat tolerance such that fatigue occurs at a lower core temperature when compared to exercise undertaken in the euhydrated state.[70,71] In horses during 40 min of exercise eliciting 40% $\dot{V}O_{2max}$, pre-exercise dehydration (4% of body weight) induced by water with-holding or furosemide administration decreased cardiac output and increased pulmonary artery blood and middle gluteal muscle temperatures (by approximately 1°C) when compared to the euhydrated state. Peak sweating rates during exercise were not affected by hydration state.[72] The authors concluded that the dehydration-induced impairment of thermoregulation was primarily due to a decreased transfer of heat from core to periphery.

The effects of dehydration on thermoregulatory function in horses are magnified during exercise in the heat. During 90 min of treadmill running at 50% $\dot{V}O_{2max}$ under hot ambient conditions (room temperature 33–35°C; relative humidity 50–55%), progressive dehydration equivalent to 6–8% of body weight was associated with decreases in stroke volume, cardiac output and sweating rate, and higher blood, muscle and rectal temperatures when compared to trials in which hydration state was maintained by the administration of oral fluid equivalent to approximately 85% of the incurred sweat fluid losses.[27] In summary, pre-exercise dehydration or the progressive dehydration incurred as a result of sweat fluid losses during prolonged exercise will impair thermoregulation in horses. This impairment of thermoregulation will be reflected by a more rapid rise in body temperature. Such an exacerbation of hyperthermia would be expected to reduce exercise capacity due to earlier attainment of a critical upper limit in core and brain temperatures.

Old age

Almost all the studies that have addressed thermoregulatory responses to exercise in horses have used young subjects.[6,13,19,38,57] As a result, there are very limited data on the effects of age on thermoregulatory function during activity in older horses. McKeever and coworkers[73] demonstrated the older horses had higher heart rates and attained a core body temperature of 40°C in approximately 50% less time than younger mares when both groups were required to work at the same absolute work output (1625 watts). Despite their inability to dissipate heat load at a similar rate during exercise when compared to the younger mares, the older horses had similar heart rates and core temperatures 10 min post exercise.[73,74]

In human studies, older subjects have been shown to have lower total body water and plasma volume and, as a result, will have a smaller fluid volume that is available to produce sweat.[75,76] There is some suggestion that older subjects are chronically hypohydrated and that these age-related alterations in fluid and electrolyte status will add to an age-related reduction in thermoregulatory capacity. However, based on the limited data available regarding older horses, it appears that the fluid shifts during exercise are of similar magnitude in the aged and young horses.[73,74]

The sweating rate in older horses has been determined to be higher when working at the same absolute work intensity as younger mares. However, it would appear that this increased sweating rate did not improve the ability of the older horses to dissipate heat when compared to their younger counterparts. This could suggest that higher sweating rates occurred in the presence of lower skin blood flow in

older versus younger horses.[73] An apparent decline in maximal heart rate and stroke volume measured in older horses may contribute to this reduced heat dissipatory capacity.[77,78] While skin blood flow measurements were not undertaken in these studies, impaired cutaneous blood flow has been demonstrated in older human subjects in response to exercise.[76] The mechanism for this age-related change in skin blood flow has not been determined. Chronic hypohydration and a concomitant decrease in plasma volume have been suggested as a contributing factor for differences in thermoregulatory capacity in older versus young human subjects.[75,76] In one study, pre-exercise plasma volume was lower in old when compared to younger mares.[73] This relative hypovolemia could impair the thermoregulatory responses of older horses.[74]

Recommendations for preparation for exercise or competition in hot conditions

Although it is not possible to eliminate the effects of adverse effects of environmental conditions on exercise performance, there is evidence from human and animal (including equine) studies that a thorough exercise training program together with a subsequent period of acclimatization will mitigate the impact of the environment. Careful planning is needed for horses transported from a temperate to a hot, humid climate, and then required to train and compete in the hot environment. These horses should attain a high level of event-specific fitness before the trip, and be given adequate time for acclimatization to exercise in the hotter conditions. The hair coat should be clipped to facilitate cutaneous heat loss.[79] For the 1996 Olympic Games in Atlanta, Georgia, the International Equestrian Federation recommended that horses arrive approximately 3 weeks in advance of the events. This recommendation was based on research studies[38,63–66] that demonstrated physiological adaptations consistent with heat acclimatization after 14 consecutive days of exercise conditioning in heat and humidity. Minimal training was recommended in the first week, to allow horses to recover from the effects of prolonged transportation. There should not be the expectation of conducting the major portion of a horse's conditioning during this period.

Initially, only light exercise should be undertaken during the heat of the day, with harder workouts performed during cooler periods, e.g. early morning. Subsequently, there should be a gradual increase in the duration and intensity of exercise performed in the heat. It is important that some exercise be performed at the intensity required of the horse during competition. Careful clinical monitoring is required to assess successful adaptation to the environment. Collection of detailed clinical data should begin 1 to 2 weeks before travel to the hotter climate. These data will provide baseline information against which to compare clinical responses during initial days of training in the hot conditions. In addition, evaluation of this information will provide an objective assessment of how well the horse is adapting to the hot environment. Water and feed intake should be measured on a daily basis. Heart rate, respiratory rate, and rectal temperature should be recorded before and after training sessions. The intensity of work efforts can be estimated by use of a heart rate monitor. Daily weighing is useful for estimation of the extent of fluid losses associated with travel and training.

Assuming similarity in the duration and intensity of exercise bouts undertaken in both cool and hot ambient conditions, the exercise-induced increase in rectal temperature will serve as an indicator of the added thermal burden associated with the hotter conditions. The monitoring of post-exercise rectal temperature is critical to early detection of heat exhaustion and other heat illnesses. As there is a lag in the rise in rectal temperature, particularly after heavy exercise in hot and humid conditions, it is important to continue to monitor rectal temperature during the first 5 to 10 min after exercise. A rectal temperature that exceeds 42°C (108°F) indicates the need for immediate and vigorous cooling. Hyperthermia of this magnitude also may signal the need for a reduction in the intensity or duration of exercise in the hot ambient conditions. There may be an increase in resting respiratory rate following the transition from cool to hot ambient conditions. This increase reflects the thermoregulatory role of the respiratory system. Similarly, the postexercise respiratory rate is typically 30–40% higher following exercise in hot ambient conditions than in cool to moderate environments. In very hot and humid conditions (temperature of 33–35°C, relative humidity 60–75%), particularly when the horse is not cooled by the application of cold water, the respiratory rate may remain increased (up to 80–100 breaths/min) for 20–30 min after exercise. Persistence of tachypnea after the horse is placed in a cooler environment or is vigorously cooled may indicate that body temperature is still markedly elevated.

Maintenance of fluid and electrolyte balance is important for successful adaptation to a hot environment. Indeed, studies in humans have demonstrated that any thermoregulatory benefits derived from heat acclimation are overwhelmed by the elevated heat stress imposed by hypohydration.[61,71] The first concern is the fluid deficit resulting from the period of transport to the new location. Even when access to food and water is maintained during travel, horses typically incur a substantial loss of weight (approximately 3 kg/h of transport). Fluid losses will be higher during road transport in hot weather. As many horses drink poorly during the initial days in a new environment, this dehydration may persist for 3 to 4 days after arrival. Oral or intravenous fluid support is often provided to recently transported horses in an attempt to hasten correction of fluid balance. Dehydration of as little as 2–3% of body weight not only impairs thermoregulation and exercise performance but also prevents the expansion in plasma volume that typically occurs during the early phases of heat acclimatization. Thus, it is imperative that dehydration is corrected before commencement of training in the heat.

Given the increased fluid losses associated with a period of exercise training in a hot climate, an increase in daily water

consumption is to be anticipated. A 30 to 50% increase in 24-h water consumption was observed in horses undergoing heat acclimation; this change occurred within 10 days of the start of heat exposure and largely reflected an increase in water consumption in the 1-h period after exercise.[63]

Electrolyte or salt supplementation is recommended for horses training and competing in hot climates (see Chapter 40). Fat supplementation has been advocated as a means for reducing thermal stress in horses exercising in hot climates. A high-fat diet (8–10% on a total diet basis) may reduce the heat generated by colonic fermentation when compared to a more traditional diet that is higher in roughage.[5] In addition, lower roughage intake may decrease 'bowel ballast', which may be beneficial during high-intensity exercise. However, the actual effects of these dietary manipulations on thermal load in exercising horses have not been quantified. A limited number of studies have demonstrated that fat supplementation has no effect on fluid and electrolyte balance in horses performing daily exercise in hot conditions (mean daily temperature of 29.2°C).[80,81]

Diseases caused by inadequate thermoregulation

In human medicine, several terms are used to describe syndromes associated with environmental heat exposure or exercise-induced hyperthermia; these include heat stress, heat exhaustion and heat stroke. Heat stress is defined as 'perceived discomfort and physiological strain associated with exposure to a hot environment, especially during physical work', whereas heat exhaustion and stroke refer to mild-to-severe illness that result from exposure to high environmental temperatures or strenuous physical exercise.[82]

As discussed above, heat stress can occur when horses are exercised in warm ambient conditions, wherein physiological strain is evidenced by a more rapid rise in core body temperature, more severe exercise-induced dehydration, and higher heart and respiratory rates during recovery when compared to similar exercise in cool or moderate environments. The horse's prodigious capacity for sweating comes at a cost; high rates of sweat fluid loss can result in moderate to severe dehydration and electrolyte abnormalities that predispose to development of muscle cramping, rhabdomyolysis and synchronous diaphragmatic flutter (SDF). Furthermore, dehydration can impair heat dissipation and contribute to the progression from heat stress to heat exhaustion or heat stroke.

Anhidrosis ('dry coat')

- Defined as an inability to sweat effectively in response to suitable stimuli such as heat or exercise.
- Occurs almost exclusively in horses living in hot or hot and humid climates.
- The mechanism of anhidrosis is not understood, but may involve down regulation of sweat gland β_2-receptors.
- Clinical signs include patchy and inadequate sweating, marked hyperthermia in response to exercise, and delayed recovery of rectal temperature, heart rate and respiratory rate after exercise. Horses with long-standing anhidrosis may exhibit dry and flaky skin with alopecia.
- Exercise during cooler periods of the day, housing the horse in an air-conditioned stall, or relocation to a more temperate climate are possible preventive strategies.

Recognition

History and presenting complaint

Affected horses often present with a history of poor or decreased exercise performance or exercise intolerance. On occasion, a dermatologic abnormality is the initial presenting complaint. An absent or inappropriate sweating response is often not detected by owners and trainers. Instead, they report poor exercise performance, labored breathing after exercise, and deterioration of the hair coat. The condition is normally more evident during hotter summer months.

Physical examination

Affected horses develop the problem in the summer months and usually recommence sweating in the winter. The primary clinical signs of anhidrosis reflect inadequate cutaneous evaporative heat loss, and include failure to sweat, tachypnea at rest, elevated rectal temperature, and a delayed postexercise recovery in rectal temperature and respiratory rate. Tachypnea (> 60–80 breaths per min) with marked nostril flare can persist for 60 or more minutes after exercise. Affected horses may seek shade or attempt to cool themselves with water (e.g. stand in water troughs), particularly during the heat of the day.

The degree of anhidrosis is variable, ranging from partial sweat production to complete absence of sweating. Body areas that may retain the ability to sweat include under the mane, the saddle and halter regions, and the axillary, inguinal and perineal regions. Sweat gland density is highest in these regions, and these areas appear to the last affected prior to onset of complete anhidrosis. Dermatologic abnormalities in horses with long-standing anhidrosis include a dry, sparse hair coat with excessive scaling and alopecia, particularly of the face, neck and shoulders.

Diagnosis

The diagnosis of anhidrosis is predominantly based on history and repeated demonstration of inadequate sweating in response to adequate thermogenic stimuli. Semiquantitative data on sweating response may be obtained by intradermal skin testing using injection of a specific β_2-agonist such as terbutaline or salbutamol. Serial dilutions (10^{-3} to 10^{-8} [w/v]) of the β_2-agonist and a control saline solution are injected into shaved

areas over the neck. Normal horses sweat in response to all dilutions, usually within 15–20 min of injection. Horses with partial anhidrosis sweat only in response to the highest β_2-agonist concentration, whereas horses with more severe anhidrosis may be refractory to all concentrations. Histological examination of skin sections may be unrewarding, although ultrastructural changes in the sweat glands and surrounding tissues may be evident. These changes include thickening of the basal lamina and connective tissues, and a marked reduction in the number of secretory cell vesicles. The lumen of sweat gland ducts may be obstructed with cellular debris, and luminal microvilli are often absent.

Anhidrosis should be differentiated from respiratory diseases that result in an increase in respiratory rate.

Treatment and prognosis

Therapy

Given the paucity of knowledge as to the underlying mechanisms for the altered pattern and intensity of sweating, no effective treatment has been determined. However, the risk of heat stress and heat stroke can be mitigated by a combination of environmental and management strategies. The only recognized effective treatment is to remove affected horses to a cooler environment, either physically (i.e. move to a more temperate climate) or by the use of air conditioning or other means of assisted cooling. Some change in exercise routine is required. Heavy training and competition during the summer months should be discouraged. On the other hand, anhidrotic horses that are rested during the summer may train and compete successfully during the cooler winter months. Anecdotally, affected horses resume a more normal sweating response as night-time temperatures begin to decline. For horses maintained in exercise training during the summer, workouts should be conducted during cooler periods of the day (e.g. early morning) and they should be cooled aggressively after exercise (e.g. the liberal and repeated application and removal of cool water over the entire body).

A variety of nutritional supplements have been advocated in the treatment of anhidrosis, but objective data on the efficacy of these products is not available. Anecdotally, some veterinarians and trainers have reported that horses with a history of anhidrosis that are treated with electrolyte supplements (especially sodium and potassium) before the onset of hot weather and during the summer months do not develop further episodes of anhidrosis. As tyrosine is thought to be important for the resensitization of β_2-receptors, supplementation with this amino acid has been recommended for horses with anhidrosis. Similarly, some veterinarians have claimed success when affected horses are supplemented with vitamin E (1000–3000 U/day) or iodinated casein (10–15 g/day for 4–8 days).

Prognosis

There is anecdotal evidence that most affected horses respond favorably to a change in environment and begin to sweat normally after a few days to weeks. A complete return to normal sweating function may take 3–4 months in some horses. There are no published reports on the long term follow-up of horses with anhidrosis. However, it is generally believed that horses with a history of anhidrosis will become anhidrotic when again exposed to hot, humid conditions.

Etiology and pathophysiology

The pathophysiological mechanisms underlying anhidrosis are not known. Various factors have been suggested, including electrolyte imbalances, hypothyroidism, sweat gland exhaustion, plugging or blocking of the sweat gland ducts to the surface, failure of secretory function, and a downregulation of glandular sensitivity. The most plausible cause is altered sweat gland receptor function. It is thought that overstimulation of sweat gland β_2-receptors results in diminished function via desensitization or downregulation of the receptors. Even apparently normally sweating horses have reduced sensitivity to intradermal epinephrine (adrenaline) in a hot and humid environment.[83] That many anhidrotic horses once again achieve adequate sweat production upon removal to a cooler climate emphasizes the importance of environmental conditions to the development of clinical disease. One hypothesis is that increased circulating epinephrine (adrenaline) concentrations result in overstimulation of the sweat glands. Beadle et al.[84] reported higher resting epinephrine (adrenaline) concentrations in anhidrotic horses compared with control horses in the same hot and humid climate. However, other studies[83,85] did not detect a difference in epinephrine (adrenaline) concentrations between control and anhidrotic horses.

For the equine athlete, the loss of an adequate sweating response translates into a reduction in the efficacy of heat loss through evaporation and an early and excessive increase in core temperature in response to moderate exercise. Exercise intolerance and poor performance can be attributed to hyperthermia. Increased respiratory rate, both at rest and after exercise, reflect an attempt to dissipate heat via the respiratory tract.

Epidemiology

Anhidrosis is almost exclusive to horses living in hot or hot and humid climates. It is estimated that as much as 20% of the population of athletic horses exercising in hot humid climates experience some degree of anhidrosis. However, more severe signs of anhidrosis are recognized in a smaller percentage of horses.[86] Anecdotally, greater susceptibility is evident in horses bred and raised in cooler climates and transported to a warm and humid climate for training or competition.

Prevention

There is no proven strategy for the prevention of anhidrosis in horses kept in hot and humid climates. However, further

episodes of anhidrosis may be prevented by relocation to a cooler climate. When physical removal from the hot climate is not possible, exercise and environmental management can prevent excessive hyperthermia and minimize the risk of heat stress or stroke.

Heat exhaustion/heat stroke

- Heat illnesses can result from exposure to high environmental temperature (non-exertional heat stroke) or, more commonly, from strenuous exercise (exertional heat stroke) undertaken in hot and/or humid ambient conditions.
- Heat exhaustion is a mild-to-moderate illness characterized by hyperthermia, tachypnea, dehydration, and fatigue. A more severe exhaustion syndrome attributed to the combined effects of hyperthermia, fluid and electrolyte deficits, and substrate depletion occurs in horses undertaking endurance exercise.
- Heat stroke is a severe illness in which there is thermoregulatory failure and development of multiorgan dysfunction, including encephalopathy.
- Clinical features common to heat exhaustion and heat stroke include hyperthermia, tachypnea with panting, tachycardia, evidence of dehydration, and fatigue. Other signs may include reduced sweat production with dry hot skin, synchronous diaphragmatic flutter (SDF), muscle cramps, and colic. With heat stroke, these signs are accompanied by neurologic abnormalities including weakness, ataxia progressing to collapse, convulsions, coma, and death.
- Exhausted horses that have sustained large sweat fluid losses may develop a 'postexhaustion syndrome' characterized by renal failure, laminitis, hepatic failure, myonecrosis and a high mortality rate.
- Therapy includes rapid assisted cooling, intravenous fluids for correction of dehydration and electrolyte and acid–base abnormalities, and judicious use of anti-inflammatory drugs.

Recognition

History and presenting complaint

Heat exhaustion and heat stroke can occur in any environmental condition but are more likely to occur in a hot and humid environment. These conditions should be viewed as a continuum; a state of heat stress can progress rapidly to heat exhaustion or heat stroke. Most often, heat stroke is recognized in association with exercise, particularly when undertaken in hot and humid ambient conditions. Affected horses may have a history of anhidrosis or prior episodes of heat exhaustion. Less commonly, heat stroke may develop in horses confined in closed trailers or buildings during hot weather. Affected horses may present with complaint of fatigue, depression, weakness, stilted gait, respiratory distress, and neurologic abnormalities including seizures.

Physical examination

The clinical signs of heat exhaustion reflect the deleterious effects of hyperthermia, dehydration, hypovolemia, and electrolyte disturbances on the function of many body systems. Hyperthermia (rectal temperature > 41–42°C), elevated heart rate (> 60–80 bpm), rapid, shallow respirations (> 80–100 breaths/min), dehydration, and evidence of fatigue are often present. Horses that have completed prolonged exercise in hot weather (e.g. an endurance race) are often dehydrated and hypovolemic. Therefore, skin elasticity may be decreased, capillary and jugular refill time delayed, and mucous membranes tacky or dry. Cardiac auscultation or electrocardiographic examination may indicate a tachyarrhythmia. Horses may be unwilling to drink despite moderate to severe dehydration. While fatigued, these horses do not necessarily appear depressed, although they might exhibit a slightly stiff gait and possibly lameness in association with muscle cramping or soreness. High metabolic heat load is often reflected in a delayed postexercise recovery of heart and respiratory rates (more than 20–30 min) and excessive sweating. Rectal temperature may continue to rise during the 5–10 min period immediately following the cessation of exercise. Decreased anal tone, muscle cramping and SDF may be evident.

By definition, both hyperthermia and central nervous system dysfunction must be present for a diagnosis of heat stroke. Signs of heat stress or exhaustion are accompanied by evidence of brain dysfunction, including a weak, staggering gait, depression or poor mentation, convulsions and coma. There may be excessive sweating with a uniformly wet hair coat or, especially in dehydrated animals, a hot dry skin with dilated cutaneous vasculature.

A number of serious complications can develop in horses with heat exhaustion or stroke. In horses undertaking prolonged exercise that results in exhaustion, glycogen depletion, and marked fluid and electrolyte deficits, such as endurance rides of 50 to 150 miles, a 'postexhaustion syndrome' characterized by multiorgan dysfunction or failure may develop. These horses may develop laminitis, colic, renal and/or hepatic failure, or myonecrosis in the 1–3-day period after the strenuous exercise. Similarly, horses that recover from the acute phases of heat stroke may develop a syndrome of multiorgan dysfunction characterized by renal and hepatic failure, laminitis, pulmonary edema and respiratory distress, and disseminated intravascular coagulation.

Diagnosis

A number of clinicopathologic abnormalities may be present in horses with heat exhaustion or stroke. Respiratory alkalosis due to hyperventilation is usually present. Metabolic alkalosis or acidosis (lactic acid accumulation) may be present depending on the nature of the exercise performed. There is an increased PCV, Hb, red cell count, and TPP and elevated creatine kinase and aspartate aminotransferase activity and decrease serum electrolytes (P, Cl, Ca [total and ionized], Mg, and possibly Na). A stress neutrophilia and lymphopenia with possible

degenerative left shift and leukopenia in face of impending diarrhea may be evident. Severe dehydration and the possible onset of renal disease may be reflected in elevated blood urea nitrogen and creatinine. Urinalysis may reveal high specific gravity (with dehydration and normal renal function) or low specific gravity when renal disease is present with or without evidence of protein or blood in urine. A clotting profile may indicate disseminated intravascular coagulation (thrombocytopenia, increased fibrin degradation products, and prolonged prothrombin time).

Treatment and prognosis

Therapy

Horses exhibiting signs of heat stroke require immediate and aggressive use of cooling techniques and intravenous fluid administration. The horse should be removed from direct sunlight to minimize further radiative heat gain. Unnecessary tack should be removed and the horse left unblanketed. If available, the horse should be positioned in front of high-output fans to increase convective heat loss. Cold water should be applied to the head, neck and body; this will increase the temperature gradient between the skin and the environment, and therefore increase conductive heat loss. The applied water must be quickly removed by use of a skin scrapper with subsequent application of further cool water to maintain this gradient. Misting fans are sometimes available at competitions held during the summer months; these also assist heat dissipation. Internal cooling techniques, such as the intragastric or rectal administration of cold water may be attempted. However, the latter obviates use of the rectum for monitoring the temperature response to therapy. Assisted cooling should be continued until rectal temperature is less than 39°C.

Large volume intravenous fluid replacement is indicated. Normal saline (0.9% NaCl) is the fluid of choice in cases of metabolic alkalosis, but any balanced polyionic solution (e.g. lactated Ringer's solution) is suitable in the face of hypovolemia and dehydration. As much as 60–80 L of fluid may be required over a 6- to 12-h period in severely dehydrated horses. Subsequent fluid therapy should be guided by clinical assessment and the results of serum biochemical analysis. Supplemental calcium may be required in horses with SDF. Oral fluid therapy may be considered providing the horse has normal gut sounds and no clinical evidence of colic or gastric reflux. Further details on the correction of exercise-induced dehydration and electrolyte disturbances are presented in Chapter 40.

The role of antipyretic and anti-inflammatory agents (e.g. non-steroidal anti-inflammatory drugs [NSAIDS]) in the management of heat stroke is unknown. Animal studies have demonstrated that the correction of hyperthermia after the onset of heat stroke may not prevent inflammation, coagulation, and progression to multiorgan dysfunction. On the other hand, treatment with glucocortocoids and immunomodulators such as interleukin-1 (IL-1) receptor antagonists improves survival in animals with heat stroke.[83] Other studies have shown that salicylates and NSAIDs enhance cellular protection against heat stress via induction of the transcription and translation of heat-shock proteins.[87] Accordingly, there may be rationale for the judicious use of NSAIDs (e.g. flunixin meglumine, 1.0 mg/kg) and glucocorticoids (e.g. methylprednisolone sodium succinate, 2–4 mg/kg i.v.) in horses with heat stroke. NSAIDs should also be administered if the horse has pain associated with colic, exertional rhabdomyolysis, or laminitis.

Rest is paramount and therefore it is advisable to transport the horse back to a stabling area once their condition has been stabilized to avoid the requirement for further exercise. Close clinical monitoring is required for a 3–5-day period after an episode of heat exhaustion or heat stroke. This should include clinical assessment of attitude, appetite, hydration status, gastrointestinal function and digital pulses. Serial measurements of serum biochemistries should also be performed. These evaluations will guide further therapy.

Prognosis

There are no reports of long-term follow-up of horses that have suffered an episode of heat stroke. Clinical experience has indicated that the prognosis for heat stroke is variable depending on severity. The recovery of central nervous system function during cooling is a favorable prognostic sign. On the other hand, persistence of neurologic abnormalities and/or the development of complications such as pulmonary edema, laminitis, renal or hepatic failure and disseminated intravascular coagulation indicate a much poorer prognosis.

Etiology and pathophysiology

A complex interplay of physiological alterations that accompany hyperthermia including circulatory failure, hypoxia, increased metabolic demand, and inflammatory and coagulation responses result in the development of heat stroke and the associated progressive multiorgan dysfunction.[82] Heat stress induces thermoregulatory, heat shock and acute phase responses. Thermoregulatory failure, altered expression of heat-shock proteins and an excessive acute phase response individually or collectively contribute to the development of heat stroke. Studies in animal models have demonstrated increased production of nitrogen or reactive oxygen species with splanchnic hypoperfusion, the result of the diversion of blood flow to the cutaneous circulation and away from the gut.[82] Subsequent mucosal injury and hyperpermeability allows the escape of endotoxin into circulation, further stimulating the acute phase response and the production of pyrogenic cytokines and nitric oxide, both of which can further interfere with thermoregulatory mechanisms. The production of these cytokines and nitric oxide can therefore precipitate hyperthermia, hypotension, and heat stroke (Fig. 41.5).

In addition to the leakage of endotoxin from the intestine, hyperthermia can also lead to the release of IL-1 and IL-6 proteins from muscle. A high level of activation of leukocytes and endothelials cells with subsequent release of pro- and anti-

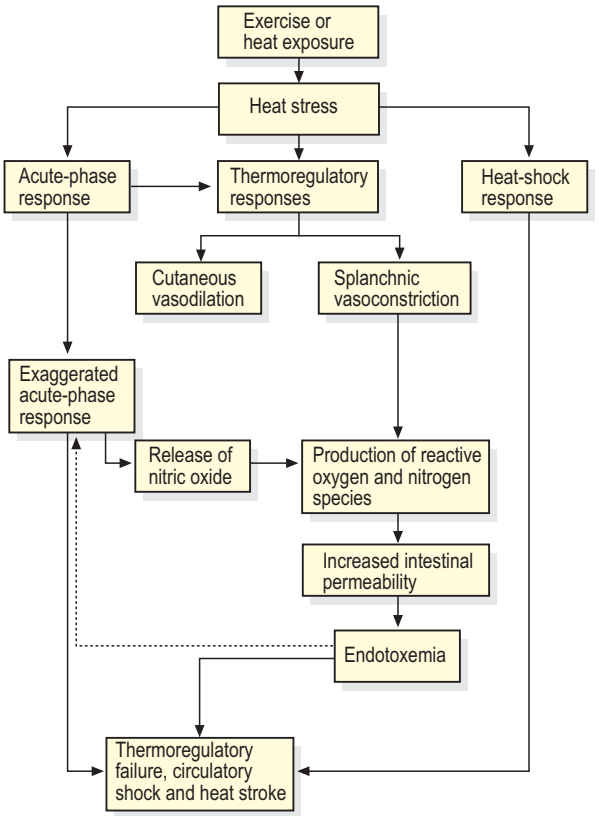


Fig. 41.5
Proposed sequence of events in the development of heat stroke in mammals. Heat stress induces thermoregulatory, acute-phase, and heat-shock responses. The redistribution of cardiac output to accommodate cutaneous heat loss results in splanchnic hypoperfusion and ischemia and the increased production of reactive oxygen and nitrogen species. These mediators may induce intestinal mucosal injury and an increase in permeability that allows the entry of endotoxin into circulation. Endotoxin enhances the acute-phase response, leading to production of pyrogenic cytokines and nitric oxide. These mediators can disrupt thermoregulation and precipitate heat stroke. Solid arrows indicate pathways for which there is experimental evidence; broken arrows indicate putative pathways. (Adapted from Bouchama and Knochel.[82])

inflammatory cytokines (IL-1, IL-6, IL-10, tumor necrosis factor α), upregulation of cell-surface adhesion molecules, and shedding of soluble cell-surface adhesion molecules as well as activation of coagulation and inhibition of fibrinolysis. Direct cytotoxic effects to cells and the inflammatory and coagulation responses result in endothelial injury and microthrombosis.[82]

A critical thermal maximum beyond which lethal injury occurs has been determined in several mammalian species.[88] In humans, critical thermal maximum is a core body temperature of 41.6°C to 42°C for 45 min to 8 h. The critical core temperature for horses has not been determined. However, exercise-associated elevation in muscle temperature above 43°C (109.4°F) results in alterations in muscle mitochondria and sarcoplasmic reticulum in horses.[89] As previously discussed, the onset of volitional fatigue in humans occurs at a core (esophageal or rectal) temperature of approximately 40°C, whereas studies in horses indicate that voluntary exhaustion does not occur until core or rectal temperatures of 42°C or greater. It is possible that horses have higher heat tolerance when compared to humans. Alternatively, the thermal limit to exercise may be very similar to that associated with the induction of heat stroke,[28] further emphasizing the need for the close monitoring of horses exercising in warm conditions.

Epidemiology

Epidemiological data on risk factors for heat stroke in horses are not available. However, poor physical conditioning, lack of heat acclimatization, prolonged exercise in hot and humid ambient conditions, dehydration, long hair coat, and obesity are factors that may increase the risk of exertional heat stroke. Horses with a history of anhidrosis are obviously at higher risk for heat stroke. In addition, the heavily muscled breeds (e.g. Warmbloods) may be at higher risk because of a low body mass to surface area ratio.

Prevention

One of the most important criteria for the prevention of heat stress is ensuring that horses have undertaken a training program that is adequate for the level of exercise or competition that will be demanded of them. However, it should be recognized that it is possible to overwhelm the thermoregulatory capacity of horses with a high level of physical conditioning when exercise is prolonged and/or there are adverse environmental conditions that will impair heat dissipatory mechanisms. Under such conditions, seeking shade at stops to reduce solar heating, using fans to improve convective cooling, and frequent, copious application of cool water will reduce the rate at which heat is stored.

As stated previously, an adequate training program will substantially improve thermoregulatory efficiency during exercise. When there is a requirement to compete in severe (i.e. hot) environmental conditions, then acclimatization to hot conditions will further enhance the horse's ability to thermoregulate in adverse conditions. Under such conditions greater attention needs to be paid to ensuring that there are an adequate number of stops during which cooling can take place. The extent of fluid losses can be ameliorated if horses are trained to drink fluids at rest stops during competition. Early recognition of hyperthermia and heat exhaustion with aggressive medical intervention will prevent development of heat stroke.

References

1. Gordon MS, Bartholomew GA, Grinnell AD, et al. Body temperature and energy metabolism. In: Gordon MS, Bartholomew GA, Grinnell AD et al, eds. Animal physiology, ed 4. New York: MacMillan; 1982; 333.

2. Brody S. Bioenergetics and growth. New York: Reinhold; 1945.
3. Kleiber M. The fire of life: an introduction to animal energetics. New York: John Wiley; 1961.
4. Lovatt Evans C. Physiological mechanisms that underlie sweating in the horse. Br Vet J 1966; 122:117–123.
5. Kronfeld D. Dietary fat affects heat production and other variables of equine performance under hot and humid conditions. Equine Vet J 1996; Suppl 22:24–34.
6. Hodgson DR, Davis RE, McConaghy FF. Thermoregulation in the horse in response to exercise. Br Vet J 1994; 150:219–235.
7. Jones JH, Carlson GP. Estimation of metabolic energy costs and heat production during a 3-day event. Equine Vet J 1995; Suppl 20:23–30.
8. Guthrie AJ, Lund RJ. Thermoregulation: base mechanisms and hyperthermia. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids and electrolytes in athletic horses. Philadelphia: WB Saunders; 1998; 14(1):45–59.
9. Ingram DL, Mount LE. Man and animals in hot environments. Berlin: Springer-Verlag; 1975.
10. Rowell LB. Human circulation: regulation during physical stress. New York: Oxford University Press; 1986; 363–407.
11. McCutcheon LJ, Geor RJ, Hare MJ, et al. Sweating rate and sweat composition during exercise and recovery in ambient heat and humidity. Equine Vet J 1995; Suppl 20:153–157.
12. Monteith JL. Specification of the environment for thermal physiology. In: Monteith JL, Mount LE, eds. Heat loss from animals and man. London: Butterworths; 1973; 1–35.
13. Geor RJ, McCutcheon LJ, Ecker GL, et al. Thermal and cardiorespiratory responses of horses to submaximal exercise under hot and humid conditions. Equine Vet J 1995; Suppl 20:125–132.
14. Baptiste KW, Naylor JM, Bailey J, et al. A function for guttural pouches in the horse. Nature 2000; 403:382–383.
15. McConaghy FF, Hales JRS, Rose RJ, et al. Selective brain cooling in the horses during exercise and environmental heat stress. J Appl Physiol 1995; 79:1849–1854.
16. Jenkinson D McE. Thermoregulatory function. In: Thody AJ, Friedman PS, eds. Scientific basis of dermatology. Edinburgh: Churchill Livingstone; 1986; 89–95.
17. McCutcheon LJ, Geor RJ. Sweat fluid and ion losses during training and competition in cool vs. hot conditions: implications for ion supplementation. Equine Vet J 1996; Suppl 22:54–62.
18. Carlson GP, Ocen PO. Composition of equine sweat following exercise in high environmental temperatures and in response to intravenous epinephrine administration. J Equine Med Surg 1979; 3:27–32.
19. Hodgson DR, McCutcheon LJ, Byrd SK, et al. Dissipation of metabolic heat in the horse during exercise. J Appl Physiol 1993; 74:1161–1170.
20. McConaghy FF, Hodgson DR, Hales JR, et al. Thermoregulatory-induced compromise of muscle blood flow in ponies during intense exercise in the heat: a contributor to the onset of fatigue? Equine Vet J Suppl 2002; 34:491–495.
21. Kingston JK, Geor RJ, McCutcheon LJ. Rate and composition of sweat fluid losses are unaltered by hypohydration during prolonged exercise in horses. J Appl Physiol 1997; 83: 1133–1143.
22. McCutcheon LJ, Geor RJ. Sweating: fluid and ion losses and replacement. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids and electrolytes in athletic horses. Philadelphia: WB Saunders; 1998; 14:75–95.
23. McConaghy FF, Hodgson DR, Evans DL, et al. Effects of two types of training on sweat composition. Equine Vet J 1995; Suppl 18:285–288.
24. Carlson GP. Thermoregulation, fluid and electrolyte balance. In: Snow DH, Persson GB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 291–309.
25. Nadel ER. Temperature regulation and prolonged exercise. In: Gisolfi CV, Lamb DR, Nadel ER, eds. Perspectives in exercise science and sports medicine. Exercise, heat, and thermoregulation. Dubuque, IA: Brown; 1988; 125–146.
26. Geor RJ, McCutcheon LJ. Thermoregulatory adaptations associated with training and heat acclimation. In: Hinchcliff KW, ed. Veterinary Clinics of North America: equine practice; fluids and electrolytes in athletic horses. Philadelphia: WB Saunders; 1998; 14:97–120.
27. Geor R, McCutcheon LJ. Hydration effects on physiological strain of horses during exercise-heat stress. J Appl Physiol 1998; 84:2042–2051.
28. Lindinger ML. Exercise in the heat: thermoregulatory limitations to performance in humans and horses. Can J Appl Physiol 1999; 24:135–146.
29. Kohn CW, Hinchcliff KW. Physiological responses to the endurance test of a 3-day event during hot and cool weather. Equine Vet J 1995; Suppl 20:31–36.
30. McConaghy FF, Hodgson DR, Rose RJ, et al. Redistribution of cardiac output in response to heat exposure in the pony. Equine Vet J 1996; Suppl 22:42–46.
31. Gonzalez-Alonzo J, Teller C, Andersen SL, et al. Influence of body temperature on the development of fatigue during prolonged exercise in the heat. J Appl Physiol 1999; 86:1032–1039.
32. Lee DT, Haymes EM. Exercise duration and thermoregulatory responses after whole body precooling. J Appl Physiol 1995; 79:1971–1976.
33. MacDougall JD, Reddan WG, Layton CR, et al. Effects of metabolic hyperthermia on performance during prolonged heavy exercise. J Appl Physiol 1974; 36:538–544.
34. Gonzalez-Alonso J, Mora-Rodriguez R, Below PR, et al. Dehydration markedly impairs cardiovascular function in hyperthermic endurance athletes during exercise. J Appl Physiol 1997; 82:1229–1236.
35. Nielsen B, Hales JRS, Strange S, et al. Human circulatory and thermoregulatory adaptations with heat acclimation and exercise in a hot, dry environment. J Physiol (Lond) 1993; 460:467–485.
36. Nielsen B, Savard G, Richter EA, et al. Muscle blood flow and muscle metabolism during exercise and heat stress. J Appl Physiol 1990; 69:1040–1046.
37. Nielsen B, Strange S, Christensen N, et al. Acute and adaptive responses to exercise in a warm, humid environment. Pflug Arch 1997; 434:49–56.
38. Marlin DJ, Scott CM, Schroter RC, et al. Physiological responses of horses to a treadmill simulated speed and endurance test in high heat and humidity before and after humid heat acclimation. Equine Vet J 1999; 31:31–42.
39. Asmussen E, Boje O. Body temperature and work capacity. Acta Physiol Scand 1945; 10:1–22.
40. Kozlowski S, Brzezinska Z, Kruk B, et al. Exercise hyperthermia as a factor limiting physical performance: temperature effect on muscle metabolism. J Appl Physiol 1985; 59:766–673.
41. Young AJ. Energy substrate utilization during exercise in extreme environments. Exer Sports Sci Rev 1990; 18:65–117.
42. Brooks GA, Hittelman KJ, Faulkner JA, et al. Temperature, skeletal muscle mitochondrial functions, and oxygen debt. Am J Physiol 1971; 220:1053–1059.

43. Willis WT, Jackman MR. Mitochondrial function during heavy exercise. Med Sci Sports Exerc 1994; 26:1347–1354.
44. Galloway SD, Maughan RJ. Effects of ambient temperature on the capacity to perform prolonged cycle exercise in man. Med Sci Sports Exerc 1997; 29:1240–1249.
45. Febbraio MA. Temperature, muscle metabolism and performance. In: Lamb DR, Murray R, eds. Perspectives in exercise science and sports medicine. carmel, In: Cooper Publishing; 1999; 315–354.
46. Nybo L, Jensen T, Nielsen B, et al. Effects of marked hyperthermia with and without dehydration on VO_2 kinetics during intense exercise. J Appl Physiol 2001; 90:1057–1064.
47. Art T, Leukeux P. Respiratory adjustments in unacclimatised horses exercised under hot, humid conditions. Equine Vet J 1995; Suppl 18:289–293.
48. Aoyagi Y, McLellan TM, Shephard RJ. Effects of 6 versus 12 days of heat acclimation on heat tolerance in lightly exercising men wearing protective clothing. Eur J Appl Physiol 1995; 71:187–196.
49. Cheung SS, McLellan TM. Heat acclimation, aerobic fitness, and hydration effects on tolerance during uncompensable heat stress. J Appl Physiol 1998; 84:1721–1739.
50. Armstrong LE, Pandolf KB. Physical training, cardiorespiratory fitness and exercise heat tolerance. In: Pandolf KB, Sawka MN, Gonzalez RR, eds. Human performance physiology and environmental medicine at terrestrial extremes. Indianapolis: Benchmark; 1988; 199–226.
51. Gisolfi GV. Work-heat tolerance derived from interval training. J Appl Physiol 1973; 35:349–354.
52. Gisolfi GV. Influence of acclimatization and training on heat tolerance and physical endurance. In: Hales JRS, Richards DAB, eds. Heat stress: physical exertion and environment. Amsterdam: Elsevier Science; 1987; 355–366.
53. Gisolfi GV, Cohen JS. Relationships among training, heat acclimation, and heat tolerance in men and women: the controversy revisited. Med Sci Sports 1979; 11:56–59.
54. Fritzsche RG, Coyle EF. Cutaneous blood flow during exercise is higher in endurance-trained humans. J Appl Physiol 2000; 88:738–744.
55. Araki T, Matsushita K Umeno K, et al. Effect of physical training on exercise-induced sweating in women. J Appl Physiol 1981; 51:1526–1532.
56. Yamauchi M, Matsumoto T, Ohwatari N, et al. Sweating economy by graded control in well-trained athletes. Eur J Physiol 1997; 433:675–678.
57. McCutcheon LJ, Geor RJ. Influence of training on sweating responses during submaximal exercise in horses. J Appl Physiol. 2000; 89:2463–2471.
58. Convertino VA. Blood volume: Its adaptation to endurance training. Med Sci Sports Exerc 1991; 23:1338–1351.
59. Roberts MF, Wenger CG, Stolwijk JAJ, et al. Cutaneous blood flow and sweating changes following exercise training and heat acclimation. J Appl Physiol 1977; 43:133–137.
60. Armstrong LE, Maresch CM. The induction and decay of heat acclimation in trained athletes. Sports Med 1991; 12:302–312.
61. Wenger CB. Human heat acclimatization. In: Pandolf KB, Sawka MN, Gonzalez RR, eds. Human performance physiology and environmental medicine at terrestrial extremes. Indianapolis: Benchmark; 1988; 153–197.
62. Nadel EF, Pandolf, KB, Roberts MF, et al. Mechanisms of thermal acclimation to exercise and heat. J Appl Physiol 1974; 37:512–520.
63. Geor RJ, McCutcheon LJ, Lindinger MI. Adaptations to daily exercise in hot and humid ambient conditions in trained thoroughbred horses. Equine Vet J 1996; Suppl 22:63–69.
64. Geor RJ, McCutcheon LJ, Ecker GL, et al. Heat storage in horses during submaximal exercise before and after humid heat acclimation. J Appl Physiol 2000; 89:2283–2293.
65. Lindinger MI, McCutcheon LJ, Ecker GL, et al. Heat acclimation improves regulation of plasma volume and plasma Na(+) content during exercise in horses. J Appl Physiol 2000; 88:1006–1013.
66. McCutcheon LJ, Geor RJ, Ecker GL, et al. Equine sweating responses to submaximal exercise during 21 days of heat acclimation. J Appl Physiol 1999; 87:1843–1851.
67. Montain SJ, Smith SA, Mattot RP, et al. Hypohydration effects on skeletal muscle performance and metabolism: a 31P-MRS study. J Appl Physiol 1998; 84:1889–1894.
68. Montain SJ, Coyle EF. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. 1992; 73:1340–1350.
69. Montain SJ, Latzka WA, Sawka MN. Control of thermoregulatory sweating is altered by hydration level and exercise intensity. J Appl Physiol 1995;79:1434–1439.
70. Sawka MN. Body fluid responses and hypohydration during exercise heat stress. In: Pandof KB, Sawka MN, Gonzalaz RR, eds. Human performance physiology and envionmental medicine at terrestrial extremes. Indianapolis: Benchmark; 1988; 227–266.
71. Sawka MN, Toner MM, Francesconi RP, et al. Hypohydration and exercise: effects of heat acclimation, gender and environment. J Appl Physiol 1983; 55:1147–1153.
72. Naylor JR, Bayly WM, Gollnick PD, et al. Effects of dehydration on thermoregulatory responses of horses during low intensity exercise. J Appl Physiol 1993; 75:994–1001.
73. McKeever KH, Eaton TL, Geiser S, et al. Thermoregulation in old and young horses during exercise. Med Sci Sport Exerc 2000; 32:S156.
74. McKeever KH. Exercise physiology in older horses. In: MacLeay JM, ed. Veterinary Clinics of North America: equine practice; geriatrics. Philadelphia: WB Saunders; 2002; 469–490.
75. Armstrong CG, Kenney WL. Effects of aging and acclimation on responses to passive heat exposure. J Appl Physiol 1993; 75:2162–2167.
76. Kenney WL. Body fluid and temperature regulation as a function of age. In: Lamb DR, Gisolfi CV, Nade ER, eds. Perspectives in exercise and sports medicine, vol 8, exercise in older adults. Carmel, IN: Cooper Publishing; 1995; 305–352.
77. McKeever KH, Kearns CF. Aging-induced alterations in plasma volume in horses. Med Sci Sport Exerc 2001; 33:S257.
78. Betros CL, McKeever KH, Kearns CF, et al. Effects of aging and training on maximal heart rate and VO_{2max}. Equine Vet J 2002; Suppl 34:100–105.
79. Morgan K, Funquist P, Nyman G. The effect of coat clipping on thermoregulation during intense exercise in trotters. Equine Vet J 2002; Suppl 34:564–567.
80. Hower MA, Potter GD, Greene LW, et al. Plasma aldosterone and electrolyte concentrations in exercising Thoroughbred horses fed two diets in summer and winter. J Equine Vet Sci 1995; 15:445–449.
81. Hoyt JK, Potter GD, Greene LW, et al. Electrolyte balance in exercising horses fed a control and a fat-supplemented diet. J Equine Vet Sci 1995; 15:429–433.
82. Bouchama A, Knochel JP. Heat stroke. N Engl J Med 2002; 346:1978–1988.
83. Lovatt Evans C, Smith DFG, Ross KA, et al. Physiological factors in the condition of 'dry coat' in horses. Vet Rec 1957; 69:1–15.
84. Beadle RE, Norwood GL, Brencick VA. Summertime plasma catecholamine concentrations in healthy and

anhidrotic horses in Lousiana. Am J Vet Res 1982; 43:1446–1448.
85. Marlin DJ, Schroter RC, Scott CM, et al. Sweating and skin temperature responses of normal and anhidrotic horses to intravenous adrenaline. Equine Vet J 1999; Suppl 30: 362–369.
86. Warner AE, Mayhew IG. Equine anhidrosis: a survey of affected horses in Florida. J Am Vet Med Assoc 1982; 180:627–630.
87. Polla BS, Bachelet M, Elia G, et al. Stress proteins in inflammation. Ann N Y Acad Sci 1998; 851:75–85.
88. Bynum GD, Pandolf KB, Schuette WH, et al. Induced hyperthermia in sedated humans and the concept of critical hyperthermia. Am J Physiol 1978; 235:R228–R236.
89. Byrd SK, McCutcheon LJ, Hodgson DR, et al. Altered sarcoplasmic reticulum function after high intensity exercise. J Appl Physiol 1989; 76:2072–2077.
90. McCutcheon LJ, Geor RJ, Hare MJ, et al. Sweat composition: Comparison of collection methods and effects of exercise intensity. Equine Vet J Suppl 1995; 18:279–284.

CHAPTER 42

Hematologic and serum biochemical responses to exercise and training

Janene K. Kingston

Blood consists of many components that play an essential role in supporting the increased metabolic rate during exercise by transporting oxygen, water, electrolytes, nutrients, and hormones to working muscles. In addition, carbon dioxide and other waste products produced during exercise are removed from muscle by the circulation. Finally, blood components are important in buffering the acid–base changes associated with exercise. The cellular components of blood include erythrocytes, leukocytes, and platelets, whereas the plasma component is made up of water, electrolytes, plasma proteins, and various hormones and enzymes.

Over the years, evaluation of the hemogram and plasma or serum biochemistry has been used to assess the health status or function of a range of body systems in the athletic horse. These tests are commonly used to assess fitness and performance potential, as well as to investigate poor performance in horses. However, there is a wide degree of variation in values of various blood constituents depending on, among other things, whether a horse is at rest or is exercising when the sample is collected. Additionally, the training status of a horse, as well as sampling techniques, can directly affect the hemogram and serum or plasma biochemistry. It is important that the veterinarian is aware of how such factors may impact test results. In this chapter, those factors that can affect the interpretation of hematology and serum or plasma biochemical profile will be detailed.

Methods

Blood samples should be collected using appropriate equipment and techniques. The jugular vein is commonly used for blood sampling and blood is collected into evacuated glass collection tubes. For routine hematology, blood samples should be collected into tubes containing ethylenediaminetetra-acetic acid (EDTA) as an anticoagulant. Given that EDTA can cause a pseudothrombocytopenia,[1] an additional sample may be collected into sodium citrate to ensure an accurate assessment of platelet numbers. Samples for serum or plasma biochemistry can be collected into tubes that do not contain an anticoagulant (serum) or into tubes containing lithium or ammonium heparin (plasma). Some laboratories prefer serum to plasma samples; it is therefore wise to ascertain the laboratory's preference prior to collection of blood samples. It is also important to note that samples collected into EDTA are unsuitable for plasma biochemistry measurements whereas samples collected into heparin are unsuitable for hematology. In addition, if plasma glucose or lactate values are to be measured, blood should be collected into tubes containing sodium fluoride/potassium oxalate as an anticoagulant.

When assessing hematology, the technique of collection, the horse's attitude and degree of excitement, relationship to feeding, and time of day can all have a profound effect on values. In addition, storage of blood samples overnight may result in a slight elevation of hematocrit and mean cell hemoglobin (MCH), probably due to enlargement of erythrocytes.[2] Storage of blood samples can also result in alterations in plasma or serum biochemistry. Therefore, it is important to standardize collection and handling techniques as much as possible.

The temperament of the horse and the technique used by the sample collector can have an important effect on both the erythrocyte and leukocyte values.[3–5] Excited horses that resist venepuncture and move about forcefully have higher

erythrocyte and leukocyte counts.[4] This may relate to the time taken to collect a blood sample in more fractious horses. It takes 30–60 s to mobilize erythrocytes from the spleen following the administration of intravenous epinephrine (adrenaline).[6] It is likely that samples collected within 30 s from less excited horses have fewer or less marked alterations in the hemogram.[4,7] At the other end of the spectrum, it is possible that very placid horses have values for red cell indices that are lower than the mean for values for the breed.[8] Therefore, it is important to note the attitude of the horse during blood collection so that the results can be correctly interpreted.

Other important factors that affect the hemogram and serum or plasma biochemistry are the diet and time of feeding. For example, in the hours after ingesting a hay meal there is a substantial increase in hematocrit and plasma protein concentration (Fig. 42.1).[9] These changes are a result of increased salivary fluid production[9] and fluid shifts from the circulation to the gastrointestinal tract.[10–12] Furthermore, feeding a large concentrate meal results in a 12% increase in plasma protein concentration with significant reductions in plasma volume.[12,13] Therefore, one should avoid collecting blood samples within 3 h of feeding a large concentrate meal or hay ration, or at least ensure that samples are collected at the same time each day and that feeding status is noted to allow for appropriate interpretation of values.

Following exercise it takes 1 to 2 h for hemogram changes to return to pre-exercise values. If blood samples are collected in the afternoon after morning exercise, there is a higher proportion of neutrophils and higher leukocyte numbers than in blood samples collected in the morning before exercise.[14] However, there does not appear to be a significant difference between hemograms for samples collected from resting horses either in the morning or afternoon.[15] It is therefore recommended that blood samples are collected either prior to exercise in the morning or on days when horses do not exercise to avoid exercise-induced effects on the hemogram.

Hematology

Structure and function

Erythrocytes

Erythrocytes are anucleate cells that normally circulate for several months in blood. Their primary purpose is to carry hemoglobin, a heme-containing protein that accounts for 95% of the total protein in erythrocytes. Erythrocyte functions include oxygen transport to the tissues, carbon dioxide transport to the lungs, and hydrogen-ion buffering, all of which are inter-related.

Oxygen transport

Oxygen is carried in the blood in two forms. Most oxygen is carried in combination with hemoglobin but some is carried as dissolved oxygen. Under normal conditions in arterial blood, 0.3 mL of dissolved oxygen is carried per 100 mL of blood.

The amount of oxygen transported by hemoglobin is much greater than that carried in the dissolved form. Hemoglobin is a tetrameric protein consisting of four polypeptide globin chains, each of which contains a heme prosthetic group. Each hemoglobin tetramer can bind four molecules of oxygen when fully saturated. Under normal circumstances, the presence of hemoglobin-containing erythrocytes increases the oxygen-carrying capacity of blood to approximately 70 times more than that that would be transported dissolved in plasma.[16] The oxygen molecule combines loosely and reversibly with the heme portion of hemoglobin. The partial pressure of oxygen (Po_2) affects the quantity of oxygen bound with hemoglobin. When the Po_2 is high, as in the pulmonary capillaries, oxygen binds with the hemoglobin, but when the Po_2 is low, as in the tissue capillaries, oxygen is

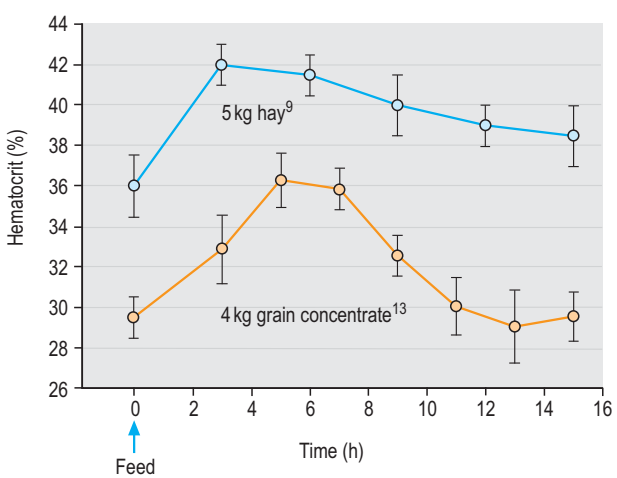


Fig. 42.1
The effect of a single feed of 5 kg of hay[9] or 4 kg of grain concentrate[13] on the hematocrit.

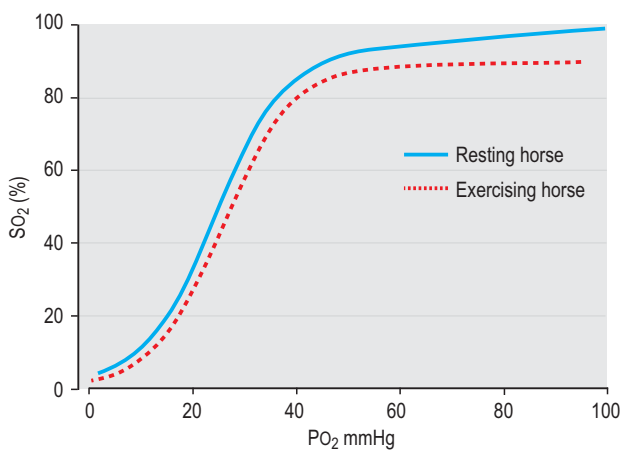


Fig. 42.2
Oxygen–hemoglobin dissociation curve in resting (solid line) and heavily exercising (dashed line) horses. Po_2, partial pressure of oxygen; SO_2, percentage saturation of hemoglobin. (Adapted from Lekeux.[17])

released from the hemoglobin. There is a progressive increase in the percentage of hemoglobin that is bound with oxygen as Po_2 increases, yielding the oxygen–hemoglobin dissociation curve (Fig. 42.2).[17] The curved nature of the oxygen–hemoglobin dissociation curve has several physiological advantages. The flat upper portion means that even if the alveolar gas Po_2 falls somewhat, loading of oxygen will be little affected. In addition, as the red cell takes up oxygen along the pulmonary capillary, a large partial pressure difference between alveolar gas and blood continues to exist when most of the oxygen has been transferred, hastening diffusion. The steep lower portion of the dissociation curve means that the peripheral tissues can withdraw large amounts of oxygen for only a small drop in capillary Po_2. This maintenance of blood Po_2 assists the diffusion of oxygen into the tissue cells.[16]

The oxygen–hemoglobin dissociation curve can be displaced such that the affinity for oxygen is altered. Factors that shift the curve include changes in carbon dioxide concentration, blood temperature, blood pH, and the concentration of 2,3-diphosphoglycerate (2,3-DPG). Changes in blood carbon dioxide and hydrogen ion concentration have a significant effect in enhancing oxygenation of blood in the lungs and enhancing the release of oxygen from the blood to the tissues through the Bohr effect.

Carbon dioxide transport

Carbon dioxide is transported in blood as either dissolved carbon dioxide (5%), bicarbonate ions (70–90%), or as carbamino compounds (5–10%). The majority of carbon dioxide is transported as bicarbonate ions. This is because erythrocytes have a high activity of carbonic anhydrase, an enzyme that catalyzes the reaction between carbon dioxide and water. This reaction makes it possible for water to interact with large quantities of carbon dioxide, enabling transport of carbon dioxide from the tissues to the lungs in the form of bicarbonate. This is particularly important during exercise as working muscles release large quantities of carbon dioxide.

As described earlier for the Bohr effect, the partial pressure of carbon dioxide and pH can loosen the binding of oxygen with hemoglobin. Conversely, oxygen can also act to displace carbon dioxide and hydrogen ions from hemoglobin; this is termed the Haldane effect. Both the Bohr and Haldane effects can be explained by the fact that deoxyhemoglobin is a weaker acid than oxyhemoglobin. Hence, deoxyhemoglobin more readily accepts hydrogen ions liberated by the dissociated form of carbonic acid at the tissue level when carbon dioxide is released into the blood from the tissues. This allows more carbon dioxide to be transported in the form of bicarbonate ions. At the same time, the association of hydrogen ions with hemoglobin lowers the affinity of hemoglobin for oxygen causing a shift of the oxygen–hemoglobin dissociation curve to the right, facilitating the unloading of oxygen at the tissue level.[16]

Leukocytes

Leukocytes have a primary role in immune function. There are normally six different types of leukocytes found in the circulating blood: neutrophils, eosinophils, basophils, monocytes, lymphocytes, and occasional plasma cells. In resting blood samples, the white cell count does not reflect the total intravascular pool, as this consists of both the circulating and marginal pools, the latter being sequestered in capillary beds and the spleen.[18] Therefore, any factors that cause mobilization of cells from the marginal pool will increase the numbers of leukocytes in the circulating pool. Such factors include plasma catecholamine and cortisol concentrations. Therefore, recent stress such as transportation or exercise of a horse can alter the white cell count in blood samples.

Platelets

Platelets are anucleate cell fragments derived from megakaryocytes in the bone marrow that normally circulate in the bloodstream for 4–5 days. Platelets interact with the endothelium and circulating coagulation factors in the maintenance of normal hemostasis. In addition, platelets are also thought to be involved in inflammatory and immunological processes.[19] Platelets are also sequestered in the spleen and are subject to increases in circulating numbers with splenic contraction. Platelets are also subject to activation following injury of the endothelium, through inappropriate handling in vitro and potentially through sheer stress in the vascular system. For the exercising horse, each of these factors is a consideration when evaluating both platelet numbers and activation status.

The normal resting hemogram

For the normal resting hemogram, the normal range for an individual horse is quite narrow, whereas there are much broader ranges across horse breeds, with further variation due to age and state/type of training. The normal ranges for various breeds, age groups, and horses in training are given in Appendices 1 and 2. The red cell indices show the greatest variation amongst breeds. This relates to factors such as plasma volume expansion seen in endurance-trained animals but not in Thoroughbred or Quarter Horse race horses. In addition as mentioned earlier, the temperament of a horse can significantly affect red cell indices.

Hematologic responses to exercise

Erythrocyte indices

Exercise has variable effects on the hemogram depending on work intensity (Fig. 42.3).[20–28] Exercise generally results in mobilization of splenic erythrocytes and, therefore, increases the oxygen transport capacity. The extent of the potential increase in circulating red cell mass is quite remarkable, as the spleen has the capacity to store up to 50% of the total red blood cell pool.[29] The release of splenic erythrocytes is under the influence of catecholamines. Both the intensity and duration of exercise are important in determining the magnitude of the catecholamine response.[30] The extent of the increase in hematocrit is a function of exercise intensity, with a linear

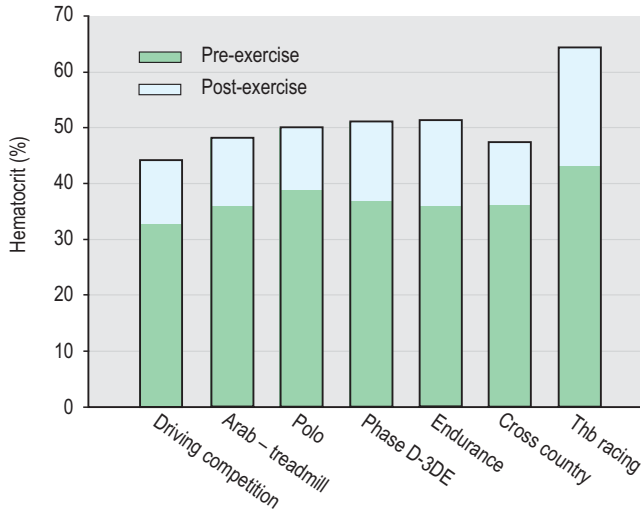


Fig. 42.3
The effect of different types of exercise including the cross-country phase of driving trail competition,[21] low-intensity treadmill exercise,[28] during a polo match,[26] phase D of a three-day event,[25] an 80-km endurance ride,[24] the cross-country phase of a three-day event,[22] and Thoroughbred racing[20] on the hematocrit.

relationship between hematocrit and speed,[23,31] up to a maximum hematocrit of approximately 60–65%.[7] There are, however, variations in splenic capacity in association with breed of the horse as well as age. Draught horses have lower relative splenic weights compared to Thoroughbred horses[32] and it appears that splenic capacity alters in response to increasing age (from 1 to 3 years) in Trotters.[31,33]

While the majority of the increase in hematocrit during high-intensity exercise is attributable to splenic contraction, exercise-induced fluid shifts also play a role. For horses performing moderate short-term incremental exercise there is a 5–10% decrease in plasma volume.[34] However, given the substantial fluid losses incurred during prolonged endurance exercise, it is likely that reductions in plasma volume play a greater role in changes in hematocrit observed in endurance exercise.

In association with the increases in hematocrit are increases in the erythrocyte count and hemoglobin concentration. As a consequence of the increase in hemoglobin concentration there is an increased oxygen transport capacity, an important factor in the horse's high aerobic capacity.[35] Indeed, studies of splenectomized horses have shown a marked reduction in exercise capacity.[29,36] However, the increase in blood viscosity associated with exercise and increased hematocrit[37–39] likely reaches a point that offsets improved oxygen-carrying capacity. This probably accounts for the marked reduction in performance in horses with red cell hypervolemia.[31]

Other erythrocyte changes associated with high-speed exercise include small increases in mean corpuscular volume (MCV) and decreases in MCH and mean corpuscular hemoglobin concentration (MCHC). In addition, erythrocytes in blood samples obtained after exercise are more resistant to osmotic stress.[40] However, although Smith et al[40] did not detect any differences in erythrocyte deformability, Geor et al[39] detected reduced erythrocyte deformability during exercise. The difference between these two studies may be attributable to the techniques used to assess erythrocyte deformability. Deformability of erythrocytes is considered to be the major determinant of resistance of blood to flow in the microcirculation,[41] with reduced erythrocyte deformability potentially increasing blood flow resistance. However, horses are remarkably resistant to changes in blood viscosity associated with increases in hematocrit, likely because of changes in red cell deformability.[42,43]

It has been reported that there are large numbers of echinocytes released during exercise.[44] However, other studies of horses exercising for shorter durations at higher intensity have found the concentration of echinocytes to be quite low.[39,40] These differences might relate to exercise intensity and duration or possibly to the breed of horse. The significance of echinocytes is unclear, however for short duration, high-intensity exercise, they are probably not of physiologic importance in changing oxygen delivery.[40] Their role in prolonged low-intensity exercise is yet to be defined.

There is a four-fold increase in oxygen extraction from blood during exercise. This increase in extraction ratio is facilitated by a rightward shift of the oxygen–hemoglobin dissociation curve. The shift occurs because of acidosis, hypercarbia, and hyperthermia in the local muscle environment.[45] There are also increases in the levels of 2,3-DPG during exercise.[46] This causes a rightward shift in the oxygen–hemoglobin dissociated curve further enhancing the release of oxygen from hemoglobin to the tissues. Low blood Po_2 stimulates erythrocyte glycolysis and the formation of 2,3-DPG. The increased oxygen extraction during exercise also makes blood more effective in the transport of carbon dioxide due to the presence of increased amounts of deoxyhemoglobin for formation of carbamino products.[45]

Leukocytes

There are significant differences in the response of leukocytes to exercise of differing intensities and duration (Fig. 42.4). Following high-intensity exercise, significant increases in leukocyte numbers are not seen. Immediately after galloping, there is a change in the neutrophil:lymphocyte ratio, but little change in the total leukocyte count. There is a transient lymphocytosis with a decrease in the neutrophil:lymphocyte ratio.[20,47] These changes are likely secondary to catecholamine release and splenic contraction. At 3 h after exercise there is an increase in the neutrophil:lymphocyte ratio, caused by an increase in neutrophils and decrease in lymphocytes due to increased plasma cortisol concentrations. However, the neutrophil:lymphocyte ratio returns to normal by 6 h after exercise.[20]

In contrast to high-intensity exercise, endurance exercise is associated with a leukocytosis, resulting from a neutrophilia and lymphopenia.[24,48] This is probably due to an increase in circulating corticosteroids,[49–51] with speed significantly affecting the extent of the neutrophilia and lymphopenia. Horses that complete an endurance ride at a faster speed have a higher neutrophil:lymphocyte ratio than slower

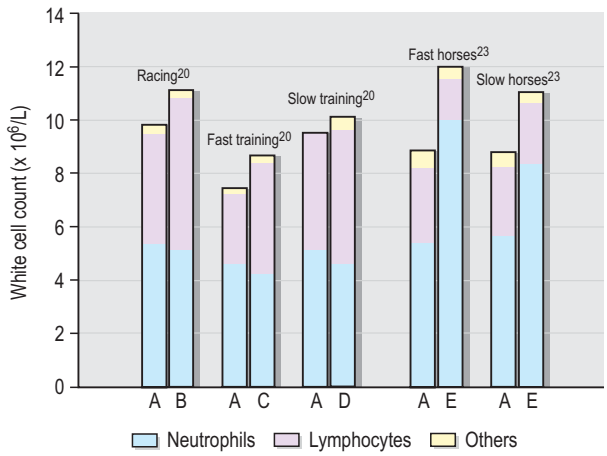


Fig. 42.4
The effect of different types of exercise on the leukocyte numbers. Data from Snow et al[20] and Rose.[23] A, resting; B, immediately after racing; C, immediately after fast training (11–12 m/s); D, immediately after slow training (13 m/s); E, immediately after a 160-km endurance ride.

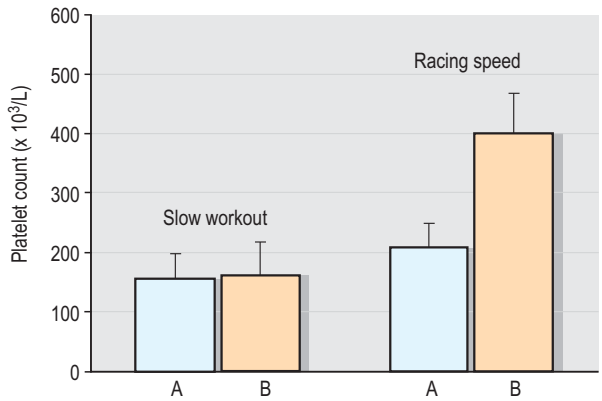


Fig. 42.5
The effect of exercise on platelet numbers. A, before exercise; B, after exercise. (Data from Johnstone et al,[55] and Bayly et al.[53])

horses.[23] Additionally, Carlson et al[52] showed that exhausted endurance horses had a significant left shift in the neutrophils when compared to clinically normal horses, even though the total white cell count was similar to that reported by Rose.[23] For samples collected the day after an endurance ride, a slower group of horses still had a significantly increased white cell count compared to a group of fast horses. However, this could be associated with the time the samples were collected, 14 h versus 21 h postexercise for the slow and fast horses, respectively.[23]

Platelets

Similar to erythrocytes, exercise has a variable effect on platelet numbers that appears to be exercise intensity dependent (Fig. 42.5). High-intensity exercise results in significant increases in circulating platelet numbers[53] whereas moderate exercise does not significantly increase platelet numbers.[54,55] With regards to platelet activation and aggregability, some studies report reduced platelet aggregability in response to high-intensity exercise,[53,55] however, others have reported increased aggregability[56] and activation of platelets.[57,58] It is likely that increases in the sodium citrate concentration associated with hemoconcentration of blood samples resulted in reduced ionized calcium concentration[59] and platelet aggregability.[53,55] No studies have looked at the effect of exercise duration, age or breed of the horse on the response of platelets to exercise.

Hematologic responses to training

Erythrocyte indices

There has been a large number of studies investigating the response of the hemogram to various types of training. The most common finding for horses undergoing high-intensity training has been significant increases in the resting red blood cell count, hematocrit, and hemoglobin concentration.[20,60–62] The increased erythrocyte numbers observed in horses training at higher intensities is thought to result from a greater demand for oxygen carriage, which stimulates erythrocyte production. Interestingly, in one study, horses with higher hematocrits (> 40%) at the start of training did not show any significant change in red cell indices compared to horses starting with a lower hematocrit.[60] This highlights some of the problems in trying to interpret the resting hemogram. Variations exist with the demeanor of the horse, as well as time of blood collection. The increased excitability of a horse as it gets fitter could result in elevations of resting red cell indices rather than the training per se and might account for the results reported by Clarkson and others.[8] Regular monitoring of the hemogram during training has little value for assessing a horse's fitness.

Despite the variability of the resting hemogram, there does appear to be an increase in total hemoglobin and total red cell volume with training. However, due to variability in individual plasma volume, an assessment of postexercise hematocrit or hemoglobin alone lacks accuracy for determination of the total erythrocyte mass.[33]

In Standardbred Trotters, prolonged training can result in an excessive increase in the red cell mass and the phenomenon known as red cell hypervolemia.[31,63] This results in reduced racing performance and appears to be due to overtraining. These horses have lower oxygen consumption. It has been hypothesized that increased blood viscosity leads to reduced capillary perfusion and inadequate utilization of oxygen by the working muscles. This phenomenon has not been observed in other breeds of performance horses, so it is unclear if it plays a role in overtraining in other breeds.

Endurance-trained horses have lower resting red cell indices than race horses. Similar to race horses, the effects of training on red cell indices are variable. In a group of Standardbred horses, after 7 weeks of low-intensity exercise training there were no significant effects on the resting or recovery hemogram.[27] Similarly, in a group of endurance horses (predominantly Arab crosses) there was no change in the resting hematocrit over 12 weeks of training, although

quieter horses had significantly lower hematocrits throughout the training period compared to more apprehensive horses. None the less, it is possible that there could be a reduction in hematocrit in endurance horses due to expansion of plasma volume.[64] It is clear from the results of these studies that hematological measurements are of little value in assessing the fitness or progress of horses during training.

Blood gas transport

Several studies have examined the effect of exercise training on blood oxygen transport properties in horses.[46,61,65] The results have been variable, although an increase in circulating blood oxygen capacity at rest, and an increase in blood oxygen affinity due to decreases in erythrocyte 2,3-DPG concentration, have been described.[61] With regards to 2,3-DPG concentration, Lewis and McLean[65] and Lykkeboe et al[61] showed a reduction in red cell 2,3-DPG concentration in response to training, whereas Pelletier et al[46] showed no change in 2,3-DPG concentration. This could potentially be due to the different training programs used in those studies. A reduced 2,3-DPG concentration could potentially impair unloading of oxygen. However, this has not been further evaluated and detrimental effects on work performance have not been reported.

Leukocytes

The total leukocyte count is unchanged during training of race horses and horses used for endurance racing. In addition, there are no alterations in the proportions of the different leukocytes. While there have been anecdotal reports of alterations in the neutrophil:lymphocyte ratio in horses that are overtrained, this was not observed by Tyler-McGowan et al.[66] However, several horses in that study developed an absolute eosinopenia together with clinical signs of illness. It was hypothesized that eosinophils may be a more sensitive indicator of training stress than other members of the leukocyte series.

Platelets

Although a large number of studies have investigated changes in the hemogram in response to training in horses, no studies have documented platelet numbers during training. Furthermore, given many of the technical problems when working with equine platelets, it is currently unknown if exercise training alters platelet function.[59]

Plasma or serum biochemistry

Muscle-derived enzymes

Creatine kinase (CK) is a relatively muscle-specific enzyme with a plasma half-life of approximately 2 h.[67] In muscle, CK makes ATP available for contraction by phosphorylation of ADP from creatine phosphate. Apart from skeletal muscle, CK activity is also present in gastrointestinal tissue, uterus, urinary bladder, kidney, heart, and thyroid gland.[68] Increased serum CK activity may be due to muscle damage, injury to organs containing smooth muscle, and be falsely increased with in vitro hemolysis.[69]

Aspartate aminotransferase (AST) has a much longer half-life (approximately 7 to 8 days)[67] than CK and is less specific for muscle, being found in most tissues.[70] It is a cytoplasmic and mitochondrial enzyme that catalyzes the deamination of aspartate to form oxaloacetate, which can enter the Kreb's cycle. Increases in plasma AST activity may be due to hepatocyte damage, muscle damage, or in vitro hemolysis.[69]

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that catalyzes the conversion of pyruvate to lactate at the end of glycolysis. Activities of LDH are high in various tissues of the body. Therefore, measurements of LDH are not organ specific. There are five isoenzymes of LDH, which can be separated by electrophoresis.[68] The isoenzyme LDH5 is the predominant form in skeletal muscle and has a plasma half-life of less than 6 h.[69] Increases in LDH activity may be due to hepatocyte damage, muscle damage, or hemolysis.

Liver-derived enzymes

γ-Glutamyltransferase (GGT) is a membrane-associated enzyme that catalyzes the transfer of glutamyl groups between peptides and is involved in glutathione reactions. Many cells have GGT activity but biliary epithelial cells, pancreas, and renal tubular cells are classically considered to have the greatest activity.[69] The half-life of GGT in horses is approximately 3 days and it is stable in serum for 2 days at room temperature, or 30 days if frozen.[71] The primary source of increased plasma GGT activity in horses is cholestasis or biliary hyperplasia.

Alkaline phosphatase (AP) catalyzes the hydrolysis of monophosphate esters and is bound to the mitochondrial membrane. Tissues that contain AP include liver, bone, intestine, kidney, placenta, and leukocytes. Increases in the serum activity of this enzyme in adult horses are secondary to induction. Cholestasis and certain drugs will cause production and the release of AP.[72]

Sorbitol (iditol) dehydrogenase (SDH) is a cytoplasmic enzyme that catalyzes the conversion of fructose to sorbitol. It has a short plasma half-life with blood levels declining within 4 h of transient hepatic necrosis. Its short half-life necessitates analysis within 12 h of collection, or 48 h if the serum is separated from blood and refrigerated.[73]

Glutamate dehydrogenase (GLDH) is found in hepatocytes, renal tissue, brain, muscle, and intestinal cells. Like SDH, GLDH has the highest tissue concentration in the liver and increases of this enzyme in blood can be considered specific for acute liver disease. The half-life for GLDH is 14 h.[71]

Plasma proteins

Albumin is synthesized by the liver and is the most prominent of the plasma proteins constituting 35–50% of total plasma

protein in animals. It is the most osmotically active plasma protein due to its abundance and small size and accounts for about 75% of the oncotic activity of plasma. A major role of albumin is as a general binding and transport protein.[74] The plasma concentration of albumin is affected by changes in plasma water content and intravascular water volume.

Globulins include α-globulins, β-globulins, γ-globulins, and immunoglobulins. Changes in the concentration of globulins generally reflect inflammation and disease, although hydration can also impact globulin concentration.

Fibrinogen is an acute phase protein, the concentration of which increases in response to inflammation. Dehydration can increase plasma fibrinogen concentration.

Changes in plasma or serum biochemistry associated with exercise

Muscle-derived enzymes

Increases in plasma CK, AST[25,70,75–78] and LDH[79] activities have been seen in response to exercise. These increases are believed to relate either to overt damage or to a change in the muscle fiber membrane causing a transient increase in permeability.[79,80] Physiological increases have been shown to occur without any tissue destruction.[81] The extent of this increase depends on the nature of the exercise.[70,79] It has been suggested that sampling at least 24 h after exercise may facilitate the differentiation between those animals showing a normal physiological response to exercise and those with an abnormal or pathological response.[70]

Liver-derived enzymes

In general, a single exercise bout has minimal effect on the activities of liver-derived enzymes. However, increases in serum AP activity have been reported in horses during endurance exercise[77] and in horses competing in three-day event competitions.[78] It is unclear whether these increases in AP are of skeletal or hepatic origin.

Plasma proteins

During maximal exercise, there is a redistribution of fluid and electrolytes from the vascular compartment to the tissue extracellular fluid spaces, with a corresponding increase in total plasma protein and albumin.[22,26,38,82–85] The extent of the fluid shift appears to be related to the duration and intensity of exercise. Less dramatic increases are seen in polo horses[26] and horses performing submaximal exercise[82] than in Thoroughbred race horses[86] and other horses performing maximal exercise.[82] Increases in plasma protein associated with short-duration exercise return to pre-exercise values within 15 to 30 min of exercise.[26,82,83] However, with hot conditions and extensive sweat losses, these fluid shifts may be more dramatic and prolonged.

While acute exercise in horses results in significant increases in total plasma protein concentrations, individual plasma protein fractions increase in a heterogeneous manner, indicating that changes in plasma protein concentrations cannot be simply attributed to changes in plasma water alone.[22,38] In a study by Coyne et al,[38] plasma albumin concentration increased by 22%, whereas fibrinogen concentration increased 12.5% and increases in the various globulin groups ranged from 25.5% to 60%. This resulted in a 10% decrease in the albumin:globulin ratio compared to resting samples. The mechanisms behind heterogeneous alterations in plasma protein fraction concentrations are unclear but could include compartmental redistribution, accelerated biosynthesis, increased degradation, and bolus release.[38] In addition, exercise-induced fibrinolysis could play a role in limiting the increase in fibrinogen concentration.[87] However, given that many laboratories consider a fibrinogen concentration above 4 g/L to be clinically significant, acute exercise does not appear to increase fibrinogen to this extent.[88]

During prolonged, low-intensity exercise, albumin and total plasma protein concentration increases.[50,51,76,77,89,90] However, despite the increase in plasma protein concentration, there is evidence that plasma volume increases during the initial stages of prolonged exercise.[31,91] Although increased plasma volume has been noted in dehydrated horses after 40 min of low-intensity exercise,[91] it is likely that plasma volume decreases in response to the substantial fluid losses incurred during prolonged endurance exercise.[24,92,93] Furthermore, those fluid losses result in increases in albumin and plasma protein concentrations that are much greater than those observed in horses performing short-duration exercise, and it takes longer for plasma protein concentrations to return to normal following prolonged endurance exercise. For horses competing in three-day event competitions[78] and driving trial competitions,[21] there are similar increases in plasma protein concentration, which remain significantly increased 30 min after exercise.

Changes in plasma or serum biochemistry associated with training

In general, there are few changes in resting biochemical values as a result of training. Although there have been some significant changes in a number of biochemical measurements, results have been variable and inconsistent.[23,62,66,94,95] The most consistent change has been in indicators of liver function, with serum GGT activity showing the greatest increase.[66,95,96] In some horses, GGT activity is greater than 100 U/L, but horses have not shown any other evidence of liver disease.[8] However, in other studies high-serum GGT

activities have been associated with poor health and overtraining in some horses.[96] Some performance horses with decreased performance have had three- to four-fold increases in serum GGT activity with no other laboratory evidence of hepatic disease. The source of the increase in GGT has not been determined and reportedly returned to normal within 30 to 60 days.[97]

Conclusion

There is no doubt that hematology and plasma or serum biochemistry are important tools for assessing the health of athletic horses. However, many factors can influence measurements, as have been outlined in this chapter. Each of these factors needs to be considered carefully when interpreting blood results. Hematology and biochemistry measures are unlikely to provide useful information regarding the fitness or performance potential of horses. However, they will continue to be useful in assessing health and disease in individual animals, particularly when samples are collected in a standardized manner and are compared to the results of horses of similar breed and training backgrounds.

References

1. Hinchcliff KW, Kociba GJ, Mitten LA. Diagnosis of EDTA-dependent pseudothrombocytopenia in a horse. J Am Vet Med Assoc 1993; 203:1715–1716.
2. Stewart GA, Riddle CA, Salmon PW. Haematology of the racehorse. A recent study of thoroughbreds in Victoria. Aust Vet J 1977; 53:353–359.
3. Archer RK, Clabby J. The effect of excitation and exertion on the circulating blood of horses. Vet Record 1965; 77:689–690.
4. Stewart GA, Clarkson GT, Steel JD. Hematology of the racehorse and factors affecting the interpretation of the blood count. Proc 16th Ann Conv Am Assoc: Equine Pract 1970; 17–35.
5. Irvine CHG. The blood picture in the racehorse. 1. The normal erythrocyte and hemoglobin status: a dynamic concept. J Am Vet Med Assoc 1958; 133:97–101.
6. Persson SG, Ekman L, Lydin G, et al. Circulatory effects of splenectomy in the horse. I. Effect on red-cell distribution and variability of haematocrit in the peripheral blood. Zentralbl Veterinarmed A 1973; 20:441–455.
7. Rose RJ, Allen JR. Hematologic responses to exercise and training. Vet Clin N Am: Equine Pract 1985; 1:461–476.
8. Rose RJ, Hodgson DR. Hematology and biochemistry. In: Hodgson DR, Rose J, eds. The athletic horse. Philadelphia, PA: WB Saunders; 1994:64–78.
9. Kerr MG, Snow DH. Alterations in haematocrit, plasma proteins and electrolytes in horses following the feeding of hay. Vet Record 1982; 110:538–540.
10. Tasker JB. Fluid and electrolyte studies in the horse. III. Intake and output of water, sodium, and potassium in normal horses. Cornell Vet 1967; 57:649–657.
11. Meyer H, Coenen M. Influence of exercise on water and electrolyte content of the alimentary tract. Equine Nutr Physiol Symp 1989; 11:3–7.
12. Clarke LL, Argenzio RA, Roberts MC. Effect of meal feeding on plasma volume and urinary electrolyte clearance in ponies. Am J Vet Res 1990; 51:571–576.
13. Clarke LL, Ganjam VK, Fichtenbaum B, et al. Effect of feeding on renin–angiotensin–aldosterone system of the horse. Am J Physiol 1988; 254:R524–530.
14. Allen BV, Kane CE, Powell DG. Leucocyte counts in the healthy English Thoroughbred in training. Equine Vet J 1984; 16:207–209.
15. Allen BV, Powell DG. Effects of training and time of day of blood sampling on the variation of some common haematological parameters in normal thoroughbred racehorses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta editions; 1983:328–353.
16. West JB. Respiratory physiology – the essentials, 5th edn. Baltimore, MD: Williams & Wilkins; 1995.
17. Lekeux P. Pulmonary function in healthy, exercising and diseased animals. Belgium: University of Ghent, 1993.
18. Schalm OW, Jain NC, Carroll EJ. Veterinary haematology. Philadelphia, PA: Lea and Febiger; 1975.
19. Herd CM, Page CP. Do platelets have a role as inflammatory cells? In: Joseph M, ed. The handbook of immunopharmacology. Immunopharmacology of platelets. London: Academic Press; 1995:1–20.
20. Snow DH, Ricketts SW, Mason DK. Haematological response to racing and training exercise in thoroughbred horses, with particular reference to the leucocyte response. Equine Vet J 1983; 15:149–154.
21. Snow DH. Haematological, biochemical and physiological changes in horses and ponies during the cross country stage of driving trial competitions. Vet Record 1990; 126:233–239.
22. Sommardahl CS, Andrews FM, Saxton AM, et al. Alterations in blood viscosity in horses competing in cross country jumping. Am J Vet Res 1994; 55:389–394.
23. Rose RJ. Haematological changes associated with endurance exercise. Vet Record 1982; 110:175–177.
24. Snow DH, Kerr MG, Nimmo MA, et al. Alterations in blood, sweat, urine and muscle composition during prolonged exercise in the horse. Vet Record 1982; 110:377–384.
25. Andrews FM, Geiser DR, White SL, et al. Haematological and biochemical changes in horses competing in a 3-star horse trial and 3-day-event. Equine Vet J Suppl 1995; 40:57–63.
26. Craig L, Hintz HF, Soderholm LV, et al. Changes in blood constituents accompanying exercise in polo horses. Cornell Vet 1985; 75:297–302.
27. Rose RJ, Allen JR, Hodgson DR, et al. Responses to submaximal treadmill exercise and training in the horse: changes in haematology, arterial blood gas and acid base measurements, plasma biochemical values and heart rate. Vet Record 1983; 113:612–618.
28. Rubio D, Riber C, Santisteban R, et al. Hematologic alterations as an index of exercise tolerance in different breeds of horses. Equine Athlete 1994; 7:10–12.
29. Persson SG, Lydin G. Circulatory effects of splenectomy in the horse. 3. Effect on pulse–work relationship. Zentralbl Veterinarmed A 1973; 20:521–530.
30. Snow DH, Harris RC, MacDonald IA, et al. Effects of high-intensity exercise on plasma catecholamines in the thoroughbred horse. Equine Vet J 1992; 24:462–467.
31. Persson SGB. On blood volume and working capacity in horses. Acta Physiol Scand 1967; Suppl 19:1–189.

32. Kline H, Foreman JH. Heart and spleen weights as a function of breed and somatotype. In: Persson SG, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:17.
33. Persson SGB. Evaluation of exercise tolerance and fitness in the performance horse. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:441–457.
34. McKeever KH, Hinchcliff KW, Reed SM, et al. Role of decreased plasma volume in hematocrit alterations during incremental treadmill exercise in horses. Am J Physiol 1993; 265:R404–408.
35. Evans DL, Rose RJ. Cardiovascular and respiratory responses in thoroughbred horses during treadmill exercise. J Exp Biol 1988; 134:397–408.
36. Persson SG, Bergsten G. Circulatory effects of splenectomy in the horse. IV. Effect on blood flow and blood lactate at rest and during exercise. Zentralbl Veterinarmed A 1975; 22:801–807.
37. McClay CB, Weiss DJ, Smith CM II, et al. Evaluation of hemorheologic variables as implications for exercise-induced pulmonary hemorrhage in racing thoroughbreds. Am J Vet Res 1992; 53:1380–1385.
38. Coyne CP, Carlson GP, Spensley MS, et al. Preliminary investigation of alterations in blood viscosity, cellular composition, and electrophoresis plasma protein fraction profile after competitive racing activity in thoroughbred horses. Am J Vet Res 1990; 51:1956–1963.
39. Geor RJ, Weiss DJ, Smith CM II. Hemorheologic alterations induced by incremental treadmill exercise in thoroughbreds. Am J Vet Res 1994; 55:854–861.
40. Smith JE, Erickson HH, Debowes RM, et al. Changes in circulating equine erythrocytes induced by brief, high-speed exercise. Equine Vet J 1989; 21:444–446.
41. Chien S. Red cell deformability and its relevance to blood flow. Ann Rev Physiol 1987; 49:177–192.
42. Fedde MR, Wood SC. Rheological characteristics of horse blood: significance during exercise. Resp Physiol 1993; 94:323–335.
43. Fedde MR, Erickson HH. Increase in blood viscosity in the sprinting horse: can it account for the high pulmonary arterial pressure? Equine Vet J 1998; 30:329–334.
44. Boucher JH, Ferguson EW, Wilhelmsen CL, et al. Erythrocyte alterations during endurance exercise in horses. J Appl Physiol 1981; 51:131–134.
45. Brooks GA, Fahey TD, White TP. Exercise physiology. Human bioenergetics and its application, 2nd edn. Mountain View, CA: Mayfield Publishing; 1996.
46. Pelletier N, Blais D, Vrins A. Effect of exercise and training on erythrocyte content of 2,3-DPG [diphosphoglycerate] and oxygen content of blood in the horse. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:484–493.
47. Rossdale PD, Burguez PN, Cash RS. Changes in blood neutrophil/lymphocyte ratio related to adrenocortical function in the horse. Equine Vet J 1982; 14:293–298.
48. Rose RJ, Hodgson DR. Haematological and plasma biochemical parameters in endurance horses during training. Equine Vet J 1982; 14:144–148.
49. Dybdal NO, Gribble D, Madigan JE, et al. Alterations in plasma corticosteroids, insulin and selected metabolites in horses used in endurance rides. Equine Vet J 1980; 12:137–140.
50. Lucke JN, Hall GM. Long distance exercise in the horse: Golden Horseshoe Ride 1978. Vet Record 1980; 106:405–407.
51. Lucke JN, Hall GN. Further studies on the metabolic effects of long distance riding: Golden Horseshoe Ride 1979. Equine Vet J 1980; 12:189–192.
52. Carlson GP, Ocen PO, Harrold D. Clinicopathologic alterations in normal and exhausted endurance horses. Theriogenology 1976; 6:93–104.
53. Bayly WM, Meyers KM, Keck MT, et al. Exercise-induced alterations in haemostasis in thoroughbred horses. In: Snow DH, Persson SGD, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 336–342.
54. Lepherd EE. Effect of exercise on platelet size and number. Vet Record 1977; 101:488.
55. Johnstone IB, Viel L, Crane S, et al. Hemostatic studies in racing standardbred horses with exercise-induced pulmonary hemorrhage. Hemostatic parameters at rest and after moderate exercise. Can J Vet Res 1991; 55:101–106.
56. Kingston JK, Sampson SN, Beard LA, et al. The effect of supramaximal exercise on equine platelet function. Equine Vet J Suppl 1999; 30:181–183.
57. Weiss DJ, Evanson OA, Fagliari JJ, et al. Evaluation of platelet activation and platelet-neutrophil aggregates in thoroughbreds undergoing near-maximal treadmill exercise. Am J Vet Res 1998; 59:393–396.
58. Kingston JK, Bayly WM, Meyers KM, et al. Evaluation of binding of fibrinogen and annexin V to equine platelets in response to supramaximal treadmill exercise. Equine Vet J Suppl 2002; 34:502–505.
59. Kingston JK, Bayly WM, Sellon DC, et al. Effects of sodium citrate, low molecular weight heparin, and prostaglandin E1 on aggregation, fibrinogen binding, and enumeration of equine platelets. Am J Vet Res 2001; 62:547–554.
60. Clarkson GT. Haematology and serum iron in the racehorse. MVSc. thesis. Melbourne, Australia: University of Melbourne, 1968.
61. Lykkeboe G, Schugaard H, Johansen K. Training and exercise change respiratory properties of blood in race horses. Resp Physiol 1977; 29:315–325.
62. Mullen PA, Hopes R, Sewell J. The biochemistry, haematology, nutrition and racing performance of two-year-old thoroughbreds throughout their training and racing season. Vet Record 1979; 104:90–95.
63. Persson SG, Osterberg I. Racing performance in red blood cell hypervolaemic standardbred trotters. Equine Vet J Suppl 1999; 30:617–620.
64. McKeever KH, Schurg WA, Jarrett SH, et al. Exercise training-induced hypervolemia in the horse. Med Sci Sports Exerc 1987; 19:21–27.
65. Lewis IM, McLean JG. Physiological variations in levels of 2,3-diphosphoglycerate in horse erythrocytes. Res Vet Sci 1975; 18:186–189.
66. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Equine Vet J Suppl 1999; 30:621–625.
67. Cardinet GH, Littrell JF, Freedland RA. Comparative investigations of serum creatine phosphokinase and glutamic-oxaloacetic transaminase activities in equine paralytic myoglobinuria. Res Vet Sci 1967; 8:219–226.
68. Cardinet GH. Skeletal muscle function. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. San Diego, CA: Academic Press; 1997; 407–440.
69. Stockham SL, Scott MA. Fundamentals of veterinary clinical pathology. Ames, IA: Iowa State Press; 2002.
70. Harris PA, Snow DH, Greet TR, et al. Some factors influencing plasma AST/CK activities in thoroughbred racehorses. Equine Vet J Suppl 1990; 9:66–71.
71. Engelking LR, Paradis MR. Evaluation of hepatobiliary disease in the horse. In: Doxey DL, ed. Clinical pathology and

diagnostic procedures. Philadelphia, PA: WB Saunders; 1987;563.
72. Kramer JW, Hoffmann WE. Clinical enzymology. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals. San Diego, CA: Academic Press; 1997;303–325.
73. Bauer JE, Asquith RL, Kivipelto J. Serum biochemical indicators of liver function in neonatal foals. Am J Vet Res 1989; 50;2037–2041.
74. Kaneko JJ. Serum proteins and dysproteinemias. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals. San Diego, CA: Academic Press; 1997; 117–138.
75. Frauenfelder HC, Rossdale PD, Ricketts SW, et al. Changes in serum muscle enzyme levels associated with training schedules and stage of the oestrous cycle in thoroughbred racehorses. Equine Vet J 1986; 18;371–374.
76. Lucke JN, Hall GM. Biochemical changes in horses during a 50-mile endurance ride. Vet Record 1978; 102;356–358.
77. Rose RJ, Purdue RA, Hensley W. Plasma biochemistry alterations in horses during an endurance ride. Equine Vet J 1977; 9:122–126.
78. Rose RJ, Ilkiw JE, Arnold KS, et al. Plasma biochemistry in the horse during 3-day event competition. Equine Vet J 1980; 12:132–136.
79. Anderson MG. The influence of exercise on serum enzyme levels in the horse. Equine Vet J 1975; 7:160–165.
80. Boyd JW. The mechanisms relating to increases in plasma enzymes and isoenzymes in diseases of animals. Vet Clin Pathol 1985; 12:9–24.
81. Cerny FJ, Haralambie AG. Exercise-induced loss of muscle enzymes. In: Knuttgen HG, Vogel JA, Poortmans J, eds. Biochemistry of exercise. Champaign, IL: Human Kinetics; 1983; 441–447.
82. Judson GJ, Frauenfelder HC, Mooney GJ. Biochemical changes in thoroughbred racehorses following submaximal and maximal exercise. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 408–415.
83. Hargreaves BJ, Kronfeld DS, Naylor JR. Ambient temperature and relative humidity influenced packed cell volume, total plasma protein and other variables in horses during an incremental submaximal field exercise test. Equine Vet J 1999; 31:314–318.
84. McKeever KH, Hinchcliff KW, Reed SM, et al. Plasma constituents during incremental treadmill exercise in intact and splenectomised horses. Equine Vet J 1993; 25:233–236.
85. Snow DH, Mackenzie G. Some metabolic effects of maximal exercise in the horse and adaptations with training. Equine Vet J 1977; 9:134–140.
86. Snow DH, Mason DK, Ricketts SW, et al. Post-race blood biochemistry in thoroughbreds. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 389–399.
87. Ferguson EW, Bernier LL, Shaughness GP, et al. Fibrinolytic activity without fibrinogenolysis during long-distance racing in horses. J Appl Physiol 1981; 50:245–249.
88. Kociba GJ, Bayly WM, Milne DW, et al. Furosemide: effects on the hemostatic mechanism of resting and exercised standardbred horses. Am J Vet Res 1984; 45:2603–2606.
89. Grosskopf JFW, Van Rensburg JJ. Haematology and blood biochemistry of horses during a 210 km endurance ride. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 416–424.
90. Grosskopf JFW, Van Rensburg JJ. Some observations on the haematology and blood biochemistry of horses competing in 80 km endurance rides. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 425–431.
91. Naylor JR, Bayly WM, Schott HC II, et al. Equine plasma and blood volumes decrease with dehydration but subsequently increase with exercise. J Appl Physiol 1993; 75:1002–1008.
92. Carlson GP, Mansmann RA. Serum electrolyte and plasma protein alterations in horses used in endurance rides. J Am Vet Med Assoc 1974; 165:262–264.
93. Carlson GP. Thermoregulation and fluid balance in exercising horses. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 291–309.
94. Judson GJ, Mooney GJ, Thornbury RS. Plasma biochemical values in thoroughbred horses in training. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983; 354–361.
95. Robertson ID, Bolton JR, Mercy AR, et al. Haematological and biochemical values in 12 standardbred horses during training. Aust Equine Vet 1996; 14:72–76.
96. Snow DH, Harris P. Enzymes as markers for the evaluation of physical fitness and training of racehorses. Adv Clin Enzymol 1988; 6:251–258.
97. Divers TJ. Hepatic disease. In: Robinson NE, ed. Current therapy in equine medicine 3. Philadelphia, PA: WB Saunders; 1992; 253–259.

CHAPTER 43

Hematologic and biochemical abnormalities in athletic horses

Sidney W. Ricketts

For horses to be successful when they race or otherwise perform they must be healthy, fit, properly prepared, well ridden, competing appropriately, and to some degree lucky. Leaving aside the effects of opposition, jockey, state of training, genetic suitability for athleticism, and how the horse feels 'on the day', this is a matter of constitution, 'heart', courage, and perhaps even intelligence. These are factors that cannot be assessed in the laboratory. This is one of the reasons why neither financial input nor veterinary/scientific endeavor guarantees success and why equine sports remain so popular for the casual punter and such a success for the betting industry. Nevertheless, within the confines of horse-training environments, health and disease remain important factors affecting fitness to compete and athletic performance.

When horses are ill or injured they are less likely to perform to their optimal potential. Therefore, veterinary surgeons attending performance-horse stables spend a great deal of their time diagnosing clinical and subclinical injury and disease, selecting and applying appropriate treatments, and assessing return to normality. The clinical pathology laboratory provides an important aid to diagnosis.[1–14] In addition, the successful race-horse trainer, in association with the attending veterinary surgeon, integrates clinical pathology assessments of individual horses and group trends into the stable's management team strategy. If interpreted with care alongside relevant reference data, specific experience, and clinical and training performance data, laboratory results can provide useful aids to the diagnosis of clinical and subclinical abnormality and therefore to training management.[15–30] As with most aspects of veterinary medicine, this is a process of 'jigsaw puzzling'. The more pieces of the puzzle that are available to the clinical pathologist, clinician, and trainer, the more likely is the team to be able to recognize the picture, make the correct diagnosis, and apply the appropriate treatment and management. If used correctly, the clinical pathology laboratory can provide important pieces of information.

It is clear that individual horses vary considerably not only in their own 'reference' results but also by the effects that variations from reference range and even clinical abnormality will have on their performance. The trainer's assessment of each horse as an individual remains essential and laboratory results should never be used to 'train' performance horses. Different types of horses are used for different forms of exercise and each requires different reference ranges and experienced interpretations.[31–38]

Groups of predominantly immature horses (Thoroughbred flat racing) that are stressed by continual population change and what must be considered unnatural housing and feeding practices, training, transport, and racing suffer a full variety of injuries and diseases for which appropriate veterinary supervision is required. Surveys have confirmed that respiratory, musculoskeletal, gastrointestinal, and skin diseases – both infectious and non-infectious – are of particular concern.[39,40]

Despite many years of clinical research into equine sports medicine, a practical laboratory measure (or measures) of fitness in race horses remains elusive.[18,21,22,25,26,29,30,41–46] Nevertheless, sensible, routine screening for subclinical disease (perhaps better called 'unfitness' tests) can be helpful to trainers and owners and may help with important management decisions, potentially preventing further injury and disease and therefore making an important contribution to the welfare of the individual horse and the others with which it is stabled.

Poor, disappointing or loss of performance[47–49] is a common problem for which owners and trainers request veterinary investigations to help provide explanations and answers to aid future management. The clinical pathology

laboratory can provide information that can be of help in this regard, if only to help rule-out obvious specific injury or illness.

All clinicians who work with performance horses should have direct access to elementary laboratory facilities that can provide quick results in urgent situations. This should include at least a simple hematologic cell counter, an elementary dry serum chemistry analyser, and a method of performing a leukocyte count and cytologic differentiation on synovial fluid samples in emergency situations such as acute collapse, myopathy and septic arthritis. The basic equipment for these tests is comparatively inexpensive, requires minimal space, and the tests can be performed quickly, accurately, and simply, using simple standard operating procedures. The equipment must be properly maintained, the staff using it must be adequately trained, and the results must be subject to elementary internal quality control and external assurance if they are to be reliable. Unreliable results are worse than no results at all because they can result in misdiagnoses and inappropriate managerial decisions.

For more demanding and less urgent laboratory work, a relationship with a specialized referral laboratory should be established. Full, modern, laboratory technology (with all the necessary facilities, equipment, technicians, quality control, and assessment) and experienced interpretations can only be justified, on economic terms, under conditions of high throughput. Referral laboratories should give clear guidance on preferred sample handling so that accurate and repeatable results can be provided efficiently, for reliable interpretation.

Sample collection and handling

Before collecting specimens for laboratory examination, clinicians should make sure that they have the necessary knowledge, experience, and equipment to obtain satisfactory samples safely. The choice of relevant tests will dictate the samples required. Results can only be as good and useful as the samples allow them to be. Samples must be collected at the appropriate time, using suitable techniques with adequate equipment, into suitable containers, and using recommended anticoagulants, preservatives or fixatives where appropriate; they must then be transported to the laboratory under satisfactory conditions. If unsure, the clinician should contact the laboratory to clarify particular sample preferences before attempting collection. In general terms, samples collected into ethylenediaminetetra-acetic acid (EDTA, sequestrene) anticoagulant are ideal for hematologic analyses and clotted (serum) samples are ideal for the majority of biochemical analyses. Adding a sample in sodium citrate anticoagulant will allow the measurement of fibrinogen by the more accurate direct coagulometry method. Therefore, three blood samples collected into EDTA and sodium citrate anticoagulants and a plain tube to allow clotting to occur, will allow the laboratory to perform all of the routinely useful tests for performance horses.

Samples should be analyzed in-house without delay or reach the referral laboratory as soon as possible after collection. Delays in postal services cause deterioration in many samples, sometimes making accurate results impossible to obtain. Ideally, serum should be separated from clotted samples by centrifugation or simple standing and then pouring or pipetting, before transit, to prevent hemolysis, which renders many enzyme analyses inaccurate. Modern blood collection and separation tubes, containing beads or gel to aid serum separation, are particularly helpful in this regard. For urgent or labile samples, rapid courier services should be used.

Samples should be indelibly labeled with full details of the horse's name or identification. Without this simple information, neither the in-house nor referral laboratory can properly certify results. A letter, or preferably the laboratory's own request form should be included, repeating the label details and adding the clinician's name, address and telephone number, either a brief or detailed case history (as appropriate), the tests requested or help required, and any other relevant information or comments. The more information the laboratory receives, the more help can be given to the clinician.

Referred samples should be carefully sealed in inner leakproof containers and securely enclosed in padded and crushproof outer containers so that they conform to relevant legislation and will withstand the handling that packages sometimes receive in the postal services. Packages must be labelled clearly to minimize the risk of going astray.

Sample analysis

It is not the purpose of this chapter to discuss laboratory management and technology. Each in-house or referral laboratory will develop under different circumstances, with different aims and priorities. There are many methods of achieving satisfactory results but it is essential to make sure that samples are received, prepared, examined, and reported as accurately and as quickly as possible. To do this, the laboratory must be well managed, technical equipment must be well maintained, technicians must be adequately qualified and experienced, and test procedures must be quality controlled and externally assured. Specific veterinary laboratory technical education and quality assurance are not universally available and thus each laboratory must make appropriate provision. Medical laboratory science courses provide an excellent foundation upon which to build in-house training in the specific veterinary requirements. Similarly, there are currently no internationally accepted general quality assurance schemes available specifically for veterinary laboratories, although medical schemes are very helpful. A combination of relevant internal and external systems is therefore essential. Modern, sophisticated biochemistry ana-

lyzers can run automatic quality controls for each assay but routine repeat analysis of split samples on different days is also necessary. Efficient secretarial services are essential for results to be reported and transmitted accurately and quickly.

Hematology

A variety of hematologic abnormalities can be recognized in blood samples collected from performance horses.

Erythrocyte abnormalities

Hemoconcentration/dehydration

Hemoconcentration/dehydration (raised total erythrocyte count, hematocrit and hemoglobin concentration) can be interpreted only in samples taken from resting horses that are relaxed at collection, which can be very difficult to achieve in some excitable individuals. Reflex splenic contraction occurs in horses in response to fright, excitement, and exercise, increasing numbers of young macrocytic erythrocytes in the circulating pool.[4,6,13,50,51] Routine sampling sessions in performance-horse stables are therefore often conducted at standard times after a period of rest and quiet, e.g. early morning or late afternoon, before mucking out and feeding, to avoid sampling excited horses and to add a degree of standardization.

Hemoconcentration is sometimes a feature of so-called 'over-trained' horses,[30] who perform poorly; appear stressed; have dry, scurfy, skin coats, lose condition and who drink inadequately. They usually respond well to fluid and electrolyte therapy administered by nasogastric tube followed by a period of rest. Chronic anhidrosis[52] can produce a similar picture.

Dehydration is a feature of horses that are clinically ill with acute enteritis or colitis,[53–55] requiring intensive fluid, electrolyte, acid–base, and supportive therapy to replace losses.[56–58]

Hemoconcentration or dehydration are features of exercise and heat exhaustion in horses performing in hot dry climates and over long distances (typically endurance races), requiring timely diagnosis and appropriate treatment/management.[57,59] The interesting condition of acute anhidrosis,[52] i.e. failure of normal sweating, occurs in some horses who are raised in temperate climates and then perform in hot, dry climates when they have failed to acclimatize, resulting in respiratory distress, labored breathing, pyrexia, collapse, and even death.

Attempts have been made to interpret the significance of results of postexercise blood samples in terms of fitness.[21,22] In terms of hematologic tests, variable degrees of hemoconcentration and leukocytosis (see below) are always a feature and without rigid standard exercise test regimes,[60] which are almost impossible to organize within most performance-horse training environments, results are usually uninterpretable. Specific muscle enzyme tests (see later), performed on serum samples collected before and after exercise, can help with the diagnosis of exertional myopathy.[61] There has been considerable interest in lactate assays[62] before, during, and after exercise to determine aerobic/anaerobic metabolic capacity, with still considerable debate and differences of opinion.

It has been shown that the osmotic fragility of erythrocytes is increased by exercise regardless of release of erythrocytes from the spleen into the peripheral circulation.[51] The precise mechanism for these changes remains unknown but they may be involved in the apparent decrease in mean cell volume (MCV) and increase in mean cell hemoglobin concentration (MCHC), which occur with exercise.

Echinocytes (spiculated erythrocytes) have been demonstrated in equine blood samples[63] in a variety of systemic diseases and in response to exercise, apparently associated with electrolyte shifts, particularly hyponatremia. Their presence decreases erythrocyte sedimentation rate but does not affect whole-blood viscosity. Although horses with echinocytosis have higher plasma lactate levels during exercise and higher serum CK levels after exercise, their presence appears to have no demonstrable effect on exercise potential.

Anemia

In horses, anemia (low total erythrocyte count, hematocrit, and hemoglobin concentration) is less commonly a primary condition and more often occurs secondary to some other primary condition, for example infection (bacterial or viral), parasitism (endo- or ectoparasitism), or metabolic abnormality (e.g. hepatopathy, nephropathy), which requires specific diagnosis and treatment.[55,64] Malnutrition is rarely seen in performance-horse stables but mineral and vitamin imbalances (involving deficiency or excess) may occur.

Acute hemorrhage can cause acute primary blood-loss anemia following accidental injury involving a major blood vessel. The hemorrhage may sometimes be visible externally but more often occurs internally within a body cavity (i.e. intraperitoneal, intrapleural or intrapericardial hemorrhage). Chronic hemorrhage, for example following castration, may cause an anemia and self-perpetuating thrombocytopenia.[55] Platelet transfusion may result in hemostasis without further surgical interference. Guttural pouch mycosis[65] may cause internal carotid artery ulceration, resulting in profound acute, and sometimes fatal, blood-loss anemia. Gastric ulceration.[66] not uncommonly seen in performance horses, can cause anemia from chronic hemorrhage. Examination of fecal samples for the presence of occult blood can be performed but results are frequently positive, most commonly because of the activity of intestinal parasites, even in well managed horses, and are therefore not reliably diagnostic of gastric ulceration. Unfortunately, serum pepsinogen assays[67] are not reliably diagnostic of gastric ulceration in horses. Where suspected, the diagnosis must be made and the significance assessed by gastroscopic examinations.

It has been reported that the repeated administration of recombinant human erythropoietin (rhEPO) to race horses results in the production of anti-rhEPO antibodies that can result in moderate to severe anemia.[68,69]

Intravascular hemolysis (i.e. erythrocyte destruction resulting in hemolytic anemia) has a variety of different causes, which require specific diagnostic testing. Equine infectious anemia[70] (Coggins' agar gel immunodiffusion test), autoimmune hemolytic anemia[55] (Coombs' antiglobulin test), piroplasmosis[71] (babesiosis) (complement fixation test), disseminated intravascular coagulopathy[55] (DIC; prolonged prothrombin and activated partial thromboplastin times) and a variety of plant and environmental toxins[72] are some causes of intravascular hemolysis.

Equine anemia is most commonly macrocytic (raised MCV), reflecting splenic replacement with juvenile erythrocytes, as seen with blood loss, infections, and parasitism. Reticulocytes are not commonly seen in equine blood samples[4,6] and so their presence or absence is not a reliable means of determining regeneration or non-regeneration, as in other species. Normocytic (MCV within the normal range) anemia is sometimes seen in horses that are being challenged by respiratory viruses but show no clinical signs. Microcytic anemia (low MCV) is uncommon but is sometimes seen in immature individuals and has been reported in horses with iron/folate deficiency.[73]

Leukocyte abnormalities

Leukocytosis and neutrophilia

Leukocytosis (raised total leukocyte count) and neutrophilia (raised segmented neutrophil count) most commonly occur in performance horses in association with septic and non-septic inflammatory conditions.[4,6,13,74] Septic inflammation is most commonly associated with bacterial infection. In performance horses this most commonly follows an injury, for example penetrating wounds followed by cellulitis, septic arthritis or tenosynovitis, upper respiratory infections, and less commonly in systemic bacterial infections. Non-septic inflammation most commonly occurs after a non-penetrating injury (e.g. bruising of soft tissues, tendons, ligaments or periosteum and traumatic arthritis or tenosynovitis) and is sometimes associated with degenerative joint disease.

Neutrophilic 'shifts to the left' (juvenile neutrophils or 'band' neutrophils), although diagnostically helpful in foalhood infections, are seldom seen in adult horses unless severely and acutely infected with conditions such as acute cellulitis or lymphangitis.[75] Some cases of acute salmonellosis, endotoxemia, peracute enterocolitis, peritonitis, and pleuritis have neutrophilic shifts to the left, more commonly associated with leukopenia and neutropenia.[76–78]

Leukopenia and neutropenia

Leukopenia (low total leukocyte count) and neutropenia (low segmented neutrophil count) are most commonly seen in adult performance horses during the acute phase of a viral challenge,[4,6,13,79] when there may or may not be clinical signs. These signs include lethargy, pyrexia, nasal discharge, coughing, and edematous legs. Leukocytic changes seen with infection very much depend upon sampling time in relation to the stage of the disease process (Fig. 43.1).

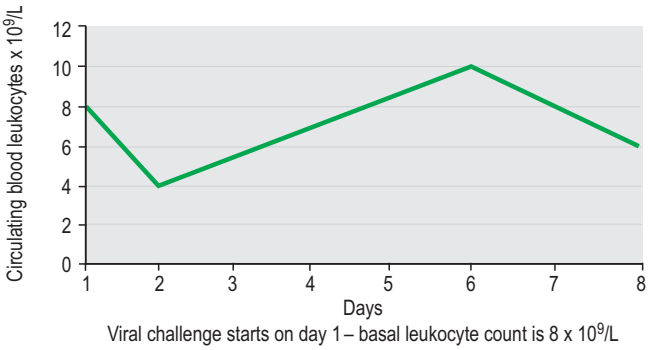


Fig. 43.1
Schematic diagram depicting total circulating blood leukocyte (WBC) response to viral challenge.

If the early acute infectious phase has passed then the leukopenic phase will be missed and hematologic examinations will reflect repair and sometimes secondary bacterial involvement with leukocytosis and neutrophilia. To help with diagnosis, epidemiology, and assessment of recovery blood samples should therefore be taken from symptomless stablemates where viral infections are suspected. Unfortunately, unless equine influenza, herpesvirus, rhinovirus, or adenovirus infections are involved (for which specific serologic assays are available), virologic 'screening' investigations are seldom rewarding.

Profound leukopenia with neutropenia and neutrophilic shifts to the left are sometimes seen in adult performance horses suffering from acute salmonellosis, peracute enterocolitis, peritonitis, and pleuritis/pleuropneumonia.[76–78] This is always a sign of severe illness, indicating the need for intensive care and suggesting a guarded prognosis.

Lymphocytosis

Lymphocytosis (raised lymphocyte count) is seen in horses in response to endogenous catecholamine release during excitement or exercise.[22] Otherwise, it is most commonly seen in response to some chronic viral infections and, more rarely, in autoimmune diseases. Massive leukocytosis (sometimes greater than 100×10^9/L) with lymphocytosis is a feature of generalized lymphoma,[80] in which neoplastic lymphocytes can be demonstrated in peripheral blood, body cavity fluid samples, and tissue biopsy samples.

Lymphopenia

The low lymphocyte count of lymphopenia is seen in horses in response to endogenous glucocorticoid release and in response to exogenous corticosteroid administration.[81] Otherwise, it can be seen in acute viral infections, severe

bacterial infections, septicemia, endotoxemia, and immune deficiency conditions. Profound, persistent leukopenia always carries a poor prognosis.

Monocytosis

Monocytosis (raised monocyte count) reflects increased phagocytic demand, as may occur with chronic suppurative conditions with tissue necrosis.[4,6,13,79] In performance horses, monocytosis is most commonly seen during the postacute or recovery phases following upper respiratory viral infections.

Eosinophilia

A raised eosinophil count occurs with antigen–antibody response in tissues rich in mast cells (e.g. skin, lung, gastrointestinal tract, and uterus) and in parasitically sensitized horses.[4,6,13,82] In performance horses, low-grade eosinophilia is most commonly seen in association with leukopenia or lymphocytosis in the acute phase of responses to viral infections.[13,79] Rare cases of eosinophilic leukemia have been seen with eosinophil counts as high as 2.5×10^9/L (25% of differential leukocyte count).

Basophilia

The raised basophil count of basophilia is very uncommon in horses, as is the presence of basophils themselves. Basophils have been a feature in cases of hyperlipidemia and in some horses that were recovering from colic.

Platelet abnormalities

Thrombocytosis (raised platelet count) is uncommon in adult horses but may occur in bacterial infections.[4,6,13,55]

Thrombocytopenia (low platelet count) may be a reflection of decreased platelet production, increased usage or from various spurious factors, e.g. drug administration, the presence of cold agglutinins in the sample, or platelet clumping in EDTA.[83] Where pseudothrombocytopenia is suspected, platelet counts should be measured on two blood samples collected at the same time, one into EDTA and the other into sodium citrate anticoagulants. If the sodium citrate sample, after correction for dilution, is considerably higher than the EDTA sample, EDTA-induced pseudothrombocytopenia is the likely answer. Decreased production may occur with neoplasia or a toxic insult to the bone marrow, the latter is diagnosable by biopsy.[84] Idiopathic thrombocytopenia is probably an immune-mediated condition and thrombocytopenia is seen in horses with disseminated intravascular coagulopathy (DIC),[55] most commonly a serious complication of acute enterocolitis.

When to use hematologic analysis

The regular, routine use of hematologic examinations to screen horses in training for subclinical disease can be helpful providing the results are interpreted carefully. Depending on the stage of sampling, Hematologic signs of viral infection (leukopenia and neutropenia) or relative lymphocytosis in a clinically normal horse may suggest 'challenge' (i.e. the horse's immune system is responding, but not succumbing, to the infection). In this condition, many horses do not perform to their best athletic potential, their recovery after exertion may be prolonged and they may be more likely to suffer secondary complications such as pneumonia, lung abscess, skeletal and/or cardiac myopathy, and/or exercise-induced pulmonary hemorrhage.

In cases of clinical disease, hematologic variations from 'normality' are often marked and obvious, but more sophisticated analytical equipment is required when screening for less obvious variations and trends. Modern automated cytochemical hematology analyzers (e.g. Bayer Advia 120) provide accurate differential cell counts that correlate closely with traditional manual differential counting techniques. Their automated differentials are highly repeatable and are likely to be more accurate than manual cell counts as they are performed on 10 000 rather than 100 leukocytes. The results provided by these analyzers are more accurate, repeatable, and therefore reliable for the routine monitoring of performance horses. However, when required by clinical history or results obtained, a traditional stained smear is still required to demonstrate erythrocyte or leukocyte abnormalities. In erythrocytes these abnormalities include Howell–Jolly bodies, nucleation, fragmentation, oxidative damage, spherocytes, basophilic stippling or *Babesia* spp. parasites in piroplasmosis. In leukocytes they include left shifts, toxic changes, hypersegmentation, neoplastic change or cytoplasmic inclusions as seen for example in ehrlichiosis.[14,85–87]

Clinical chemistry

Proteins

Total protein, albumin and globulin estimations are useful in the assessment of general bodily condition and nutritional status, and the response to infectious or parasitic disease.[20] Electrophoresis helps determine the significance of raised total globulin levels.[7,13,88] Horses in training, although not at pasture, usually have access to areas of communal grazing that can become contaminated with parasitic larvae. Yearlings usually leave stud farms having received comprehensive worm-control programs and have therefore had little opportunity to develop natural immunity to intestinal parasites. It is therefore essential that adequate worm-control programs are maintained throughout training or problems with large strongylosis, cyathostomiasis, or tapeworm infestations may occur, sometimes with fatal consequences.[89,90] Specific tapeworm ELISA assays are now available commercially.[91] Serum protein assays can be very useful as part of the stable's routine worm-control monitoring program. Low serum albumin and/or rising globulin levels are a 'red flag' warning,

most commonly seen with cyathostomiasis[92] (hypoalbuminemia), large strongylosis[93] (raised β-1 globulin), mixed helminthiasis (hypoalbuminemia and raised β-1 globulin), hepatopathy (hypoalbuminemia and raised β-2 globulin), antibody response to infection (raised γ globulin) or abscess formation (raised α-2 and γ globulins).[13] Globulins can be differentiated by electrophoresis (Fig. 43.2).

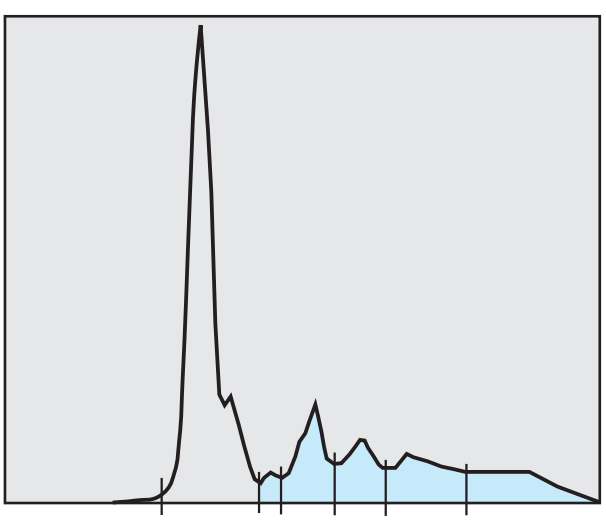
Protein electrophoresis

This identifies elevations in specific globulin fractions:

- α-2 globulin: acute-phase inflammatory protein responses (Fig. 43.3).
- β-1 globulin: *Strongylus vulgaris* and mixed strongyle larval activity (Fig. 43.4).
- β-2 globulin: hepatopathy (Fig. 43.5).
- γ globulin: antibody responses to bacterial or viral infections (Fig. 43.6).

Horses with abscesses will often show characteristic α-2 and γ globulin responses. Serum samples should be used for protein electrophoresis, as raised fibrinogen levels in heparinized plasma samples will cause confusing rises in β-2 globulins (Fig. 43.7).

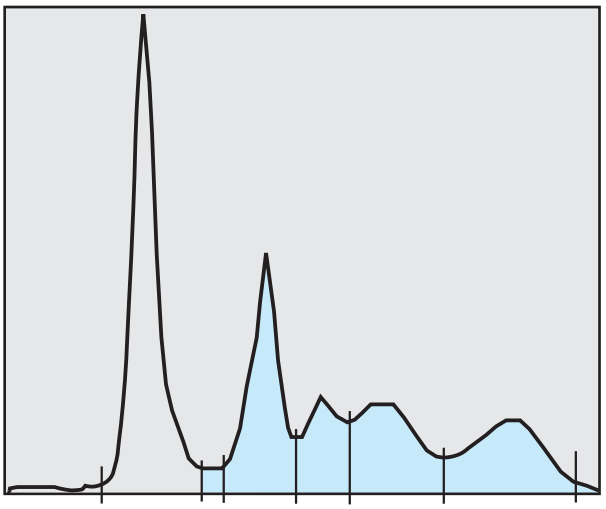
Occasionally, horses with generalized lymphosarcoma[80] or plasma cell myeloma[94] have massively increased total protein and globulin levels, for which protein electrophoresis shows a massively raised, discrete, 'skyrocket' peak, usually in the β-2 globulin range (Fig. 43.8) suggesting monoclonal lymphoma protein production.[95]



Fraction	Rel %	g/L
1	5.0	1.10
2	26.1	5.74
3	20.6	4.53
4	24.9	5.48
5	23.5	5.17

Total g/L 22.0

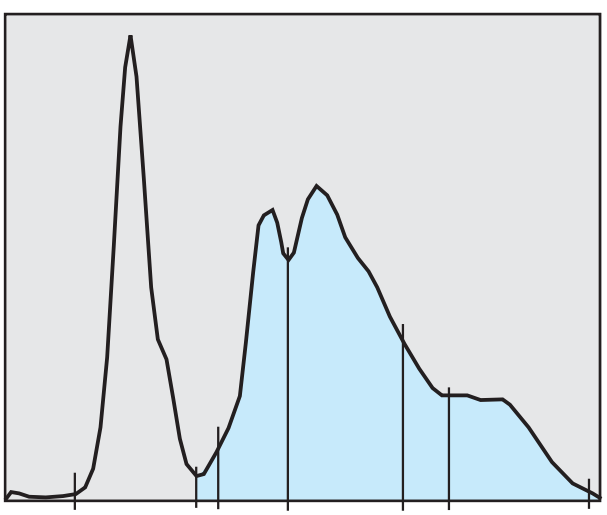
Fig. 43.2
Serum protein electrophoresis – normal horse.



Fraction	Rel %	g/L
1	2.0	0.78
2	33.7	13.14
3	16.4	6.40
4	24.5	9.56
5	23.4	9.13

Total g/L 39.0

Fig. 43.3
Serum protein electrophoresis – α-2 globulin response in a horse with an acute-phase inflammatory protein response.



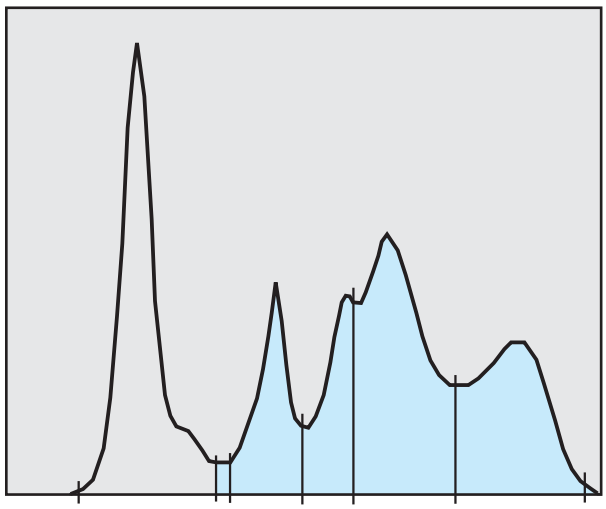
Fraction	Rel %	g/L
1	1.3	0.62
2	24.0	11.52
3	48.2	23.14
4	10.4	4.99
5	16.2	7.78

Total g/L 48.0

Fig. 43.4
Serum protein electrophoresis – β-1 globulin response in a horse with large strongyle larval migratory activity.

Plasma fibrinogen

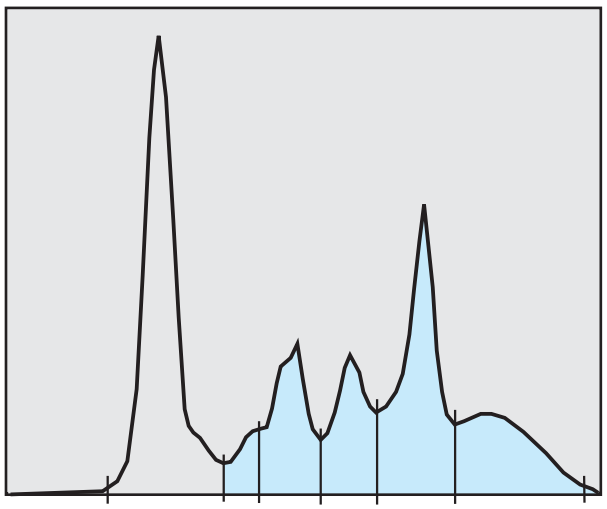
This is an acute-phase reactive protein, which increases in response to inflammation.[74,96] Elevations are found in the



Fraction	Rel %	g/L
1	0.9	0.49
2	17.0	9.18
3	15.2	8.21
4	39.3	21.22
5	27.6	14.90

Total g/L 54.0

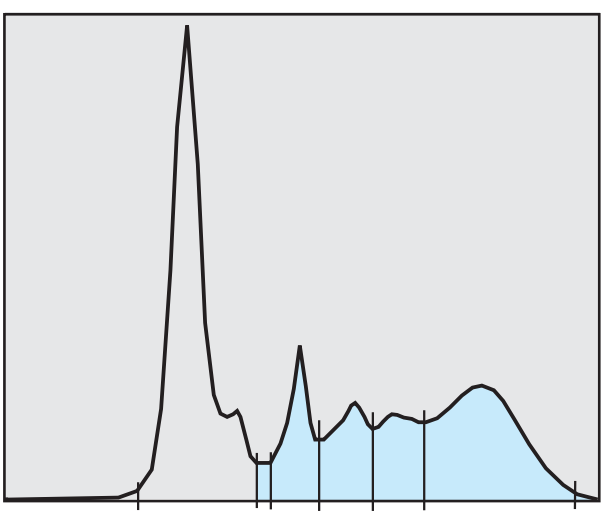
Fig. 43.5
Serum protein electrophoresis – β-2 globulin response in a horse with hepatopathy.



Fraction	Rel %	g/L
1	5.4	2.48
2	19.8	9.11
3	17.5	8.05
4	36.0	16.56
5	21.3	9.80

Total g/L 46.0

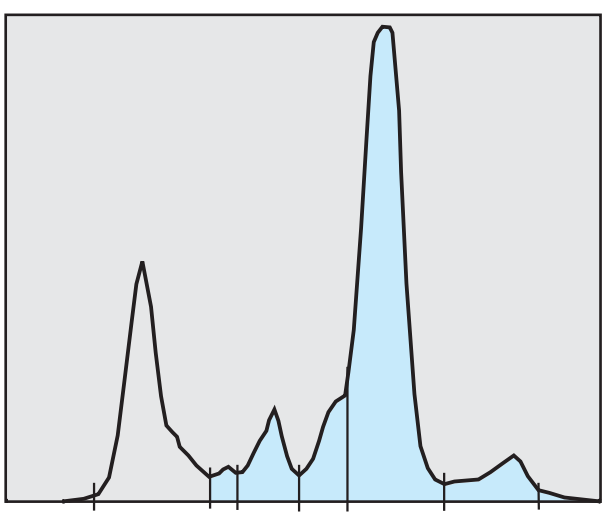
Fig. 43.7
Serum protein electrophoresis – high β-2 globulin peak measured in a heparinized plasma sample from a horse with a high fibrinogen level but no serum liver enzyme abnormalities.



Fraction	Rel %	g/L
1	2.1	0.76
2	18.3	6.59
3	17.5	6.30
4	17.1	6.16
5	45.1	16.24

Total g/L 36.0

Fig. 43.6
Serum protein electrophoresis – γ-globulin response in a horse with an antibody response to infection.



Fraction	Rel %	g/L
1	2.1	1.91
2	9.5	8.65
3	9.5	8.65
4	71.2	64.79
5	7.6	6.92

Total g/L 91.0

Fig. 43.8
Serum protein electrophoresis – massive 'skyrocket' peak in β-2 globulin range, suggesting monoclonal lymphoma protein production in a horse with generalized lymphosarcoma.

presence of tissue damage and this assay may help with diagnosis and prognosis in cases of internal abscessation, chronic infectious or parasitic disease and in cases of exercise-induced pulmonary hemorrhage (EIPH). The test can be performed on fresh, paired, non-hemolyzed EDTA and serum samples by subtraction of serum protein from plasma protein results, but more accurate results are obtained from samples collected into sodium citrate anticoagulant to measure values by direct coagulometric assay. When measured serially with serum amyloid A (see below) the kinetics of the inflammatory response can often be determined (Fig. 43.9) and this can be very helpful when monitoring response to treatment.

Plasma viscosity (PV)

This is a very non-specific measure of inflammation and acute tissue damage, which may help with the diagnosis and prognosis of inflammatory response. Fresh, non-hemolyzed sequestrated or heparinized blood samples are required. Some trainers of performance horses like to monitor PVs as a crude guide to health and fitness. It has superseded the use of erythrocyte sedimentation rate (ESR), which was used in a similar manner. Because of the horse erythrocyte's tendency to form rouleaux, ESR is a highly inaccurate test and it is much more satisfactory to measure PV directly.[97] Plasma viscometers have become difficult to source and fibrinogen and amyloid A assays will probably replace the use of PV assay because their results are inherently more accurate and useful.

Serum amyloid A (SAA)

This is a highly sensitive, rapidly reacting inflammatory protein, which can be very helpful in monitoring early responses to infection and their response to treatment.[98] Most normal horses have zero measurable levels and in the face of acute, particularly septic inflammation, levels increase quickly (within 24 h) to over 20 mg/L and sometimes more than 100 mg/L. Levels peak and fall similarly quickly with subsidence of inflammation when the infection responds to antibiotic therapy (see Fig. 43.9).

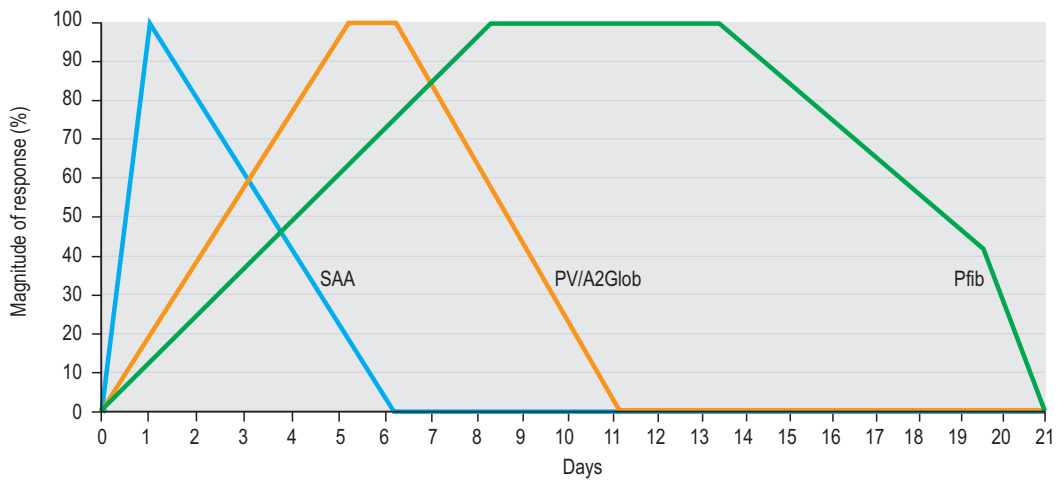


Fig. 43.9 Schematic diagram depicting inflammatory protein (plasma viscosity and fibrinogen, Pfib; serum α-2 globulin and amyloid A, SAA) dynamics during an inflammatory response.

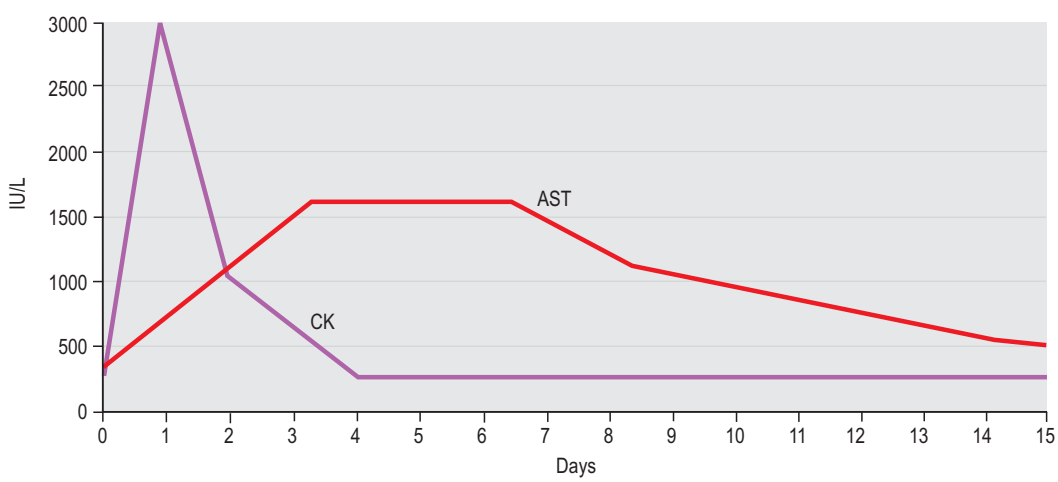


Fig. 43.10 Schematic diagram depicting serum muscle enzyme (AST and CK) levels following a relatively mild episode of exercise-induced myopathy.

Aspartate aminotransferase (AST, AAT, SGOT)

Elevations are seen in the presence of acute myopathy[61,99,100] or hepatopathy.[101–105] After myopathy, levels peak at 24–48 h and return to baseline by 10–21 days, assuming that no further damage occurs. This test, taken with CK at first visit and then 10–14 days later, can therefore be a useful guide to recovery from acute myopathy (Fig. 43.10).

Creatine kinase (CK, CPK)

Elevations are specifically seen in the presence of acute myopathy.[61,99,100,106] CK isoenzyme analysis[107] was (before routine ultrasound diagnosis) used in human medicine to help differentiate cardiac and skeletal myopathy from brain pathology, but has never become routinely established in equine sports medicine. Cardiac troponin assays (see later) are now used to differentiate skeletal from cardiac myopathy in horses.

CK levels peak at 6–12 h and return to baseline by 3–4 days, assuming that no further myopathy occurs. When measured alongside AST, which takes longer to rise, peak and return to normal, the timing and response to treatment of myopathy in horses can be usefully monitored (see Fig. 43.10). Paired CK assays taken before and 2–3 h after strenuous exercise can form a useful diagnostic test for exercise-induced myopathy, in horses where the diagnosis may be in doubt. Some respiratory virus infections, notably equine herpesvirus-1, appear to increase muscle cell membrane fragility and predispose to exercise-induced myopathy in horses in training.[108] This condition is sometimes

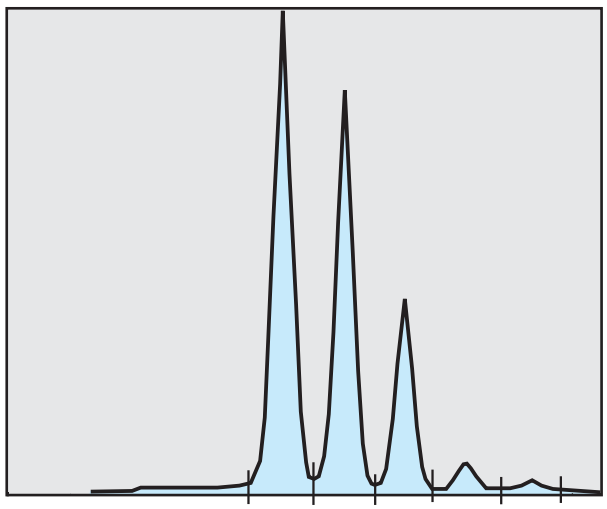


Fig. 43.12
Serum lactate dehydrogenase (LD) isoenzyme analysis – high LD1 in a horse with intravascular hemolysis.

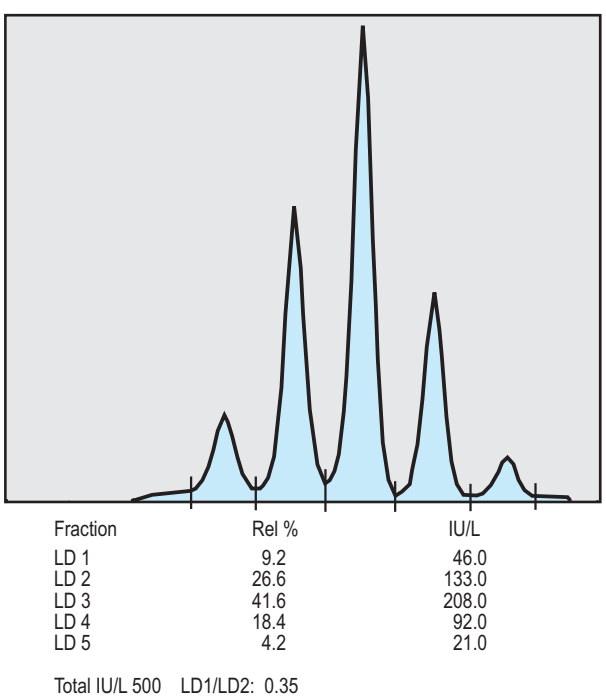


Fig. 43.11
Serum lactate dehydrogenase (LD) isoenzyme analysis – normal horse.

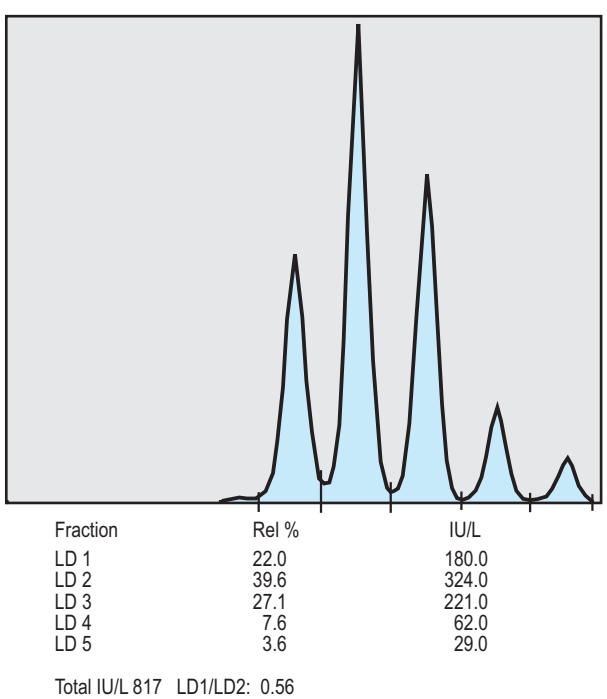
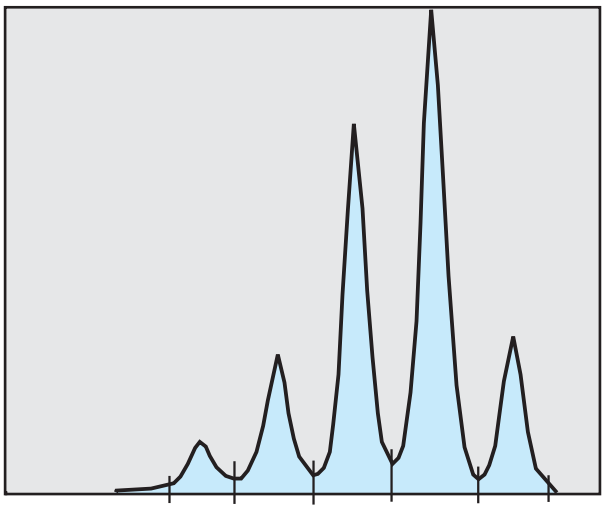


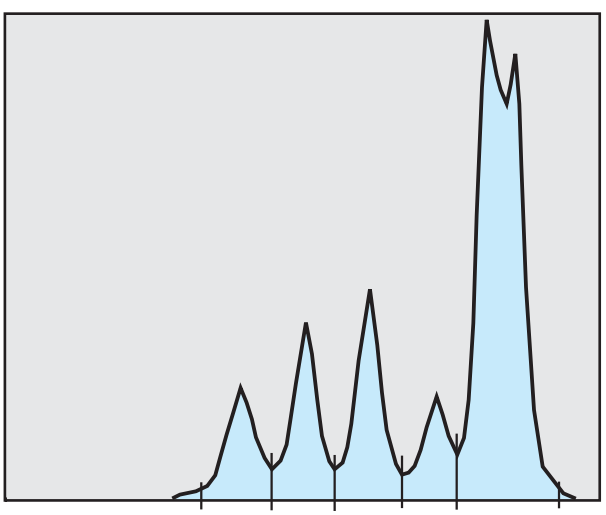
Fig. 43.13
Serum lactate dehydrogenase (LD) isoenzyme analysis – high LD2 in a horse with cardiac abnormality.



Fraction	Rel %	IU/L
LD 1	4.9	39.0
LD 2	12.1	96.0
LD 3	29.4	233.0
LD 4	41.4	328.0
LD 5	12.2	97.0

Total IU/L 792 LD1/LD2: 0.40

Fig. 43.14
Serum lactate dehydrogenase (LD) isoenzyme analysis – high LD4 in a horse with enteropathy.



Fraction	Rel %	IU/L
LD 1	9.3	205.0
LD 2	12.7	280.0
LD 3	15.8	348.0
LD 4	7.3	161.0
LD 5	54.8	1207.0

Total IU/L 2203 LD1/LD2: 0.73

Fig. 43.15
Serum lactate dehydrogenase (LD) isoenzyme analysis – high LD5 in a horse with exertional myopathy.

associated with clinical signs of fatigue and stiffness in performance horses.[109]

Significant myopathy, demonstrable by higher serum CK and AST levels, occurs more often after exercise in unfit rather than in fit horses. The conditioning process protects equine muscle cells from exercise-induced injury.[106]

Lactate dehydrogenase (LD)

A variety of disease conditions can cause elevations in total LD and more useful differentiation can sometimes be provided by isoenzyme analysis[7,13,110] (Fig. 43.11):

- LD isoenzyme 1: most dramatically increased by intravascular hemolysis (Fig. 43.12).
- LD isoenzyme 2: elevated in some cases of cardiac pathology, an indication for cardiac troponin assay (Fig. 43.13).
- LD isoenzyme 3: no known disease association in the horse.
- LD isoenzyme 4: most commonly elevated by intestinal pathology (Fig. 43.14).
- LD isoenzyme 5: rises seen with skeletal myopathy and hepatopathy, requiring further differentiation with CK and liver enzyme assays (Fig. 43.15).

Cardiac troponin (cTnI)

Two proteins (tropomyosin and troponin) work in concert with calcium to regulate muscle contraction.[111] Troponin is a globular protein complex composed of three single-chain polypeptide subunits: TnI (troponin inhibitory component), which prevents muscle contractions in the absence of calcium; TnT (tropomyosin-binding component), which connects the troponin complex with tropomyosin; and TnC (calcium-binding component), which binds calcium. The cardiac-muscle-specific isoform cTnI (24 kDa) exhibits approximately 60% homology with the skeletal isoforms (sTnI) and has a unique 31-amino-acid extension of the N-terminus. Experience in human medicine has shown that after acute myocardial infarction (AMI), elevated cTnI levels appear in the circulation within 3–6 h. Serum levels peak within 14–20 h and return to normal after 5–7 days. The measurement of cTnI can therefore be a useful diagnostic aid for AMI and an aid for the monitoring of recovery.[111]

Myocardial infarction is rarely diagnosed in horses but myocardial necrosis is seen in conditions such as atypical myoglobinuria.[112] Myocarditis is sometimes suspected on the basis of echocardiographic abnormalities and/or raised serum lactate dehydrogenase isoenzyme-2 levels, most commonly following upper respiratory viral infections, which can predispose to exercise-induced cardiomyopathy. Horses who have suffered in this way will need rest and supportive treatment, followed by follow-up to normality before returning to strenuous exercise if potentially serious complications are to be avoided. Raised cTnI levels in a performance horse in training are an indication for cardiac ultrasound examinations and monitoring.[112]

Cardiac troponin (cTnI) levels are measured in serum samples. Clinically normal horses have serum cTnI levels of less than 0.2 ng/mL. Experience so far suggests that greater than 0.3 ng/mL is abnormal, i.e. suggests myocardial

pathology and 0.2–0.3 ng/mL is currently a 'gray' zone. Levels of 0.9–5.4 ng/mL have been measured in horses with ultrasound-confirmed cardiomyopathy.

Sorbitol dehydrogenase (SDH)

This is an enzyme found in the cytoplasm of hepatocytes and is therefore virtually liver specific,[113] although rises are sometimes seen in horses with skin conditions and enteropathy. It is useful for the identification of acute hepatocellular damage for in-house laboratory conditions, but the enzyme is highly labile. Therefore, samples must be handled with care and assays must be performed within 8–12 h of sampling, making SDH assays unsatisfactory for transported samples.

Glutamate dehydrogenase (GLDH)

Elevations are seen in the presence of acute hepatocellular damage. This is a mitochondrial enzyme found mainly in liver, heart muscle, and kidney. It is a relatively stable enzyme and is a suitable replacement for sorbitol dehydrogenase (SDH) in transported samples.[13] GLDH rises are sometimes seen in horses with skin conditions and enteropathy.

L-gamma glutamyltransferase (GGT)

GGT is found in cell membranes of hepatocytes and biliary epithelial cells, but the enzyme is also found in the pancreas and kidney.[101,102,104,105] Elevations in serum levels are seen in the presence of acute hepatitis, chronic liver cirrhosis, and in very rare cases of pancreatitis. Nephropathy does not usually result in significantly raised serum GGT levels so high levels measured in the horse are usually a sign of biliary or cholestatic disease. Chronic pyrrolizidine alkaloid toxicity (ragwort, i.e. *Senecio jacobea*, poisoning) causes bile duct hyperplasia and biliary stasis and therefore typically results in raised serum GGT and alkaline phosphatase levels.[114] This remains an important cause of hepatopathy in horses and ponies in the UK, who ingest the plant unknowingly in poor-quality hay. Toxicity is uncommon in well-managed performance horses.

Idiopathic GGT elevations are not uncommonly seen in horses in training who appear otherwise healthy but perform poorly. The cause of these GGT rises has not yet been satisfactorily defined, although plant and fungal hepatotoxins have been suspected. In most cases, other liver enzymes are within normal range as are urea and creatinine levels, and liver biopsy reveals insignificant histopathologic findings. It is therefore not certain that primary hepatopathy or nephropathy is involved. Some cases have raised muscle enzymes suggesting an association with myopathy, either directly or secondarily, again perhaps via respiratory virus-induced increased muscle cell membrane fragility. Most cases respond (GGT levels return to normal) to a period of rest from exercise.

Urine GGT:creatinine ratios are elevated (> 4.0) in renal tubular pathology.[115]

Alkaline phosphatase (SAP)

Elevations in this brush-border enzyme are most commonly seen in the presence of chronic biliary obstructive liver pathology (e.g. chronic pyrrolizidine alkaloid toxicity).[101–105] High levels are also seen with abnormalities of bone metabolism and intestinal malfunction.[116]

Intestinal phosphatase (IAP)

Elevations relative to total SAP are seen in the presence of intestinal pathology.[116]

Reference ranges for serum SAP and IAP levels are age-related[10] and apparently high results must be interpreted carefully in immature performance horses.

Bilirubin

The analysis of bilirubin levels is seldom useful in the horse but may aid the classification of anemia and jaundice in some cases.[5,101,102,117] Owing to the horse's unusual biliary excretion system, indirect (unconjugated) bilirubin levels may be higher than those in other species, without clinical disease, and the significance of elevations without other abnormalities may therefore be difficult to interpret. A period of anorexia, inanition, or intestinal malfunction typically increases indirect bilirubin levels spuriously.

Bile acids

This is a much better guide to hepatobiliary status than bilirubin assays. High bile acid levels occur with embarrassed hepatic function[118] and are a useful diagnostic and prognostic liver function guide in horses.

It is important to remember that none of the liver enzymes, measured singly or in a 'profile', give any useful information about liver function.[103] The liver has a large functional reserve and compensatory capacity. Liver enzyme rises suggest hepatopathy that can be differentiated to a degree into acute, chronic, biliary obstructive, or mixed pathology, but bile acid assays and bromsulfalein clearance test results reveal either adequate (normal levels) or impaired (high levels) functional compensation. Impaired hepatic function suggests a guarded prognosis. Liver biopsy and ultrasound examinations are required to confirm an etiologic diagnosis on the basis of histopathologic and echographic features.

Bromsulfalein (sulfobromophthalein, BSP) clearance

Abnormally long clearance half-times for this liver-cleared dye are seen in the presence of gross liver malfunction and results may provide a useful diagnostic and prognostic guide to liver function.[119] Its use has decreased now that bile acid

assays (whose results appear to correlate well) have become available. After a baseline (time zero), jugular venous serum sample is taken, two vials of prewarmed reagent are injected intravenously. Serum samples are then taken from the other jugular vein at 2, 4, 8, and 16 min, after injection. Half-time clearances of more than 90 s are considered abnormal in horses.

Amylase

Elevations occur in the presence of pancreatitis,[120] but this condition is rarely diagnosed in the horse.

Glucose

Other than for oral glucose and xylose absorption tests,[121] useful for the diagnosis and evaluation of intestinal malabsorption cases, the value of this assay in adult horses is limited to cases of pituitary adenoma (equine Cushing's syndrome).[122,123] This condition is seldom seen in young horses in training. Cases are frequently hyperglycemic.

Samples for glucose assay must be taken into fluoride anticoagulant and must reach the laboratory within hours of collection.

Cholesterol and triglycerides

Elevations are seen in the presence of abnormal lipid metabolism and hyperlipidemia.[124] These conditions, which are typically seen in the Shetland and other small ponies, are seldom recognized in well-managed performance horses.

Urea

Urea is produced in the liver from the metabolism of ammonia.[125] Elevations are seen in the presence of abnormal renal function. Urea levels may rise in the hemoconcentrated and 'over-trained' horse, associated with fluid balance shifts rather than renal disease. Many cases of equine dysautonomia ('grass sickness')[126] have a degree of uremia but this is usually caused by catabolism. A period of anorexia can have a similar result.

Creatinine

Creatinine is formed in muscles from creatine breakdown and is excreted via the kidneys.[125] In normal horses, daily production and excretion are remarkably constant, leading to its use as an arithmetic constant for use with urinary fractional excretion rates (see below). Therefore serum elevations reflect renal malfunction (reduced glomerular filtration), levels being controlled by excretion rate. This may occur in horses with prerenal (e.g. circulatory disturbances, dehydration or shock), renal (insufficiency) or postrenal (obstructive) conditions.[7]

Urinary fractional electrolyte and mineral clearance ratios

In horses with normal renal tubular function, urinary excretion rate of creatinine is almost constant. It can therefore be used as an arithmetic constant to produce a measure of the fractional excretion of electrolytes and minerals in equine urine.[7,127–129] Concentrations of electrolytes or minerals are measured in serum and urine samples collected at the same time or at least within 1 h of one another. Diuretics must not be used to stimulate urination.

The percentage excretion of an electrolyte is calculated from the following equation:

$$\text{Fractional urinary excretion (\%)} = \frac{(E)u}{(E)s} \times \frac{(Cr)s}{(Cr)u} \times 100$$

Where: (E)u is the concentration of electrolyte in the urine, (E)s is the concentration of electrolyte in the serum, (Cr)u is the concentration of creatinine in the urine and (Cr)s is the concentration of creatinine in the serum.

Fractional excretion rates for sodium, potassium, chloride, magnesium, calcium, and phosphate are most commonly measured. The result provides an assessment of the horse's homeostatic regulatory status for that electrolyte or mineral, e.g. sodium and chloride may be selectively excreted at an increased rate because of excessive dietary salt intake. Phosphate may be excreted at an increased rate to try to maintain a normal serum calcium:phosphate ratio in the face of inadequate calcium intake.[7] The use of this method applies only to horses with normal renal function. Impaired renal tubular function results in high urine excretion rates for all the electrolytes and minerals, from failure of retention, and in such cases, creatinine is not a valid arithmetic constant.

Electrolyte imbalance may predispose to exercise-induced myopathy in horses in training and so fractional clearance ratios may sometimes be helpful in the investigation and management of recurrent cases.[127,129] Dietary deficiencies, excesses, or imbalances can be corrected and return to normal excretion rates monitored, sometimes with useful results in terms of resolution of myopathy.

In secondary nutritional hyperparathyroidism,[7] which is commonly seen in horses on a high-phosphate training diet, phosphate excretion rate is high, indicating the need for oral calcium supplementation and phosphate reduction, to restore balance. Experience has shown that, in the UK, many healthy, fit, stabled and well-performing horses receiving high cereal training rations have urinary fractional phosphate excretion rates in excess of 9%, emphasizing the need for calcium supplementation. Higher excretion rates are seen in horses with clinical manifestations of secondary nutritional hyperparathyroidism, which include shifting lameness, periosteal thickening, and facial and mandibular swelling.

Sodium, phosphate, and chloride

Electrolyte imbalance and fluid loss may occur with diarrhea, endotoxemia, intestinal crises, and exertional

exhaustion.[46,53–59,130] The latter is of particular importance for endurance horses and for other horses performing in hot and humid weather conditions.[131] Serial assays are helpful with intensive care cases. In other cases, urinary fractional electrolyte excretion rates (see above) are a much better assessment than single serum assays.

Calcium, phosphate and magnesium

Mineral analysis may be helpful in young horses, i.e. yearlings and 2-year-olds coming into training, with signs suggesting abnormalities of bone metabolism.[132] As homeostatic mechanisms are efficient, serum levels are often normal even in the face of whole body abnormality, and thus urinary fractional excretion rates are of greater value.

Plasma lactate

A number of hand-held and bench-top blood lactate analyzers have been used in horses. Most have been designed to help assess the human response to exercise. Results have been used to describe and predict aerobic endurance capacity in horses and it has been suggested that the rate of decline in blood lactate concentration, which occurs after exercise, may be a useful index of fitness.[62,133–136] Persistent high blood lactate concentrations may suggest metabolic fatigue. Anerobic capacity is essential for sprinters and so increases in blood lactate concentrations for fast, short-distance Thoroughbred flat race horses may be an advantage. Successful long-distance endurance race horses need to be able to maintain mainly aerobic metabolism (low blood lactate levels) rather than switching to increased dependence on anaerobic metabolism (high blood lactate levels) for prolonged periods of time.

In horses, high circulating erythrocyte counts, particularly in response to exercise, make measurement of whole blood lactate levels less accurate, repeatable, and meaningful than plasma lactate levels.[137] This necessitates deproteinization and centrifugation before analysis of plasma samples, which is much less convenient than whole blood analyses, which can be performed for human athletes with instant-reading hand-held machines.

For race horses, results are uninterpretable without carefully controlled standard exercise testing conditions,[45,60] which are often difficult to organize, especially under Thoroughbred race horse training conditions.

Serology

Feed allergen precipitin tests

These may be useful in intractable cases of allergic dermatologic or enteric disease. Serum samples can be tested against a panel of equine food allergens prepared previously or specific allergens can be prepared from representative samples of all the individual horse's feed constituents. Bran appears to be the most common feed constituent that produces positive precipitin responses in equine serum. Occasionally, exclusion from the diet has resulted in clinical improvement in sensitized horses.

Fungal allergen precipitin tests

These have been used occasionally in cases of recurrent allergic pulmonary disease.[138]

Blood gas analysis

Analyses are useful in cases of respiratory and intestinal abnormality, where acidosis or alkalosis are suspected, prior to therapeutic correction.[56,58,139] Analyses are helpful, alongside fluid and electrolyte balance assessments, for enterotoxemic and other critically ill horses under intensive care and for endurance horses and others performing in hot, humid conditions, suffering exertional exhaustion and/or heat stress.

Samples must be taken in heparinized, airtight syringes (preferably glass), and transported on ice to the laboratory within an hour or two of collection, so are practically limited to immediate in-house testing.

Interpretation of laboratory results

With a differential diagnosis in mind, the first task is to examine laboratory results in relation to appropriate reference values[10,140] and to decide whether significant variations occur. If all figures lie within reference ranges, this can help to rule out some possibilities, opening paths for further investigation. For example, the horse that is 'stiff' after exercise, yet whose serum AST and CK levels (in a sample collected later the same day or the following day) are not elevated, can be confirmed to be not suffering from exertional myopathy.[61] Further examinations and spinal/pelvic radiographic examinations may be indicated if clinical signs persist. The horse that coughs with normal leukocyte figures may not be suffering from a systemic infection and the next logical step is endoscopic and tracheobronchial wash cytologic examination[141,142] to investigate further.

Where there are variations from reference values, physiologic and pathologic causes must be differentiated.

Physiologic and collection technique effects

Marked elevations in erythrocyte parameters can occur following epimephrine (adrenaline) release and reflex splenic contraction, especially in the temperamentally 'nervous' horse.[4,6,13,50,51] This may occur when the horse is presented

with an unusual situation (e.g. a veterinary surgeon with blood collection equipment) or following exercise. In most cases, such excitement is obvious to the clinician but, if a laboratory interpretation is required, a note should be made on the laboratory request form to avoid misinterpretations. Alternatively, other people, prior to the clinician's arrival and unknown to him or her, may have excited the horse and this may only be apparent on examination of the results. Under these circumstances, marginal effects are difficult to assess. For these reasons, blood samples should be taken from horses following periods of rest, with the minimum of restraint and with a gentle reassuring technique. In UK Thoroughbred racing stables, 4 p.m., before the staff arrive to feed and groom, is usually a convenient time for sampling standardization. Despite all efforts, it is impossible to collect blood from some individual horses without eliciting a degree of excitement that makes the interpretation of erythrocyte parameters impossible.

The delineation between physiologic alterations and pathologic changes can sometimes be indistinct. Exercise, especially strenuous exercise, produces physiologic alterations in circulating leukocyte numbers, the concentrations of circulating muscle cell enzymes, fluid, electrolyte, and acid–base balance, which must be taken into consideration when trying to interpret postexercise laboratory results.[21,22] Excessive alterations in these parameters may occur as the result of pathologic changes in the unfit, overexerting and/or exhausted horse.[46,131] It can sometimes be very difficult to determine where physiologic alteration finishes and pathologic change begins. For example, degrees of exercise-induced myopathy can be diagnosed in serum samples taken from most, if not all, race horses during their training process on the basis of raised serum muscle enzyme levels. Some horses show no clinical signs and perform well whereas others with similar magnitudes of circulating AST and CK appear stiff and perform poorly. It is sometimes difficult to determine where physiologic muscle 'stress' becomes pathologic myopathy. There appears to be considerable individual variation and this is where the veterinarian and trainer must get to know their horses as individuals.

Pathologic abnormalities

Once artifactual and physiologic effects have been considered, the next step is to identify those that suggest pathologic abnormality. In some cases these will be highly specific, for example high serum AST and CK levels in a clinical case of exertional myopathy[61] or the isolation of equine influenza virus from a nasopharyngeal swab sample of an acutely coughing horse.[143] In other cases, the initial results may require clarification by the application of further tests, for example LD isoenzyme analysis, bile acids, BSP clearance test, liver ultrasound imaging and biopsy following high serum AST, LD, GLDH, GGT, and SAP levels.[103] Urine analysis, urinary electrolyte fractional excretion rates, renal and bladder ultrasound examinations, and cystoscopic examinations may be required following high serum urea and creatinine results in cases of weight loss. In some instances, parallel tests must be performed to make accurate interpretations, for example concurrent tracheobronchial cytopathologic and bacteriologic examinations of tracheal wash samples in race horses.[141,142] Without information regarding the presence or absence of septic leukocytic inflammatory change, the interpretation of the ubiquitous equine skin and mucosal aerobe *Streptococcus zooepidemicus* in relation to bronchitis in the absence of obvious clinical signs is impossible.

Where abnormal results indicate organ pathology (e.g. AST, LD, GLDH, GGT, and SAP indicate hepatopathy), it is important to determine its effect on organ function.[103] Normal bile acid results indicate insufficient pathology to compromise liver function and therefore a better prognosis for response to treatment than where raised bile acids confirm sufficient pathology to cause functional impairment.

Once pathologic abnormality has been identified, this must be correlated with the clinical history and an assessment made of primary or secondary significance. In a horse with clinical signs of acute, postexercise myopathy, high serum AST and CK levels are consistent with primary significance.[61] However, in a horse that is collapsed and jaundiced with very high serum SAP and GGT levels and history of ingestion of contaminated hay, suggesting chronic *Senecio jacobea* poisoning, high β-1 globulin levels may be a sign of underlying and perhaps opportunist large or mixed strongyle larval activity. Treatment of the latter case with larvicidal doses of anthelmintics would be unlikely to cure the collapse, jaundice, and hepatopathy and may be deleterious, until the hepatopathy has been treated and resolved. Mixed pathology is not uncommon in young and adult horses and multiple laboratory result abnormalities must be interpreted with care. The 'jigsaw puzzle' analogy is again appropriate.

Response to treatment

Clinicians recognize that clinical examinations alone may be misleading in the assessment of response to treatment. Again, the race horse with exercise-induced myopathy provides a good example. This horse may appear clinically normal after a period of rest and treatment but experience suggests that if exercise is resumed before serum AST levels have returned to within normal reference limits there is a greater risk of immediate recurrence. This especially applies to those fillies who repeatedly 'tie-up'[144] and are suspected to have a genetic predisposition to this condition. Race horses that are returned to strenuous exercise before respiratory viral-induced leukopenia and raised inflammatory protein and cardiac troponin levels have resolved are at significantly greater risks of developing chronic fatigue syndrome[109] and/or cardiopulmonary complications. Horses that have been treated with larvicidal doses of anthelmintics for intestinal parasitism should be re-examined 4 weeks after treatment to look for return to normal β-1 globulin levels. If there is an unsatisfactory response, a change in management, anthelmintic type, repeat treatment, or search for a primary

predisposing factor or other primary disease is indicated. Horses that have been treated for hepatopathy should be re-examined 3 weeks later to look for return to normal liver enzymes and bile acid results.

The future

Equine veterinary research will continue to generate information leading to the development and refinement of laboratory aids to diagnosis, including hematologic and serum biochemical tests, which are of help to the clinician. Clinicians will continue to improve their knowledge and expertise in the application and interpretation of these aids and will require access to efficient laboratory support. Equine diagnostic laboratories will continue to develop to provide this support to the benefit of race horses and their owners and trainers.

For clinical disease diagnosis, tests with improved specificity will continue to develop and find their place in practice. The importance of preventive medicine, in terms of both humane and economic considerations, will continue to increase and developments in knowledge and techniques will improve laboratory support.

Research into equine exercise physiology will continue to provide information, which may help to improve the efficiency of the performance-horse industries. Interest in exercise physiology, involving standardized exercise schedules, on and off treadmills, with pre-, during and postexercise sampling, cardiopulmonary monitoring, and muscle cell histochemical assessments have and will continue to improve our understanding of this subject. Unfortunately, few trainers of race and performance horses have embraced or are even willing to try these techniques. Frequently, trainers covet their art and are suspicious of recommended science. It is to be hoped that scientific progress in equine exercise physiology can be converted into practical and reliable tests that can help veterinarians give advice to trainers with respect to the true assessment of fitness in performance horses and the management of the training process. Once convinced, trainers will be more willing to use these techniques.

References

1. Ricketts SW, Rossdale PD. Laboratory measurements as an aid to equine practice. Veterinary Annual. Bristol: John Wright; 1973:94.
2. Ricketts SW, Rossdale PD. The equine practice laboratory. Vet Record 1975; 97:320–324.
3. Schalm OW. Equine hematology as an aid to diagnosis. Proc 1st Int Symp Equine Hematology. AAEP; 1975:3–16.
4. Schalm OW, Jain NC, Carroll EJ. Veterinary haematology. Philadelphia: Lea, Febiger; 1975.
5. Tennant B, Baldwin BH, Silverman SL, et al. Equine hematology as an aid to diagnosis. Proc 1st Int Symp Equine Hematology. AAEP; 1975:246–254.
6. Jeffcott LB. Clinical haematology of the horse. In: Archer RK, Jeffcott LB, eds. Comparative clinical haematology. Oxford: Blackwell Scientific; 1977:161–213.
7. Coffman JR. Equine clinical pathology and pathophysiology. Kansas: Veterinary Medical Publishing; 1981.
8. Ricketts SW. Laboratory aids to diagnosis in the horse. In Practice 1981; 3:5.
9. Schalm OW. Manual of equine haematology. Santa Barbara: Veterinary Practice Publishing; 1984.
10. Ricketts SW. The laboratory as an aid to clinical diagnosis. Vet Clin N America: Equine Practice 1987; 3:445–460.
11. Ricketts SW. Clinical pathology as an aid to equine practice. Proc 6th Congresso Nazionale Multisala Societa Italiana Veterinari per Equini: Pisa; 2000:375–395.
12. Ricketts SW. Clinical chemistry and endocrinology in equine clinical pathology. Proc 6th Congresso Nazionale Multisala Societa Italiana Veterinari per Equini: Pisa; 2000:343–355.
13. Barrelet A, Ricketts SW. Haematology and blood biochemistry in the horse: a guide to interpretation. In Practice 2002; 24(6):318–327.
14. Latimer KS, Andreasen CB. Peripheral blood smears. In: Cowell RL, Tyler RD, eds. Diagnostic cytology and hematology of the horse, 2nd edn. St Louis: Mosby; 2002:200–216.
15. Sykes PE. Haematology as an aid in equine track practice. Proc Am Ass Equine Practnr 1966; 12:159–167.
16. Gillespie JR. A review of hematological response to exercise. Proc 1st Int Symp Equine Hematology. AAEP; 1975; 435–443.
17. Snow DH. Biochemical changes in blood and muscle associated with exercise. Proc 1st Int Symp Equine Hematology. AAEP; 1975:427–434.
18. Stewart GA, Steel JD. Haematology of the fit racehorse. J S Afr Vet Ass 1975; 45:287–291.
19. Milne DW, Skarda RT, Gabel AA, et al. Effects of training on biochemical values in standardbred horses. Am J Vet Res 1976; 37:285–290.
20. Mullen PA, Hopes R, Sewell J. The biochemistry, haematology, nutrition and racing performance of two-year-old thoroughbreds through their training and racing season. Vet Record 1979; 104:90–95.
21. Snow DH, Mason DK, Ricketts SW, et al. Post-race biochemistry in thoroughbreds. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:389–399.
22. Snow DH, Ricketts SW, Mason DK. Haematological response to racing and training exercise in thoroughbred horses, with particular reference to the leucocyte response. Equine Vet J 1983; 15:149–154.
23. Carlson GP. Hematology and body fluids in the equine athlete: a review. In: Gillespie JR, Robinson NR, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:393–425.
24. Harkins JD, Kammerling SG, Bagwell CA, et al. A comparative study of interval and conventional training in thoroughbred racehorses. Equine Vet J 1990; 9 (Suppl):14–19.
25. Rose RJ. Exercise and performance testing in the racehorse: problems, limitations and potential. Proc Am Ass Equine Practnr 1990; 36:491–504.
26. Rose RJ, Evans DL. Training horses – art or science? Equine Vet J 1990; 22:2–4.
27. Rose RJ, Hendrikson DK, Knight PK. Clinical exercise testing in the normal thoroughbred racehorse. Aust Vet J 1990; 67:345–348.
28. Sheerman HA, Morris EA, O'Callaghan MW. The use of sports medicine techniques in evaluating the problem equine

athlete. Vet Clin N Am: Equine Pract, Racetrack Practice 1990; 6:239–274.
29. Harkins JD, Beadle RE, Kammerling SG. The correlation of running ability and physiological variables in thoroughbred racehorses. Equine Vet J 1993; 25:53–60.
30. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Equine Vet J 1999; 30(Suppl):621–625.
31. Lindholm A, Saltin B. The physiological and biochemical response of standardbred horses to exercise of varying speed and duration. Acta Vet Scand 1974; 15:310–324.
32. Carlson GP. Hematologic alterations in endurance trained horses. Proc 1st Int Symp Equine Hematology. AAEP; 1975:444–449.
33. Gerber H, Tschudi P, Straub R. 'Normal' values for different breeds of horses. Proc 1st Int Symp Equine Hematology. AAEP; 1975:266–275.
34. Allen BV, Archer RK. Some haematological values in English thoroughbred horses. Vet Record 1976; 98:195–196.
35. Lucke JN, Hall GM. Biochemical changes in horses during a 50-mile endurance ride. Vet Record 1980; 102: 356–358.
36. Rose RJ, Ilkiw JE, Arnold KS, et al. Plasma biochemistry in the horse during 3-day event competition. Equine Vet J 1980; 12:132–136.
37. Allen BV. Comparison of the haemogram between three-year-old thoroughbred stayers and sprinters. Vet Record 1986; 118:555–556.
38. Allen BV. Age differences in the haemogram of the National Hunt trained racehorse. Equine Vet J 1989; 21:309–310.
39. Rossdale PD, Hopes R, Wingfield Digby NJ, et al. Epidemiological study of wastage among racehorses 1982 and 1983. Vet Record 1985; 116:66–69.
40. Williams RB, Harkins LS, Hammond CJ, et al. Racehorse injuries, clinical problems and fatalities recorded on British racehorses from flat racing and National Hunt racing during 1996, 1997 and 1998. Equine Vet J 2001; 33:478–486.
41. Persson SGB. On blood volume and working capacity in horses. Acta Vet Scand 1967; 19(Suppl):1–189.
42. Persson SGB. Evaluation of exercise tolerance and fitness in the performance horse. In: Snow DH, Persson SGB, Rose TJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:441–457.
43. Persson SGB. Practical aspects of blood volume measurement: procedure for determination of total red cell volume (CV) in the horse. Proc Int Conf Equine Sports Med 1986:51–53.
44. Snow DH. Assessment of fitness in the horse. In Practice 1987; 9:26–30.
45. Seehrman HA, Morris EA. Application of a standardised treadmill exercise test for clinical evaluation of fitness in 10 thoroughbred racehorses. Equine Vet J 1990: (Suppl 9):26–34.
46. Snow DH. Fatigue and exhaustion in the horse. Aust Equine Vet 1991; 9:108–111.
47. Mumford JA, Rossdale PD. Virus and its relationship to the 'poor performance' syndrome. Equine Vet J 1980; 12:3–9.
48. Morris A, Seeherman HJ. Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. Equine Vet J 1991; 23:169–174.
49. Rose RJ, King CM, Evans DL, et al. Indices of exercise capacity in horses presented for poor racing performance. Equine Vet J 1995; 18(Suppl):418–421.
50. Persson SGB. The circulatory significance of the splenic red cell pool. Proc 1st Int Symp Equine Hematology. AAEP; 1975:303–310.
51. Hanzawa K, Kubo K, Kai M, et al. Effects of exercise on erythrocytes in normal and splenectomised thoroughbred horses. Equine Vet J 1995; 18(Suppl):439–442.
52. McEwan Jenkinson D, Loney C, Elder HY, et al. Effects of season and lower ambient temperature on the structure of the sweat glands in anhidrotic horses. Equine Vet J 1989; 21:59–65.
53. Burrows GE. Hematologic alterations associated with acute *E. coli* endotoxemia. Proc 1st Int Symp Equine Hematology. AAEP; 1975:505–515.
54. Scrutchfield WL. Hematologic preconceptions of acute diarrhea. Proc 1st Int Symp Equine Hematology. AAEP; 1975:501–504.
55. Morris DD. Diseases of the hemolymphatic system. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders; 1998:558–601.
56. Carlson GP. Fluid, electrolyte and acid-base balance. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. London: Academic Press; 1997:485–516.
57. Rose RJ, Arnold KS, Church S, et al. Plasma and sweat electrolyte concentrations in the horse during long distance exercise. Equine Vet J 1980; 12:19–22.
58. Carlson GP. Interrelationships between fluid, electrolyte and acid-base balance during maximal exercise. Equine Vet J 1995; 18(Suppl):261–265.
59. Carlson GP. Fluid and electrolyte alteration in endurance trained horses. Proc 1st Int Symp Equine Hematology. AAEP; 1975:473–480.
60. Dubreucq C, Chatard JC, Courouce A, et al. Reproducibility of a standard exercise test for Standardbred trotters under field conditions. Equine Vet J 1995; 18(Suppl): 108–112.
61. Hodgson DR. Exertional rhabdomyolysis. In: Robinson NE, ed. Current therapy in equine medicine, 2nd edn. Philadelphia: WB Saunders; 1987:487–490.
62. Bayly WM, Grant BD, Pearson RC. Lactate concentrations in thoroughbred horses following maximal exercise under field conditions. In: Gillespie JR, Robinson NR, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:426–437.
63. Weiss DJ, Geor RJ, Clark MS. Effects of echinocytes on hemorrheologic values and exercise performance in horses. Am J Vet Res 1994; 55:204–210.
64. Carlson GP. Evaluation of responsive anemias in horses. Proc 1st Int Symp Equine Hematology. AAEP; 1975: 327–335.
65. Greet TRC. Outcome of treatment in 35 cases of guttural pouch mycosis. Equine Vet J 1987; 19:483–487.
66. Murray MJ, Schusser GF, Pipers FS, et al. Factors associated with gastric lesions in thoroughbred racehorses. Equine Vet J 1996; 28:368–374.
67. Wilson JH, Pearson MM. Serum pepsinogen levels in foals with gastric or duodenal ulcers. Proc 31st Ann Conv Am Ass Equine Practnr 1985:149–156.
68. Geor RJ, Weiss DJ. Drugs affecting the hematologic system of the performance horse. Vet Clin N Am: Equine Practice 1993; 9:649–667.
69. Woods PR, Campbell G, Cowell LR. Nonregenerative anaemia associated with administration of recombinant human erythropoietin to a thoroughbred racehorse. Equine Vet J 1997; 29:326–328.
70. Lucas MH, Davies THT. Equine infectious anaemia. Equine Vet Education 1996; 7:89–92.
71. Phipps LP. Equine piroplasmosis. Equine Vet Education 1996; 8:33–36.

72. Knight AP. Plant poisoning of horses. In: Lewis LD, ed. Equine clinical nutrition: feeding and care. Philadelphia: William & Wilkins; 1995:447–502.
73. Seckington IM, Huntsman RG, Jenkins GC. The serum folic acid levels of grass-fed and stabled horses. Vet Record 1967; 81:158–160.
74. Becht JL. Interpretation of erythrocyte and leukocyte responses, dynamics of plasma proteins and assessment of fibrinogen. Proc 32nd Ann Conv Am Ass: Equine Practnr 1986; 605–612.
75. Abu-Samra MT, Imbabi SE, Mohmed KA, et al. Ulcerative lymphangitis in a horse. Equine Vet J 1980; 12:149–150.
76. Kuesis B, Spier SJ. Endotoxaemia. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders; 1998:639–650.
77. Ricketts SW. Peritonitis. In: Robinson NE, ed. Current therapy in equine medicine, 2nd edn. Philadelphia: WB Saunders; 1987:79–81.
78. Ainsworth DM, Biller DS. Pleuropneumonia. In: Reed SM, Bayly WM, eds. Equine internal medicine. Philadelphia: WB Saunders; 1998:275–277.
79. Allen BV, Frank CJ. Haematological changes in two ponies before and during an infection with equine influenza. Eq Vet J 1982; 14:171–172.
80. Allen BV, Wannop CC, Wright IM. Multicentric lymphosarcoma with lymphoblastic leukemia in a young horse. Vet Record 1984; 115:130–131.
81. Straub R, Gerber H. Effects of prolonged use of corticoids. Proc 1st Int Symp Equine Hematology. AAEP; 1975:536–553.
82. Archer RK. Eosinophils. Proc 1st Int Symp Equine Hematology. AAEP; 1975:113–119.
83. Hinchcliffe KW, Kociba GJ, Mitten LA. Diagnosis of EDTA-dependent pseudothrombocytopenia in a horse. J Am Vet Med Assoc 1993; 203:1715–1716.
84. Latimer KS, Rakich PM. Bone marrow. In: Cowell RL, Tyler RD, eds. Diagnostic cytology and hematology of the horse, 2nd edn. St Louis: Mosby; 2002: 217–226.
85. Prasse KW, George LW, Whitloch RH. Idiopathic hypersegmentation of neutrophils in a horse. J Am Vet Med Assoc 1981; 178:303–305.
86. Simpson CF, Kirkham WW, Kling JM. Comparative morphologic features of *Babesia caballi* and *Babesia equi*. Am J Vet Res 1967; 28:1693–1697.
87. Korbutiak E, Schneiders DH. A confirmed case of equine ehrlichiosis in Great Britain. Equine Vet Education 1994; 6:303–304.
88. Pierce KR. Assay of equine serum proteins by clinical chemical and electrophoretic methods. Proc 1st Int Symp Equine Hematology. AAEP; 1975:144–151.
89. Herd RP. Diagnosis of internal parasites. In: Robinson NE, ed. Current therapy in equine medicine, 2nd edn. Philadelphia: WB Saunders; 1987:323–327.
90. Proudman CJ. The role of parasites in equine colic. Equine Vet Education 1999; 11(4):219–224.
91. Proudman CJ, French NP, Trees AJ. Tapeworm infection is a significant risk factor for spasmodic colic and ileal impaction colic in the horse. Equine Vet J 1998; 30(3): 194–199.
92. Mair TS, Cripps PJ, Ricketts SW. Diagnostic and prognostic value of serum protein electrophoresis in horses with chronic diarrhea. Equine Vet J 1993; 25:324–326.
93. Ogbourn CP, Duncan JL. *Strongylus vulgaris* in the horse: its biology and veterinary importance, 2nd edn. Commonwealth Institute of Parasitology, Commonwealth Agricultural Bureaux of the United Kingdom. Miscellaneous publication 9; 1985.
94. Drew RA, Greatorex JC. Vertebral plasma cell myeloma causing posterior paralysis in a horse. Equine Vet J 1974; 6:131–134.
95. Traub-Dargatz J, Bertone A, Bennett D, et al. Monoclonal aggregating immunoglobulin cryoglobulinaemia in a horse with malignant lymphoma. Equine Vet J 1985; 17:470–473.
96. Schalm OW. Significance of plasma fibrinogen concentration in clinical disorders of the horse. Proc 1st Int Symp Equine Hematology. AAEP; 1975:159–167.
97. Allen BV. Relationships between the erythrocyte sedimentation rate, plasma proteins and viscosity, and leucocyte counts in thoroughbred racehorses. Vet Record 1988; 122:329–332.
98. Pepys MB, Baltz ML, Tennant GA, et al. Serum amyloid A (SAA) in horses: objective measurement of the acute-phase response. Equine Vet J 1989; 21:106–109.
99. Valberg S, Essén-Gustavsson B, Lindholm A, et al. Blood chemistry and skeletal muscle metabolic responses during and after different speeds and durations of trotting. Equine Vet J 1989; 21:91–95.
100. Harris PA, Greet TRC, Snow DH, et al. Some factors influencing plasma AST/CK activities in Thoroughbred racehorses. Equine Vet J 1990; 22(Suppl 9):66–71.
101. Tennant BC. Hepatic function. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. London: Academic Press; 1997:327–352.
102. Carlson GP. The liver. In: Mansmann RA, McAllister ES, Pratt PW, eds. Equine medicine and surgery, 3rd edn. American Veterinary Publications 1982; 1:633–643.
103. Ricketts SW. Assessment of equine liver function. Vet Record 1985; 117:561.
104. West HJ. Clinical and pathological studies in horses with hepatic disease. Equine Vet J 1996; 28:146–156.
105. McGorum BC, Murphy D, Love S, et al. Clinicopathological features of equine primary hepatic disease: a review of 50 cases. Vet Record 1999; 145:134–139.
106. Siciliano PD, Lawrence LM, Danielsen K, et al. Effect of conditioning and exercise type on serum creatine kinase and aspartate aminotransferase activity. Equine Vet J 1995; 27(Suppl 18):243–247.
107. Argiroudis SA, Kent JE, Blackmore DJ. Observations on isoenzymes of creatine kinase in equine serum and tissues. Equine Vet J 1982; 14:317–321.
108. Harris PA. An outbreak of the equine rhabdomyolysis syndrome in a racing yard. Vet Record 1990; 127: 468–470.
109. Ricketts SW, Young A, Mowbray JF, et al. Equine fatigue syndrome. Vet Record 1992; 131:58–59.
110. Littlejohn A, Blackmore DJ. Blood and tissue content of the isoenzymes of lactate dehydrogenase in the thoroughbred. Res Vet Sci 1978; 25:118–119.
111. Adams JE, Boder GS, Davilia-Roman VG. Cardiac troponin 1. A marker with high specificity for cardiac injury. Circulation 1993; 88:101–106.
112. Cornelisse CJ, Schott HC, Oliver NB, et al. Concentration of cardiac troponin 1 in a horse with a ruptured aortic regurgitation jet lesion and ventricular tachycardia. J Am Vet Med Assoc 2000; 217:231–235.
113. Bernard WV, Divers TJ. Variations in serum sorbitol dehydrogenase, aspartate transaminase and isoenzyme 5 of lactate dehydrogenase activities in horses given carbon tetrachloride. Am J Vet Res 1989; 50:622–623.
114. Giles CJ. Outbreak of ragwort (*Senecio jacobea*) poisoning in horses. Equine Vet J 1983; 15:248–250.

115. Rossier Y, Divers TJ, Sweeney RW. Variations in urinary gamma glutamyl transferase/urinary creatinine ratio in horses with or without pleuropneumonia treated with gentamicin. Equine Vet J 1995; 27:217–220.
116. Davies JV, Geering EL, Goodburn R, et al. Experimental ischaemia of the ileum and concentrations of the intestinal isoenzyme of alkaline phosphatase in plasma and peritoneal fluid. Equine Vet J 1984; 16:215–217.
117. Gronwall R. Bilirubin metabolism in the horse. Proc 1st Int Symp Equine Hematology. AAEP; 1975:237–240.
118. West HJ. Evaluation of total plasma bile acid concentrations for the diagnosis of hepatobiliary disease in horses. Res Vet Sci 1989; 46:264–270.
119. Mullen PA. Sodium sulfobromophthalein (BSP) clearance tests to assess hepatic function. Equine Vet J 1968; 1:92.
120. Parry BW, Crisman MV. Serum and peritoneal fluid amylase and lipase reference values in horses. Equine Vet J 1991; 23:390–391.
121. Roberts MC, Hill FWG. The oral glucose tolerance test in the horse. Equine Vet J 1973; 5:171–173.
122. Eustace R. Equine pituitary neoplasia. In Practice 1991; 13:147–148.
123. van der Kolk JH, Kalsbeek HC, van Garderen E, et al. Equine pituitary neoplasia. A clinical report of 21 cases (1990–1992). Vet Record 1993; 133:594–597.
124. Watson TDG, Burns L, Love S, et al. Plasma lipids, lipoproteins and post-heparin lipases in ponies with hyperlipaemia. Equine Vet J 1992; 24:341–346.
125. Kerr, M. Renal disease in the horse. Equine Vet Education 1990; 2:123–126.
126. Doxey DL, Milne EM, Gilmour JS, et al. Clinical and biochemical features of grass sickness (equine dysautonomia). Equine Vet J 1991; 23:360–364.
127. Harris PA, Colles C. The use of creatinine clearance ratios in the prevention of equine rhabdomyolysis: a report of four cases. Equine Vet J 1988; 20:459–463.
128. Harris PA, Snow DH. Role of electrolyte imbalances in the pathophysiology of the equine rhabdomyolysis syndrome. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:435–442.
129. Harris PA, Gray J. The use of the urinary fractional electrolyte excretion test to assess electrolyte status in the horse. Equine Vet Education 1992; 4:162–166.
130. Dunavant ML, Murray ES. Electrolyte imbalances in racing horses. Proc 1st Int Symp Equine Hematology. AAEP; 1975:533–535.
131. Marlin DJ, Scott MC, Schroter RC, et al. Physiological responses of horses to a treadmill simulated speed and endurance test in high heat and humidity before and after humid heat acclimation. Equine Vet J 1999; 31(1):31–42.
132. Schryver HF, Hintz HF. Factors affecting calcium and phosphorus nutrition in the horse. Proc 24th Ann Conv Am Ass Equine Practnr; 1978:499–503.
133. Harris PA, Snow DH. The effects of high intensity exercise on the plasma concentrations of lactate, potassium and other electrolytes. Equine Vet J 1988; 20:109–113.
134. Evans DL, Harris RC, Snow DH. Correlations of racing performance with blood lactate and heart rate after exercise in thoroughbred horses. Equine Vet J 1993; 25:441–445.
135. Evans DL, Rainger JE, Hodgson DR, et al. The effect of intensity and duration of training on blood lactate concentrations during and after exercise. Equine Vet J 1995; 27(Suppl 18):422–425.
136. Persson SGB, Essén-Gustavsson B, Funkquist P, et al. Plasma, red cell and whole blood lactate concentrations during prolonged treadmill exercise at $V_{LA}4$. Equine Vet J 1995; 27(Suppl 18):104–107.
137. Ferrante PL. Lactate measurements and interpretation: blood vs. plasma. Equine Vet J 1995; 27(Suppl 18): 478–479.
138. Lawson GHK, McPherson EA, Murphy JR, et al. The presence of precipitating antibodies in the sera of horses with chronic obstructive pulmonary disease (COPD). Equine Vet J 1979; 11:172–176.
139. Gillespie JR, Kaufmann A, Steere J, et al. Arterial blood gases and pH during long distance running in the horse. Proc 1st Int Symp Equine Hematology. AAEP; 1975: 450–468.
140. Blackmore DJ. A new concept of 'normal' in haematology. Proc 1st Int Symp Equine Hematology. AAEP; 1975:276–285.
141. Whitwell KE, Greet TRC. Collection and evaluation of tracheobronchial washes in the horse. Equine Vet J 1984; 16:499–508.
142. Ricketts SW. Tracheal washes and bronchoalveolar lavages: cytological interpretation in equine health and respiratory disease. Proc 6th Congresso Nazionale Multisala Societa Italiana Veterinari per Equini, Pisa; 2000:317–327.
143. Morley PS, Bogdan JR, Townsend HGG, et al. Evaluation of Directigen Flu A assay for detection of influenza antigen in nasal secretions of horses. Equine Vet J 1995; 27:131–134.
144. Frauenfelder HC, Rossdale PD, Ricketts SW, et al. Changes in serum muscle enzyme levels associated with training schedules and stage of the oestrous cycle in Thoroughbred racehorses. Equine Vet J 1986; 18:371–374.

CHAPTER 44

Abnormalities of the erythron

Colin C. Schwarzwald and Katarina Schuback

Anemia

Anemia is defined as a decrease in red-cell mass leading to a reduction in measured erythrocyte concentration, hemoglobin concentration, or hematocrit below the reference value.[1,2] As hemoglobin is the major determinant of the arterial oxygen content (Cao_2), anemia is functionally characterized by the reduced oxygen-carrying capacity of the blood.[3–5]

Several compensatory mechanisms serve to increase tissue oxygenation in the presence of anemia.[1,2,6] One of the initial adaptations to anemia is an increase in the 2,3-diphosphoglycerate (2,3-DPG) content of the red blood cells. This is probably caused by a change in intracellular pH and leads to a decreased oxygen-affinity of hemoglobin; oxygen is therefore more readily released to the tissue. Blood viscosity is markedly decreased, with lower erythrocyte concentrations,[7] and tissue hypoxia activates mechanisms of local blood flow regulation and causes peripheral vessels to dilate.[8] This results in a dramatic fall in peripheral vascular resistance, an increase in cardiac output, and improvement in oxygen delivery to the tissues.[1,2,6,9] Individual changes in vascular tone result in redistribution of blood from non-vital areas (skin, intestine) to highly oxygen-dependent tissues (heart, brain, muscles). Finally, diminished oxygen supply to the kidneys leads to increased synthesis of erythropoietin, which accelerates erythropoiesis in the bone marrow and elicits a regenerative response to anemia.[2]

These mechanisms can, at least partially, compensate for the decreased hemoglobin concentration and attenuate the decrease in oxygen delivery to tissues. Even severe anemia is therefore relatively well tolerated at rest, as long as it meets the following criteria:

- it does not occur acutely
- it is not associated with acute hemolysis or blood loss
- there is no loss of blood volume
- no other disease processes or conditions (such as infection, fever, severe injury, exercise, agitation, or advanced pregnancy) are present which increase oxygen demand.

Free hemoglobin in solution, as present in intravascular hemolysis, exerts strong vasoconstrictor effects due to binding of nitric oxide,[10] and has an increased affinity for oxygen due to a loss of 2,3-DPG.[11] The resulting decline of effective oxygen delivery and release into the tissues contributes to the pathophysiologic effects of hemolytic anemia. When tissue oxygen demand is increased, or when anemia becomes severe enough to exceed the compensatory capacity of the organism, the degree of oxygen extraction from the blood cannot be increased and the oxygen uptake by the tissue decreases as the oxygen supply decreases (supply-dependent oxygen uptake; Fig. 44.1). The resulting anaerobic metabolism leads to an accumulation of lactate and metabolic acidosis.[3,4,12] Ultimately, tissue hypoxia and limited metabolic capacity of the affected tissue can lead to tissue damage and organ failure.[2,13]

Diagnosis of anemia

Clinical signs

Decreased oxygen-carrying capacity of the blood and related compensating mechanisms are responsible for most of the clinical signs associated with anemia. The severity and rate of development of anemia determine the efficacy of physiologic compensatory mechanisms. Patients with chronic anemia tolerate a much lower red-blood-cell mass than do patients with rapidly developing acute anemia.

Subtle anemia is difficult to detect and has mild clinical effects. Total red-cell volume and hemoglobin concentration are correlated with the exercise capacity of a horse.[14–16] During exercise, tissue demand for oxygen is increased. Small decrements in red-cell mass lower the level of exercise

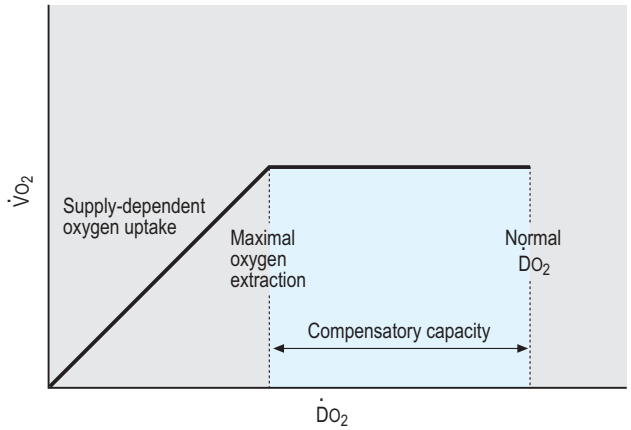


Fig. 44.1
Relationship between oxygen delivery ($\dot{D}O_2$) and oxygen uptake ($\dot{V}O_2$).

intensity at which tissue hypoxia occurs, and therefore result in exercise intolerance.[6]

More severe anemia is characterized by depression, weakness, tachypnea, tachycardia, hyperkinetic pulses, and pale or icteric mucous membranes. Systolic, functional heart murmurs are frequently associated with anemia. Hemoglobinuria or bilirubinuria may be seen in horses with hemolytic anemia. Cardiac arrhythmias may indicate myocardial hypoxia. Abdominal pain and signs of functional intestinal ileus are likely related to splanchnic ischemia, which may lead to sloughing of the intestinal mucosa, endotoxemia, and bacteremia.[12,13]

Hematology

Anemia is diagnosed when hematocrit, hemoglobin concentration, and erythrocyte concentration on a complete blood count (CBC) are below the reference range for the respective breed. The clinical definition of anemia can be problematic, as hydration status and splenic contraction due to exercise, excitement, or stress can also influence the hematologic values. Changes in hematocrit and hemoglobin concentration may therefore not reflect the true change in oxygen-carrying capacity of the blood.[1,17]

The traditional approach to determine the etiology and pathogenesis of anemia is to establish whether the anemia is regenerative or non-regenerative.[18] In horses, assessment of a regenerative response is difficult based on a routine hemogram, because reticulocyte maturation is completed in the bone marrow and release of reticulocytes into the blood is minimal, even in response to severe anemia.[17,19,20] Rarely, reticulocytes and nucleated red blood cells may be found in cases with severe hemolysis.[21] Young erythrocytes are usually larger than normal erythrocytes. Therefore, a regenerative response is in most species characterized by release of macrocytes into the bloodstream, independent of reticulocytosis.[18,19] Macrocytosis and anisocytosis may be the only indicators of regeneration in peripheral blood of horses.[18] It can be detected by determination of erythrocyte indices (mean corpuscular volume and red blood cell distribution width), red blood cell cytograms and volume distribution histograms, or blood smear evaluation.[18]

The mean corpuscular volume (MCV) is not a very sensitive test for the detection of abnormal or variable sizes of erythrocytes. Large numbers of macrocytes are necessary to increase the MCV above the normal range.[18,19,22,23] Macrocytosis is more pronounced in hemolytic anemia than in anemia due to acute blood loss.[24,25] The mixture of pre-existing normocytes and newly produced macrocytes during the recovery period in regenerative anemias leads to anisocytosis.[26] The red blood cell distribution width (RDW) is an index of anisocytosis and is calculated by many automated hematology systems as a coefficient of variation of the erythrocyte volume distribution.[19,23] Significant increases in MCV and RDW are detectable 14 to 20 days after onset of anemia and can persist for several weeks.[19,23] Although the RDW might be somewhat more sensitive than the MCV in detecting a regenerative response in horses, its increase is not a consistent indicator of regeneration, and it does not occur in mildly anemic horses.[19] Therefore, absence of these two findings does not exclude regenerative anemia.

Red blood cell (RBC) cytograms, RBC volume distribution curves, and hemoglobin concentration histograms are more sensitive in detecting changes in erythrocyte size or hemoglobin content and allow earlier detection of abnormal erythrocyte subpopulations than the routine erythrocyte indices (MCV, RDW).[18,19,22,23,27] Most modern automated hematology analyzers will report this information on request (Fig. 44.2).

Single hematologic measurements may be difficult to assess. Series of samples can reveal the severity of anemia and the presence of a regenerative response. The nadir of the hematocrit is reached around 2 to 7 days after acute blood loss and as late as 13 to 22 days after onset of hemolysis.[19,20,23–25] Reported daily increases in hematocrit following hematocrit nadir in regenerative anemias in horses vary between 0.32 and 0.67%, and are slower than reported in other species.[19,20] The rate of erythrocyte and hemoglobin production after hemolysis is higher than after acute blood loss, probably because iron and protein is not lost from the body and is readily available for erythropoiesis.[17,23,25,26]

Concurrent measurements of total plasma protein concentration may also be useful for determination of the type of anemia. Regenerative anemia, associated with a low, increasing plasma protein concentration, is consistent with blood loss, whereas a normal protein concentration more likely indicates hemolysis.[17]

Blood smears Blood smear evaluation is an easy and very important procedure in diagnosing anemia. Autoagglutination, alterations in erythrocyte morphology, presence of blood parasites, or the brown color of methemoglobin cannot be accurately detected by automated hematology analyzers.[18,28]

The physiologic property of equine erythrocytes to aggregate and form rouleaux on the peripheral blood smear (Fig. 44.3) requires special consideration and should be distinguished from pathologic autoagglutination. The latter leads to formation of irregularly shaped erythrocyte clusters of different sizes, whereas rouleaux formation leads to a more

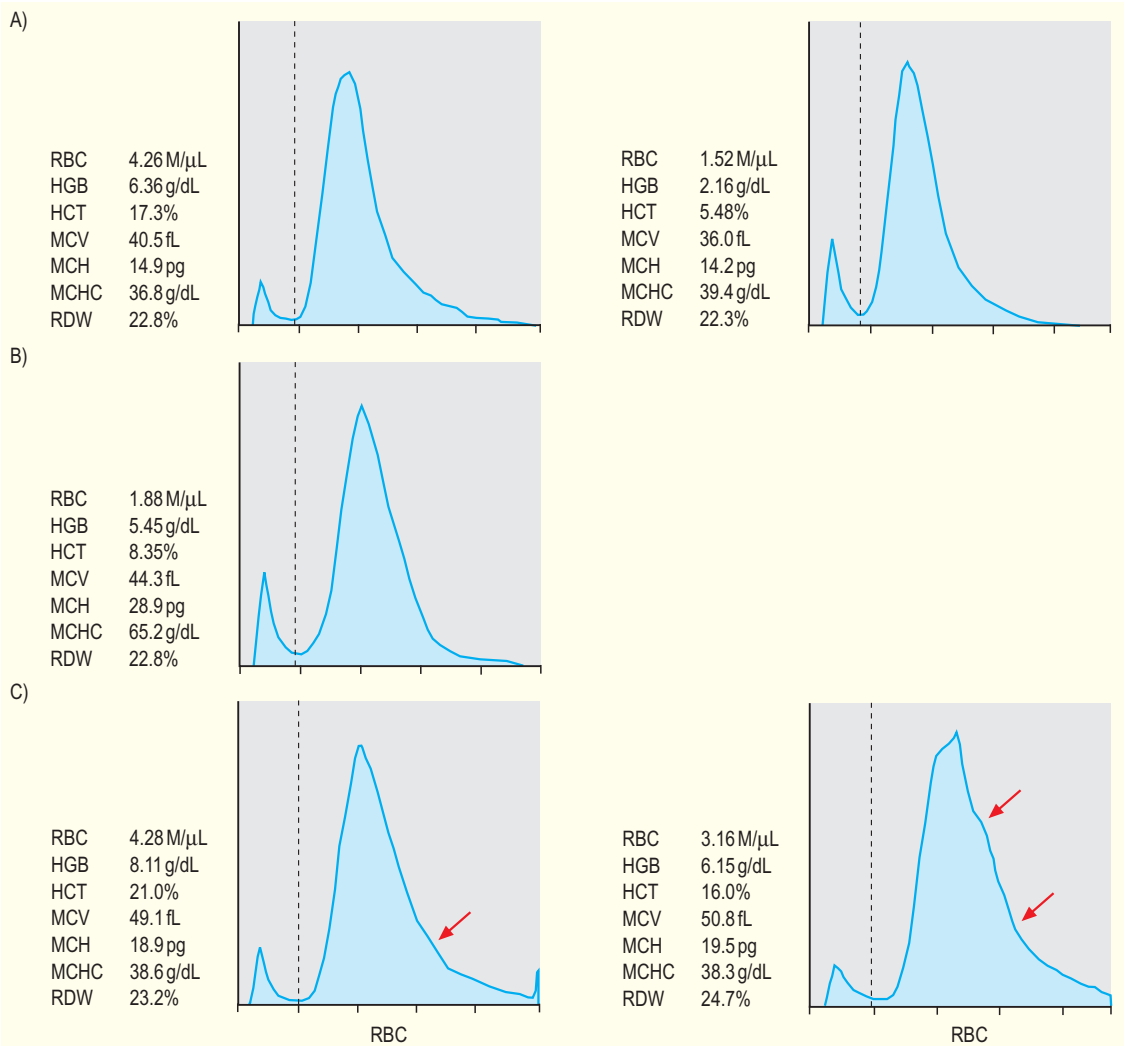


Fig. 44.2
Red blood cell indices and erythrocyte volume histograms.
(A) Pure red cell aplasia associated with administration of rhEPO. The RBC indices and erythrocyte volume histograms of two examinations 80 days apart indicate lack of regenerative response despite decreasing hematocrit (PCV). (B) Heinz body hemolytic anemia due to maple leaf toxicity. RBC indices and erythrocyte volume histograms 4 days after onset of the clinical signs do not indicate regeneration. (C) Erythrocyte volume histograms of the horse in (B) 2 days (left) and 8 days (right) later. Widening of the right tail of the histograms (arrows) indicates increased numbers of macrocytes consistent with a regenerative response. Note that the MCV and RDW are increasing over time but do not exceed the upper limit of the normal range (normal ranges: MCV 43–55 fl; RDW 19.8–25.4%).

orderly association with the erythrocytes lining up in rows. Mixing of the blood with normal saline (in a ratio of 1 part blood to 4 parts saline) will break up rouleaux but not agglutinated erythrocytes.[17,29,30]

Wedge smears of EDTA-anticoagulated whole blood can be made using two clean glass slides. The smears are then air dried and stained with Romanowsky-type stains (e.g. Wright, Giemsa, Diff–Quick).[28] New methylene blue stain can be used to detect Heinz bodies. Normal equine erythrocytes are approximately 5.4 µm in diameter. Changes in erythrocyte morphology may be useful to determine the underlying mechanism of anemia.[28] Table 44.1 summarizes common findings in blood smears of anemic horses.

Bone marrow evaluation

Bone marrow evaluation is the most accurate method for assessment of a regenerative response in horses. It is indicated in cases for which the hemogram does not adequately provide evidence of normal bone marrow function.[18,26,31] Bone marrow aspirate cytology allows evaluation of individual cellular morphology and the use of special stainings and procedures, but may not reflect true cellularity of the bone marrow and can be affected by hemodilution. Core biopsy examination is indicated if repeated aspirates are of marginal cellularity, if hypoplasia, aplasia, inflammation, necrosis, or myelofibrosis are suspected, or when megakaryocyte

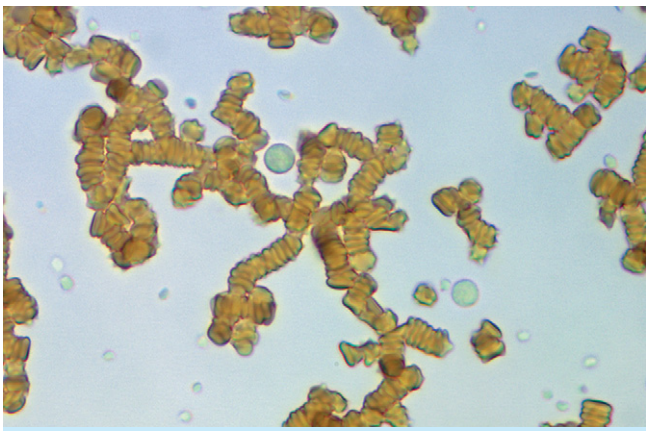


Fig. 44.3
Normal rouleaux formation of equine erythrocytes.

numbers should be determined.[32] In some cases only a combination of both techniques provides the desired information. Both procedures are easy to perform on the standing sedated horse and carry a small risk of complications. Standard techniques for bone marrow collection, sample preparation, and staining have been described.[32–35]

For aspirates, a 13- to 15-gauge, 2-inch needle with stylet is recommended. For core biopsies, a larger needle (11 to 13 gauge) should be used (Fig. 44.4). Several types of bone marrow collection needles are commercially available. An alternative biopsy technique using an electric drilling machine has been described.[36] Possible sites for bone marrow sampling in horses are the cranial sternum, tuber coxae, and the dorsal third of the ribs, where hematopoietic activity is maintained throughout life; the sternum is most frequently used. The sampling is performed in the ventral midline on an

Table 44.1 Common findings on peripheral blood smears in anemic horses[17,18,28]

Finding	Description/appearance	Cause
Rouleaux formation	Erythrocytes lining up in rows, very prominent in equine blood	Normal
Howell–Jolly bodies	Round, basophilic inclusion bodies, found near the periphery of the erythrocytes	DNA remnants, found in 0.1% of normal erythrocytes; more often with severe (regenerative) anemia
Heinz bodies	Pale pink (Romanowsky stain) or dark blue (new methylene blue stain) round protrusions of the erythrocyte membrane or bodies within the cell	Denaturated aggregates of hemoglobin due to oxidative damage (maple leaf, onion, or phenothiazine toxicity)
Eccentrocytes ('hemighosts')	Erythrocytes with small peripheral cytoplasmatic clearing	Alterations in the erythrocyte membrane and condensation of hemoglobin in the remainder of the cell due to severe oxidative damage (maple leaf toxicity)
Schistocytes (erythrocyte fragments)	Small, irregularly shaped erythrocyte fragments with two to four angular or pointed projections	Endothelial damage and alterations in the microcirculation, associated with DIC, neoplasia, or inflammation of very vascular organs (liver, spleen, lung, kidney, bone marrow, placenta)
Autoagglutination	Irregularly shaped erythrocyte clusters of different sizes	Immune-mediated hemolytic anemia, adverse effect of unfractioned heparin, occasionally incidental finding as a result of anti-erythrocyte IgM antibodies present in normal animals
Echinocytes	Uniformly spaced, pointed membrane projections	Crenation artifact, electrolyte depletion
Macrocytosis	Large erythrocytes	Regenerative anemia, prolonged storage of blood
Microcytosis	Small erythrocytes	Iron deficiency, chronic blood loss
Spherocytes	Small round erythrocytes with lack of central pallor (difficult to detect in horses)	Result from partial removal of red cell membrane by macrophages secondary to antibody or complement attachment (immune-mediated) or oxidative damage (maple leaf toxicity)
Parasites	Teardrop-shaped inclusions with two or four ('Maltese cross') organisms per cell	*Babesia caballi* or *Theileria equi*

DIC, disseminated intravascular coagulation; IgM, immunoglobulin M.

imaginary line between the two elbows. The site is clipped, aseptically prepared, and 5 to 10 mL of a local anesthetic is injected into the subcutis down to the periosteum. A stab incision is then made at the sampling site and the bone marrow needle with stylet is inserted through the skin to the sternum. To take a bone marrow aspirate, the needle is then advanced approximately 1 to 1.5 cm with a rotational movement using firm pressure. The stylet is removed, a 10-mL syringe is attached, and aspiration is performed. The risk of extensive contamination of the sample with peripheral blood can be reduced by forceful, rapid aspiration. The suction should be released when blood becomes evident in the syringe. The marrow specimen should be processed immediately to avoid coagulation and to preserve cellular morphology. The sample is transferred through the needle to several glass slides and direct smears are made before the sample clots. Alternatively, bone marrow aspirates can be transferred onto a Petri dish containing 0.5 to 1 mL 2% to 3% EDTA or a citrate–phosphate–dextrose solution for anticoagulation. The marrow particles adhere to the Petri dish and can be easily detected as small, granular, gray particles, even when some blood contamination is present. They are selected and transferred to glass slides using a Pasteur pipette. Bone marrow squash preparations are made using a second slide. The slides are then air-dried. Multiple smears (4 to 10, depending on volume of material obtained) should be submitted for routine stains and for additional special stains.

To obtain a core biopsy, the needle is inserted through the skin and the cortex of the sternum as described above. After removing the stylet, the needle is advanced with a rotating motion an additional 1 to 2 cm into the bone marrow cavity. The needle is then withdrawn rapidly from the sternum, and the biopsy specimen is removed retrograde from the lumen of the needle with a probe or with the stylet. Some needles require particular handling and the manufacturer's instructions should be followed carefully. Core biopsy samples are fixed in 10% neutral buffered formalin. Before placing in formalin, the specimen should be rolled gently across a glass slide to obtain impression smears for cytologic examination.

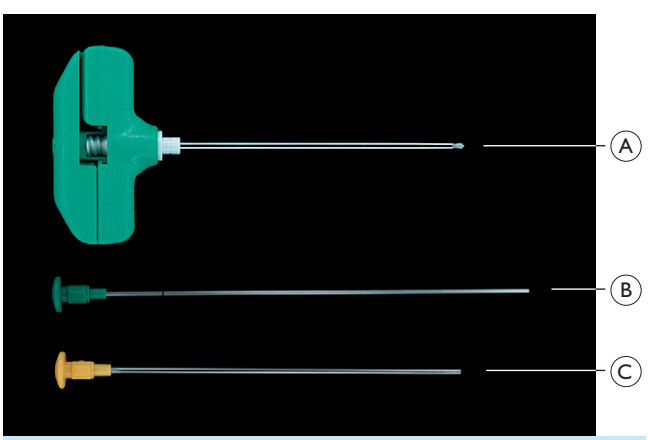


Fig. 44.4
Bone marrow sampling device. (A) Needle with stylet, (B) probe, (C) extraction cannula (optional use). (TrapSystem™ Bone marrow biopsy/aspiration needle.)

Common problems encountered when performing these procedures are failure to obtain a bone marrow aspirate or biopsy, and excessive blood contamination of aspirate specimens. In this case, multiple attempts at slightly different sites should be made to obtain diagnostically interpretable samples. Complications of bone marrow aspiration or biopsy are rare. Iatrogenic infections can be avoided by sterile technique. Excessive bleeding in patients with coagulation disorders, pneumothorax, hemothorax, and cardiac laceration may occur. The risk can be minimized by sedation of the horse, proper restraint, use of a needle guard, and careful monitoring of the needle length during the procedure. Bone marrow collection from the ribs contains similar risks, as the needle can slip off the bone and enter the thoracic cavity. Bone marrow sampling at the tuber coxae appears safer for examiner and horse, and may be associated with less complications. However, it is difficult to obtain bone marrow samples from the tuber coxae of older horses.

Cytologic examination of bone marrow aspirates or histologic examination of bone marrow biopsies should be assessed together with a complete blood count and differential taken on the same day and, if available, with results from previous CBCs and bone marrow evaluations.[18,32,35] Accurate interpretation of bone marrow samples requires training and considerable expertise. Routine bone marrow aspirate cytology is performed using Romanowsky-type stains (e.g. Wright, Giemsa, Diff–Quick). These stains allow the determination of particle cellularity; megakaryocyte numbers and maturity; erythroid and myeloid development, maturation, and morphology; and the presence of lymphoid cells, macrophages, stromal cells, and unusual cell populations.[35]

Normocellular bone marrow particles contain 50% fat and 50% cells (Table 44.2). Hypocellularity is consistent with decreased hematopoiesis, whereas hypercellularity suggests hematopoietic response, infiltrative disease, or neoplasia.[35] Normocellular bone marrow with normal-appearing erythroid cells and increased iron deposits in the marrow is seen in anemia of inflammatory disease.[18,37] Erythroid hyperplasia, accompanied by a lack of hemosiderin in macrophages, is seen in iron deficiency.[18] Aplastic anemia (aplastic pancytopenia) is characterized by peripheral pancytopenia and bone marrow panhypoplasia. The bone marrow space is replaced by adipose tissue.[38] Infiltration and replacement of the bone marrow by inflammatory cells, neoplastic cells, or fibrous tissue (myelofibrosis) is referred to as myelophthisis. The marrow usually appears normocellular or hypercellular.[38] Myelodysplasia is characterized by morphologic abnormalities in hemic cells. Excessive blast cell content of the bone marrow is indicative for leukemia.[18] Severe suppression of only the erythroid cell line is called pure red cell aplasia.[38]

Although subjective microscopic evaluation is a valuable and important method, it is often inadequate to assess regenerative response to anemia. Differential cell counts should be determined to increase the accuracy of quantification of

myeloid and erythroid cells.[31] The myeloid to erythroid ratio (M:E ratio) is commonly used to assess the erythroid compartment. The ratio is determined by counting 200 to 500 cells and dividing the number of cells of the myeloid series by the number of cells of the erythroid series. The normal M:E ratio in horses is between 0.5 and 1.5. A regenerative response leads to a decrease in M:E ratio, whereas a hypoproliferative anemia is characterized by an increased M:E ratio.[31,39–41] The regenerative response after acute loss of 25% of blood volume (20 mL/kg) leads to an expansion of the erythroid compartment within the first 3 days, and the peak erythroid response is reached after 9 days, corresponding with the lowest M:E ratio. The regenerative response in horses is prolonged and may be detected for more than 1 month.[31] Coexisting changes in the myeloid compartment can also influence the M:E ratio and should be taken into consideration. Leukocytosis with left shift, as detected on complete blood count, results from augmented granulopoiesis. In this instance an activation of the myeloid series increasing the M:E ratio may be expected.

In addition to the M:E ratio, determination of the number of young erythrocytes in bone marrow is useful to assess erythropoietic activity.[42] Anucleate erythrocytes in Romanowsky-stained smears are referred to as polychromatophilic erythrocytes (PRBC). In new methylene blue-stained smears, these cells appear as reticulocytes.[35] The presence of more than five PRBCs per high power field (100× oil immersion) and more than 3% reticulocytes (up to 66%) in relation to the total red blood cells confirm a regenerative response.[17,31,42–44]

Prussian blue stain allows semiquantitation of iron storage in the bone marrow. Normal bone marrow particles contain a moderate to large amount of erythroblasts with hemosiderin granula.[40] The amount of stainable iron is decreased in horses with chronic blood loss and iron deficiency.[41] Normoblasts and macrophages containing iron-rich granules (siderocytes, sideromonocytes) can be seen in horses with hemolytic anemia.[45,46] Anemia of inflammatory (chronic) disease leads to increased iron storage,[37,40] whereas iron-deficiency anemia leads to decreased iron storage in bone marrow.[47,48]

Serum biochemistry

Determination of the serum bilirubin concentration may be useful in diagnosis of anemia. Bilirubin is a breakdown product of hemoglobin metabolism. Horses frequently develop mild increases in serum unconjugated (indirect, prehepatic) bilirubin concentrations (up to 6–8 mg/dL [103–137 μmol/L]) as a result of anorexia. Larger increases of unconjugated bilirubin concentrations in anemic horses support the diagnosis of hemolysis. The degree of elevation depends on the rate of red cell destruction and the capacity of the liver to conjugate and excrete the newly formed bilirubin.[49] Monitoring of the serum creatinine and serum urea nitrogen concentrations is critical in horses with hemolytic anemia, as hemoglobinuria and bilirubinuria can lead to acute tubular nephrosis (pigment nephropathy). Hypovolemia associated with acute blood loss is characterized by prerenal azotemia. Furthermore, moderate non-regenerative anemia can occur secondary to chronic renal failure.[49,50] Serum activities of sorbitol dehydrogenase (SDH), other liver-derived enzymes, and bile acid concentrations may be increased with severe acute anemia due to hypoxic or ischemic liver damage or increased iron storage and iron overload with severe hemolytic anemia.[49,51] Increased cardiac troponin I serum concentrations may indicate hypoxic myocardial damage.

Urinalysis

Hemoglobinuria and bilirubinuria are common features associated with severe intravascular hemolysis, potentially leading to acute tubular nephrosis. Monitoring of renal

Table 44.2 Normal and abnormal bone marrow findings used for assessment of anemia in horses

Finding (staining method)	Normal	Regenerative response	Hypoproliferative bone marrow
Cellularity	50% fat, 50% cells	> 50% cells, dense cellular aggregates	< 50% cells, mainly fat
M:E ratio	0.5–1.5	< 0.5	> 1.5
PRBCs (Romanowsky)	< 2/HPF	> 5/HPF	
Reticulocytes (new methylene blue)	0.5–1% of erythroid cells	> 3–5% of erythroid cells	
Stainable iron (Prussian blue)	Many or all erythroblasts contain one to many hemosiderin granules	Normal in blood loss anemia	⇓ or absent in iron deficiency anemia
		⇑ in hemolytic anemia	Normal or ⇑ in anemia of inflammatory disease

HPF, high power field (100x oil immersion); M:E ratio, myeloid-to-erythroid ratio; PRBC, polychromatophilic erythrocytes.

function in cases with hemolytic anemia includes repeated analyses of urine samples.[49]

Blood gas analysis and lactate

Blood gas analysis and measurement of blood or serum lactate concentration may be useful for assessment of tissue oxygenation in horses with severe anemia. Metabolic acidosis, increased anion gap, and elevated blood or serum lactate concentration are consistent with tissue hypoxia or ischemia. A low venous or (preferably) mixed venous oxygen partial pressure (Pvo_2 < 25 mmHg) in association with normal pulmonary function and adequate arterial oxygenation (Pao_2 > 90 mmHg) indicates increased oxygen extraction from the blood secondary to inadequate oxygen delivery.[1,4,52] However, the clinical application of these measurements to assess the severity of anemia, tissue oxygenation, and the need for blood transfusions in horses with anemia has not been established and requires further investigation.

Assessment of minerals, trace elements, and vitamins

Iron Iron exists in several anatomically, chemically, and functionally distinct compartments in the organism.[53,54] The functional pool contains approximately 70% of the total body iron. It consists of hemoglobin, myoglobin, and several iron-containing or iron-dependent enzymes. Iron is stored primarily in bone marrow, spleen, and liver, either in a soluble form (ferritin), or as insoluble, aggregated deposits (hemosiderin). Plasma transferrin is the major iron transport protein.

The iron content of several of these compartments can be determined to assess a patient's iron metabolism. Hemoglobin, the largest iron compartment of the body, is most commonly measured and routinely included in complete blood counts. However, hemoglobin is probably the least sensitive variable for detection of iron deficiencies. Overt anemia occurs only in late stages of severe iron deficiency.[53,54] Serum iron, ferritin, iron-binding capacity, and evaluation of the iron content of bone marrow are more accurate indicators of the iron status.[47,48,53,54] Total serum iron concentration is low with chronic iron deficiency, but it is also decreased in inflammatory disease, hypoproteinemia, and renal disease.[55] Serum ferritin concentration correlates well with body iron stores and is a sensitive indicator of iron deficiency.[55,56] It is also an acute-phase reactant protein and can increase secondary to inflammation or liver disease, leading to an overestimation of total body iron content. Serum ferritin should therefore be assessed together with a complete blood count and plasma fibrinogen concentration.[57] Plasma transferrin is indirectly measured after complete saturation with iron, with the resulting iron content referred to as total iron-binding capacity (TIBC). The TIBC is typically increased in iron deficiency states, but decreased with acute-phase reactions and inflammatory disease. The amount of stainable iron in bone marrow samples correlates well with iron stores[58] and is a sensitive indicator for evaluation of the iron metabolism (see above). The amount of marrow stainable iron is decreased with iron deficiency, and increased with inflammatory disease (Tables 44.3 and 44.4).

Copper Copper deficiency may commonly be overdiagnosed in horses due to inappropriately high reference ranges available for horses. Normal serum copper concentrations in healthy horses probably vary between 0.5 and 1.5 mg/L (8–24 μmol/L).[63–66] Concentrate ration feeding and copper supplementation increase the serum copper concentrations to 1–1.7 mg/L (17–26.6 μmol/L).[67] Serum copper

Table 44.3 Variables used for assessment of iron status in horses[47,48,53,54,57,59]

	Increased	Decreased
Serum iron	Hemolytic anemia Refractory anemia Iron overload Liver disease	Iron deficiency Acute phase reactions Chronic inflammation Hypoproteinemia Renal disease Stress response (transport)
Serum ferritin	Iron overload Hemolysis Acute-phase reaction Inflammation Liver disease Some neoplasia	Iron deficiency
Total iron-binding capacity	Iron deficiency	Acute phase reactions Chronic inflammation Hypoproteinemia Renal disease
Bone marrow stainable iron	Acute phase reaction Inflammation	Iron deficiency

Table 44.4 Normal values for the evaluation of the iron status in horses

Value	(*n*) Breed	Normal values*	Reference
Serum iron (μg/dL)	n.d.	111 ± 11	60
	(14) Arabian	129 ± 29	61
	(33) Quarter Horse	154 ± 34	61
	(18) Thoroughbred	109 ± 12	61
	(28) n.d.	124 ± 36.9	55
	(23) Standardbred	147 ± 36.8	62
Serum ferritin (ng/mL)	(28) n.d.	152 ± 54.6	56
	(23) Standardbred	88.4 ± 31.8	62
TIBC (μg/dL)	n.d.	330 ± 32	60
	(14) Arabian	189 ± 17	61
	(33) Quarter Horse	337 ± 49	61
	(18) Thoroughbred	297 ± 47	61
	(28) n.d.	343 ± 56	55
Transferrin saturation (%)	(14) Arabian	68.3	61
	(33) Quarter Horse	45.7	61
	(18) Thoroughbred	36.7	61

n.d., not determined.
* Normal values expressed as mean ± SD where applicable.

concentrations lower than 0.7 mg/L (11.5 μmol/L) may indicate copper deficiency.[68]

Liver copper concentration and plasma ceruloplasmin activity may be used in addition to serum copper concentration to assess copper status of an animal.[64,68,69] Normal copper concentrations in liver tissue vary between 3.2 and 11 mg/kg (51–176 μmol/kg) fresh weight.[68,70,71] Mean plasma ceruloplasmin activity in mature Standardbreds has been determined to be 39.1 ± 0.5 IU/L (mean ± s.d.),[65] and serum ceruloplasmin concentration in adult horses varies between 4.07 ± 0.41 and 6.06 ± 0.74 mg/mL.[72] Acute-phase reactions may increase copper metabolism and cause the plasma copper concentration and ceruloplasmin activity to rise.[63,69,72] Complete blood count and plasma fibrinogen concentration should therefore be assessed together with serum copper concentrations to detect falsely elevated values.

Folic acid and vitamin B_{12} (cobalamin) Data on normal folate and vitamin B_{12} serum concentrations for horses are limited, and comparison between different studies is complicated by differences in feeding and management regimen. Serum folate concentrations in non-supplemented stabled horses and intensively training Thoroughbreds and Standardbreds (range: 1.5–15.1 ng/mL) are generally lower than in pastured horses (range: 6.4–21.7 ng/mL) or in race horses receiving dietary folate supplements (range: 2.0–21.1 ng/mL).[73–76] Similar differences were found for red cell folate concentrations, with race horses in training having lower values (35–372 ng/mL) than stabled horses (70–630 ng/mL) or horses on pasture (123–986 ng/mL).[76] Measurement of red cell folate concentration may be more accurate for the assessment of the folate metabolism of horses.[76,77] Serum vitamin B_{12} concentrations in non-supplemented horses vary between 1.25 and 5.4 μg/L.[75,76] Vitamin B_{12} levels do not seem to be significantly affected by feeding and exercise. Measurements of serum or red cell folate concentrations and vitamin B_{12} levels may be indicated in horses with macrocytic or normocytic anemia, leukopenia, and hypoplastic bone marrow. However, interpretation of the results may be difficult, as specific cut-off values for determination of vitamin deficiency are not established.

Specific causes of anemia

Anemia is caused by hemorrhage (blood loss anemia), red blood cell destruction (hemolytic anemia), or lack of erythrocyte production (hypoproliferative anemia) (Table 44.5).[17,18] Blood loss anemias and hemolytic anemias are referred to as regenerative anemias, whereas hypoproliferative anemias are non-regenerative.

Table 44.5 Causes of anemia in athletic horses

Regenerative anemia		Non-regenerative (hypoproliferative) anemia
Blood loss anemia	**Hemolytic anemia**	
Acute Trauma Surgery Guttural pouch mycosis Internal abdominal or thoracic bleeding Coagulation disorders **Chronic** Gastrointestinal (ulceration, neoplasia, parasites) Respiratory (ethmoidal hematoma, guttural pouch mycosis, pulmonary hemorrhage) Urogenital Coagulation disorders	**Infectious** Equine infectious anemia (EIA) Piroplasmosis (*Babesia caballi*, *Theileria equi*) **Immune-mediated hemolytic anemia (IMHA)** Secondary IMHA (Clostridial infection, penicillin, lymphoma, purpura hemorrhagica) Autoimmune hemolytic anemia Transfusion incompatibility **Oxidative injury (Heinz body anemia and methemoglobinemia)** Maple leaf toxicity Onion poisoning Phenothiazine poisoning **Others** Terminal liver failure Intravenous administration of concentrated dimethyl-sulfoxide (DMSO) or hypotonic solutions	**Anemia of inflammatory (chronic) disease** Chronic infection Chronic inflammation Severe trauma Neoplasia **Nutritional deficiencies** Iron deficiency Folate deficiency **Immune-mediated hypoproliferative anemia** Recombinant human erythropoietin (rhEPO)-induced pure red cell aplasia Immune-mediated hemolytic anemia affecting erythroid precursors **Infectious** Equine infectious anemia **Others** Chronic organ dysfunction Aplastic anemia Myelophthisic disorders Myelodysplastic syndromes

Blood loss anemia

Acute blood loss

- External or internal bleeding can lead to decreased circulatory volume and hypovolemic shock.
- External bleeding is usually obvious, whereas internal bleeding may be difficult to diagnose.
- Anemia and hypoproteinemia usually become evident within 12 to 24 h of the onset of acute hemorrhage.
- Treatment consists of controlling the hemorrhage and reversing hypovolemia, rather than increasing the hemoglobin content of the blood.
- The prognosis is favorable for controlled hemorrhage, but guarded for uncontrolled hemorrhage.

Acute hemorrhage is defined as major external or internal hemorrhage that occurs within a few minutes to several hours. Severe acute blood loss results in acutely reduced blood volume, cardiovascular collapse, hypovolemic shock, and death.[12,13,78,79]

History and presenting complaint A history of recent trauma or surgery may be obtained. Overt bleeding is a common but not invariate presenting sign. Exercise intolerance, weakness, depression, anorexia, colic, and dyspnea may be present.[80]

Physical examination Clinical signs principally reflect the loss of blood volume rather than the loss of hemoglobin.[78] They vary depending on the underlying cause and rapidity, severity, and duration of blood loss. Depression, weakness, tachycardia, tachypnea, pale mucous membranes, weak peripheral pulses, dehydration, and cold extremities are signs of hypovolemia and hypovolemic shock. Occasionally, anxiety and agitation may occur. Death due to cardiovascular collapse can occur within 30 min with severe acute hemorrhage.[80–82]

Hemothorax is generally associated with dyspnea,[82] whereas hemoperitoneum commonly presents with signs of abdominal pain.[80,81,83] Colic may also arise from malperfusion of the intestine and tissue ischemia resulting from compensatory cardiovascular mechanisms.[81]

Special examination Endoscopic examination of the upper airways and guttural pouches is indicated to determine the cause of severe epistaxis. Rectal examination, ultrasonographic examination of the abdominal and thoracic cavity, followed by abdominocentesis or thoracocentesis, should be performed if internal hemorrhage is suspected.[80,81,84]

Laboratory examination Initially, hematocrit and erythrocyte count are normal due to the simultaneous loss of blood cells and plasma. Splenic contraction may initially increase the hematocrit in horses with acute blood loss. The hematocrit is therefore not an accurate indicator of the severity of blood loss, especially in early stages of hemorrhage.[78,82,84] The severity of blood loss must therefore be estimated from clinical signs or, if possible, from measurement of the volume of blood loss. Blood volume is restored by shifting water from the interstitial fluid compartment to the intravascular compartment and by gastrointestinal and renal reabsorption of fluid. Anemia and hypoproteinemia usually become evident within 12 to 24 h of acute hemorrhage, indicating blood loss anemia.[17,24,78,84] The plasma protein concentration usually begins to increase within 2 to 3 days and reaches normal values within 5 to 7 days, unless there is ongoing blood loss.[78,84] Three to seven days after acute blood loss, regenerative response can be detected by sequential measurements of the hematocrit.[20,23,24,78]

Internal hemorrhage may be more difficult to detect based on measurements of hematocrit and plasma protein concentration, because up to two-thirds of the erythrocytes and most of the plasma proteins are recycled. The hematocrit can therefore increase more rapidly and the plasma protein concentration may be normal or only slightly decreased.[78,80,84]

The diagnostic work-up should include a platelet count and coagulation profile (activated partial thromboplastin time and prothrombin time) if the etiology of the hemorrhage is not obvious.[81] Bone marrow evaluation is rarely indicated, unless inadequate regenerative response to blood loss anemia is suspected. Erythroid hyperplasia and decreased M:E ratio usually become apparent within the first 3 to 5 days after hemorrhage.[78,82] The increase in red cell production reflects the severity of the anemia. However, concomitant iron deficiency, chronic renal disease, inflammation, bone marrow disorders, or blood transfusions may decrease the erythrocyte response.[78]

Diagnostic confirmation Ongoing blood loss or signs of recent hemorrhage are usually evident on physical examination. However, hematologic examination, abdominal ultrasonography, abdominocentesis, and thoracocentesis may be required to detect internal bleeding.

Therapeutic aims Initial treatment is aimed at controlling the hemorrhage and reversing the hypovolemic shock rather than increasing the hemoglobin concentration in the blood.[1,78,84] If blood pressure, circulatory volume, and tissue perfusion are adequate, tissue oxygenation will be maintained even in severely anemic horses.[52,84]

Therapy External hemorrhage can usually be controlled by external pressure or surgical ligation of large vessels. Control of internal hemorrhage can often not be achieved effectively and surgical intervention is rarely practical.[82,84]

The circulatory volume can be restored by rapid administration of crystalloid solutions, hypertonic saline, colloid solutions, or equine plasma (Table. 44.6).[79,81,84] Hypertonic saline[85–87] and colloid solutions[88–92] allow resuscitation with smaller volumes of fluids. A plasma protein concentration of less than 4.0 g/dL indicates the need for colloid solutions or equine plasma. The latter not only contains albumin as oncotic active component but, if fresh frozen plasma is used, also provides coagulation factors.[81]

Excessive volume replacement in the setting of uncontrolled hemorrhage may exacerbate the bleeding tendency and increase blood loss, due to the increased blood pressure and cardiac output.[81,83] The practice of restrictive volume replacement is referred to as hypotensive resuscitation.[93,94] Reduction of stress, placement in a quiet environment, and moderate fluid therapy are essential points of treatment of uncontrolled bleeding. Sedation with acepromazine (0.02–0.055 mg/kg i.v. or i.m.) leads to peripheral

Table 44.6 Therapies for intravenous volume restoration and increase of oxygen-carrying capacity of the blood[81,82,84,85,98,99]

Treatment	Dosage recommendations	Comments
Isotonic crystalloid solutions	3 times estimated volume of blood loss at a rate of 40–80 mL/kg/h	Shock dose
Hypertonic saline (7.2%)	4–6 mL/kg over 10–15 min	Followed by 40 mL/kg of an isotonic solution within 2 h
Hetastarch 6%	10 mL/kg	Colloid solution
Equine fresh-frozen plasma	12–16 mL/kg	Estimate: 7 L plasma (70 g/L) raises plasma protein concentration by 10 g/L in a 500-kg horse
Polymerized ultrapurified bovine hemoglobin (Oxyglobin®)	10–30 mL/kg at a rate of 10 mL/kg per h	Estimated half-life 40 h Shelf life 2 years (room temperature)
Whole blood	12–16 mL/kg or 20–40% of estimated blood loss at a rate of 20 mL/kg per h (initial rate: 0.1 mL/kg for 10 min, monitor for adverse reactions)	May need to repeat due to destruction of transfused red blood cells Estimate: 1 L blood (PCV 40%) raises PCV by 1% in a 500-kg horse

vasodilation and drop in blood pressure, which potentially reduces severity of hemorrhage and permits clot formation. However, acepromazine can exacerbate shock and cause acute collapse. Flunixin meglumine (0.5 to 1.0 mg/kg i.v.) and butorphanol tartrate (0.02 to 0.04 mg/kg i.v.) may be used to control pain, especially in cases with internal hemorrhage.

Several pharmacologic agents are occasionally recommended to treat acute hemorrhage, although clinical efficacy has not been proven in horses. The antifibrinolytic agents aminocaproic acid and tranexamic acid have been used in horses with the intention to stabilize fibrin clots and stop further hemorrhage (Table 44.7).[80,81,84] Intravenous administration of 10% buffered formalin may help to control bleeding,[81,95,96] although no effect on hemostatic variables can be detected in healthy horses.[97] Adverse effects at the recommended doses are rare. The mechanism of action remains unknown.[97] Naloxone hydrochloride, an opiate antagonist with dopaminergic activity may reverse the effects of endogenous opioids on cardiovascular dynamics and attenuate cardiovascular responses associated with acute hemorrhage,[81,84] but can potentially result in increased pain perception.[80]

Table 44.7 Commonly used dosages for anecdotal treatment of acute hemorrhage in horses[80,81,84,95,96]

Treatment	Dosage recommendations	Comments
Aminocaproic acid	20–80 mg/kg i.v., diluted in 1 L 0.9% saline, over 30–60 min	Antifibrinolytic agents Can be redosed as needed Contraindications: thromboembolic disease, DIC
Tranexamic acid	2 mg/kg i.v.	
Naloxone hydrochloride	0.01–0.02 mg/kg i.v.	Opiate antagonist
10% buffered formalin	0.02–0.08 mL/kg i.v., diluted in 1L 0.9% saline	

DIC, disseminated intravascular coagulation.

Following volume replacement and stabilization, the patient should be reassessed for the necessity of whole blood transfusion. The decision for transfusion should be based on clinical and clinicopathologic assessment. Transfusion is indicated if:

- the hematocrit rapidly falls below 15% and continues to decrease
- the hematocrit is below 10%
- there is uncontrolled bleeding
- the quantitated blood loss is more than 30% of the total blood volume
- the tissue oxygen demand increases due to fever or agitation
- gastrointestinal signs (colic, diarrhea) indicate possible intestinal ischemia or hypoxia
- cardiac arrhythmia and increased cardiac troponin I serum concentrations indicate myocardial hypoxia
- tachycardia, tachypnea, depression and weakness persist after initial restoration of the circulatory volume.[82,84,100,101]

The use of blood gas measurements and oxygen extraction ratios (O_2ER) as transfusion triggers has not been well established in horses. However, a low venous oxygen partial pressure ($Po_2 < 25$ mmHg) with normal pulmonary function, the presence of metabolic acidosis, and increased blood lactate concentrations indicate inadequate tissue oxygenation and the need for blood transfusion.[1,4,52] If available, cross-match testing should precede transfusion. Alternatively, blood can be transfused without cross-matching if the donor (preferably a gelding or stallion) and the recipient have not received prior transfusions.[81,82,100,101] Adult horses can safely donate

10 to 16 mL/kg (5 to 8 L for a 500-kg horse) whole blood without fluid replacement, and up to 25 mL/kg (12.5 L for a 500-kg horse) whole blood when the withdrawn volume is replaced with isotonic solutions. Potential adverse effects of administration of whole blood are transfusion reactions, and suppression of the normal bone marrow response to anemia.[100] Blood transfusions are only temporarily effective, and further transfusions may be required, when the transfused erythrocytes are degraded or removed from the circulation.[81,82,100,101]

The transfusion of polymerized ultrapurified bovine hemoglobin (PUBH, Oxyglobin®, Biopure Corporation, Cambridge, MA, USA) can be a valuable, but very expensive, alternative to whole-blood transfusion when compatible whole blood or packed red cells are not available. It increases the oxygen-carrying capacity of the blood, exerts a profound oncotic effect resulting in volume expansion, and causes peripheral vasoconstriction.[10,11,102] The use of PUBH in hemorrhagic shock or as a low-volume resuscitation fluid is currently being investigated in a variety of species but its safety and efficacy in horses has not been completely established and its optimal use is undefined. Treatment with PUBH has been reported in a miniature horse with intra-abdominal hemorrhage[98] and in ponies with experimentally induced normovolemic anemia.[99]

Prognosis Generally, the prognosis for anemias caused by acute hemorrhage is good, provided that the hemorrhage can be controlled and appropriate treatment is initiated.[78] The erythrocyte variables usually return to prehemorrhage levels within 8 to 14 weeks after acute hemorrhage.[24,78] The prognosis for internal, uncontrolled bleeding is usually guarded.[80]

Etiology and pathophysiology Acute blood loss anemia occurs with severe hemorrhage due to trauma or surgery. Infectious, neoplastic, or parasitic lesions can cause erosion of vessel walls. Severe epistaxis can occur due to trauma or guttural pouch mycosis, and less commonly as a result of pulmonary hemorrhage or nasal neoplasia.[82,84] Occasionally, internal hemorrhage can occur into the abdominal or thoracic cavity. It is caused by trauma, vascular abnormalities, neoplasia, abscesses, amyloidosis, parasite damage, or postoperative complications, and originates from large vessels, liver, spleen, kidneys, intestine, reproductive tract, or lungs. However, the underlying cause is often not found.[79–81,83,84] Rarely, coagulation disorders (warfarin intoxication, thrombocytopenia, disseminated intravascular coagulation, hemophilia) lead to significant acute hemorrhage.[84]

While the decreased oxygen-carrying capacity of the blood and the increased cardiac output are the main pathophysiologic effects in other types of anemia (see above), decreased circulatory blood volume, hypotension, decreased cardiac output, and hypovolemic shock are the primary sequelae in severe hemorrhagic anemia.[1,78,84] The total blood volume equals approximately 8% of bodyweight (40 L in a 500-kg horse). A small amount of acute blood loss is well tolerated, while a loss of larger volume may lead to overt clinical signs. Acute blood loss of more than 30% of total blood volume (13 L) results in hypovolemic shock, whereas loss of 50% or more (20 L) leads to death if untreated.[78,84]

Chronic blood loss

- Chronic blood loss is uncommon in horses.
- Diagnosis is made by identification of the source of bleeding and exclusion of other causes of anemia.
- Differential diagnoses of chronic blood loss anemia are anemia of inflammatory disease, iron-deficiency anemia, and low-grade hemolysis.

Recognition of disease Pale mucous membranes and clinical signs associated with the underlying disease may be noted. Physiologic adaptation to the gradually developing anemia usually masks overt signs of anemia until the hematocrit is less than 15%. The anemia is typically regenerative, unless chronic blood loss results in iron deficiency and depletion of the iron stores (see below). Plasma protein concentration is usually normal, although in some cases hypoproteinemia (e.g. intestinal blood and protein loss) or hyperproteinemia (hyperglobulinemia, chronic immunologic stimulation) can be present.

Diagnostic confirmation Diagnosis is based on characterization of the anemia, identification of a source of chronic blood loss, and exclusion of other causes for anemia. Diagnostic procedures may include complete blood count, bone marrow aspirate, coagulation profile, gastroscopy, fecal occult blood test, fecal parasite egg count, abdominocentesis, endoscopy of upper and lower airways, bronchoalveolar lavage, urinalysis and Coggins test for equine infectious anemia. Differential diagnoses for anemia of chronic blood loss are anemia of inflammatory disease, iron-deficiency anemia, and low-grade hemolysis.

Treatment and prognosis Treatment of the underlying cause is the cornerstone in management of chronic blood loss. Treatment of the anemia is rarely indicated, although horses with secondary iron-deficiency anemia may benefit from oral supplementation with ferrous sulfate. The prognosis depends on the underlying disease.

Etiology and pathophysiology Chronic blood loss may result from bleeding gastrointestinal ulcers, parasites, gastrointestinal neoplasia, exercise-induced pulmonary hemorrhage, ethmoid hematoma, guttural pouch mycosis, or urogenital hemorrhage. Coagulopathies should always be considered.[82,84,103] Chronic blood loss can lead to iron depletion and iron-deficiency anemia.

Red cell destruction (hemolytic anemia)

Equine infectious anemia (EIA)

- Equine infectious anemia is a viral disease characterized by development of persistent subclinical infections with possible recrudescence of disease. Chronic carriers remain infectious.
- Transmission occurs most commonly via insect vectors.
- Anemia occurs due to immune-mediated intravascular and extravascular hemolysis and bone marrow suppression.
- Depression, peripheral edema, weight loss, and recurrent episodes of fever are typical clinical signs of EIA. Laboratory abnormalities include anemia and thrombocytopenia.

- The diagnosis is based on serologic testing with agar gel immunodiffusion (Coggins') or ELISA tests.
- EIA is a reportable disease. Prevention and regulatory measures are important for control of the disease.
- No effective treatment is available.

The equine infectious anemia virus (EIAV) is a retrovirus of the *Lentivirinae* subfamily, closely related to caprine arthritis–encephalitis virus of goats, Maedi/Visna virus of sheep, and the human and feline immunodeficiency viruses.[104] Development of persistent infections is characteristic of lentiviruses. Infected animals remain life-long carriers and a potential source of infection for other animals. Performance of chronically infected horses is impaired, despite lack of clinical signs of disease.[105] Equine infectious anemia occurs in all parts of the world and has important implications on horse trading as well as national and international equestrian sports. Equine infectious anemia is a reportable disease (World Organization for Animal Health (OIE) List B of infectious diseases).[106]

History and presenting complaint The clinical signs of EIA depend on the virulence of the virus, the infectious dose, host resistance factors, and environmental stressors.[104,107] Horses with acute EIA are usually presented for depression, anorexia, and fever. Less virulent strains may lead to less severe clinical signs, and infection may remain undetected. The subacute to chronic stage is characterized by recurrent episodes of fever, depression, peripheral edema, and weight loss. Most EIAV-infected horses, however, do not show clinical signs of disease. Periodic exacerbation of clinical disease may be associated with environmental stressors, transportation, strenuous exercise, concomitant diseases, or corticosteroid therapy.

Physical examination The acute form is characterized by high fever, depression, petechial hemorrhages, pale or icteric mucous membranes, and occasionally death within days. Horses with subacute to chronic EIA show additional signs of lymphadenopathy, edema, and weight loss. Recurrent fever is typical. Neurologic signs have been reported.[104,108]

Laboratory examination Thrombocytopenia and marked anemia are seen during active febrile episodes. The Coombs' test may be positive during these periods. Increase in serum bilirubin is present if significant hemolysis occurs. Leukopenia or leukocytosis with lymphocytosis and monocytosis may be present. Platelet counts usually rebound following resolution of the acute viremic phase. Chronic carriers show low normal erythrocyte parameters or occasionally mild to moderate anemia. Persistent non-specific hypergammaglobulinemia may indicate low-grade chronic infection.[104,107,108]

Serologic testing for EIA should be performed in all horses with anemia if the etiology is not obvious or if concurrent clinical signs, such as intermittent fever, edema, petechiation, and weight loss, indicate possible EIA infection. Horses usually seroconvert within 14 to 45 days after infection.[109] The most widely accepted diagnostic test is the Coggins' test, an agar gel immunodiffusion procedure that is sensitive and specific for antibodies against the EIA p26 core protein antigens.[104,107,110] Two highly sensitive enzyme-linked immunosorbent assays are available which test for antibodies against p26 core proteins (competitive ELISA) or gp 45 transmembrane glycoproteins (synthetic antigen ELISA).[104,107,110] Both tests are rapid and highly specific for EIA infection, even in chronic carriers. However, confirmation of positive ELISA results by Coggins' test and Western blot may be required due to possible false-positive results of the ELISA tests.[104,107,110]

During febrile periods, serum iron decreases, whereas the total iron-binding capacity does not change significantly.[111] Bone marrow evaluation reveals a normal M:E ratio despite anemia, indicating hyporesponsive bone marrow. The content of stainable iron in the reticuloendothelial cells of the bone marrow (and other organs like the liver) is increased.[104,111]

Necropsy examination Necropsy findings vary with the stage of the disease process. During active disease, splenomegaly, hepatomegaly, lymphadenopathy, hemorrhages, and edema are common findings. Histopathologic findings include lymphoid necrosis and perivascular lymphocytic infiltrates of most organs and widespread hemosiderosis, especially in the liver. Glomerulonephritis may be present.[104,107]

Diagnostic confirmation The diagnosis of EIA is based on a positive Coggins' test or EIA ELISA. Virus isolation is usually not necessary.[110] Differential diagnoses include equine viral arteritis, equine ehrlichiosis, purpura hemorrhagica, and other causes of immune–hemolytic anemia. For chronic forms, other causes for chronic weight loss should be considered.

Therapeutic aims No effective treatment is available to eliminate the infection.

Therapy Clinical recovery can be achieved with rest and supportive treatment.

Prognosis The prognosis is unfavorable. Most horses spontaneously recover from the initial viremic episode but latent infection persists and recrudescence of clinical signs is common. Most horses become inapparent carriers with time and a few progress to a debilitating form of the disease.[104]

Etiology and pathophysiology Equine infectious anemia virus is a non-oncogenic retrovirus that infects and replicates primarily in tissue macrophages and integrates into the host genome.[104,112,113] Transmission of the disease requires a vector allowing blood transfer from an infected to a susceptible horse. Interrupted feeding of large hematophagous insects (*Tabanidae*; horseflies, deerflies, stable flies) is the principal mechanism of disease transmission.[108,114] Iatrogenic transmission via blood transfusion, blood-contaminated instruments, or needles is possible. Transplacental passage, infection of nursing foals through the colostrum or milk, and venereal transmission by asymptomatic stallions can occur.[104,107,115] The incubation period is 1 to 3 weeks, but can be as long as 3 months.[104,110]

Infection causes a strong cellular and humoral immune response, which cannot clear the virus completely from the body but finally leads to a remission of clinical signs and latent infection. Recurrence of the disease is associated with recrudescence of viremia due to production of antigenetically novel virus strains that temporarily escape the host's immune system.[104,107] Treatment with corticosteroids or environmental stress can also elicit viremic and symptomatic episodes. Infection of a naive host leads to acute EIA. The severity of clinical signs then decreases with each viremic

episode and the host mounts an immune response against all common variants of EIAV, leading to the chronic subclinical carrier stage.[104] Viral titers in infected animals vary depending on the stage of the disease, being highest during febrile periods. However, chronic infected subclinical carriers may remain viremic and can be a source of infection of other animals.[104,115]

The manifestations of the disease are associated with the host's immune response rather than being the result of direct viral replication.[104] Thrombocytopenia is one of the earliest and most consistent hematologic abnormalities. Anemia is primarily caused by complement-mediated intravascular and extravascular hemolysis secondary to virus–antibody complex attachment to erythrocytes.[104,108] Furthermore, direct bone marrow suppression and sequestration of iron in the reticuloendothelial system occurs,[111] presumably as a direct viral effect[116] and as a response to inflammation as commonly seen in anemia of inflammatory disease (see below).

Immune-complex-mediated glomerulonephritis is common in EIAV-infected horses, but clinical proteinuria is uncommon.[104]

Epidemiology Equine infectious anemia occurs worldwide with variable prevalence. The potential of chronic inapparent carriers to serve as a source of infectious virus is of epidemiologic importance and emphasizes the need for rigorous disease control measures.

Prevention Equine infectious anemia is a reportable disease. Coggins' test or ELISA are obligatory for many health certificates required for traveling and participation in equestrian sports events. Testing of horses at prepurchase exams or before introduction into a new population of horses is recommended. Tests should be performed after a quarantine of 60 days duration after potential exposure to EIAV. Control measures are usually aimed at elimination of inapparent carriers, although the regulations for Coggin's-positive horses may vary. In certain circumstances keeping affected horses in isolation is permitted. Separation from other horses by 200 m is effective in preventing transmission of the disease because the vectors are unlikely to fly a long distance before completing an interrupted meal. Insect control and strict prevention of iatrogenic transmission is required.[104,107,109,114]

Equine piroplasmosis (babesiosis, theileriosis)

- Equine piroplasmosis is a tick-borne protozoal disease characterized by hemolytic anemia, fever, peripheral edema, and weight loss.
- Development of immunity leads to a chronic carrier state, characterized by chronic anemia and poor performance.
- *Theileria equi* is considered more pathogenic than *Babesia caballi*.
- The diagnosis is based on direct detection of intraerythrocytic parasites or indirect serologic tests (complement fixation test or indirect fluorescent antibody test).
- Treatment is aimed towards resolution of the clinical signs. Infections with *T. equi* are difficult to eliminate with the currently available drugs.
- The worldwide distribution of the disease is related to the presence of the tick vectors.
- Equine piroplasmosis is a reportable disease. Regulatory measures are important for international equestrian sports and horse trading.

Piroplasmosis is a tick-borne disease of horses, caused by the intraerythrocytic protozoa *B. caballi* and *T. equi* (formerly *B. equi*). The disease has important implications in the international equestrian sports and trade of horses.[117–119] Potential tick vectors are present in many disease-free countries and would allow the disease to become endemic once introduced into the native horse population by carrier animals. Equine piroplasmosis is therefore classified as an OIE List B disease.[106] Import regulations of various countries restrict entering of horses with antibodies against *B. caballi* or *T. equi*.

History and presenting complaint Piroplasmosis can occur in acute, subacute, and chronic forms.[120] Clinical cases are more frequently caused by *T. equi*; *B. caballi* seems to be less pathogenic.[117,120] Acute forms usually present with depression, anorexia, fever, and peripheral edema. Subacute cases show similar signs, accompanied by weight loss, and occasionally colic and diarrhea. The fever can be intermittent. In chronic cases, unspecific clinical signs including poor performance, mild inappetence, and weight loss are the major complaints. A detailed traveling history should be obtained for horses with suspicious clinical signs, which are not living in endemic areas. Excessive tick infestation may be reported.

Physical examination The clinical signs are often nonspecific.[117,120] Acute piroplasmosis is characterized by high fever, tachycardia, tachypnea, congestion of mucous membranes, peripheral edema, swelling of the eyelids, icterus, and hemoglobinuria. Subacute disease presents with similar signs. The mucous membranes appear from pale pink to pale yellow or bright yellow. Occasionally, petechiae and ecchymoses are found. Physical examination in chronic cases does often not reveal significant abnormalities. Untreated cases become severely anemic and weak. Infection with *B. caballi* is often not clinically apparent, or causes unspecific clinical signs of chronic inappetence, poor performance, weight loss, and persistent anemia.[117,120] Acute renal failure, colic, enteritis, pneumonia, loss of fertility, and abortion are reported complications of equine piroplasmosis. Occurrence of central nervous signs has also been reported.[117]

Special examination Splenomegaly is usually detected on rectal examination and ultrasonographic evaluation of the abdomen.[120]

Laboratory examination The laboratory findings are generally similar to those found in immune-hemolytic anemia, often associated with thrombocytopenia.[121] Neutropenia and lymphopenia are common in acute infections. Varying degrees of hemoglobinuria are observed.[117]

Direct detection of the parasites during the acute phase of the infection can be achieved by examination of Giemsa-stained blood smears.[117,119,122] The presence of large, paired intraerythrocytic merozoites forming an acute angle is indicative for *B. caballi* (Fig. 44.5A). *T. equi* is typically characterized by four small merozoites arranged in a tetrad ('Maltese cross'; Fig. 44.5 B).[121] In carrier animals and in most cases of *B. caballi* infection, parasitemia is very low and

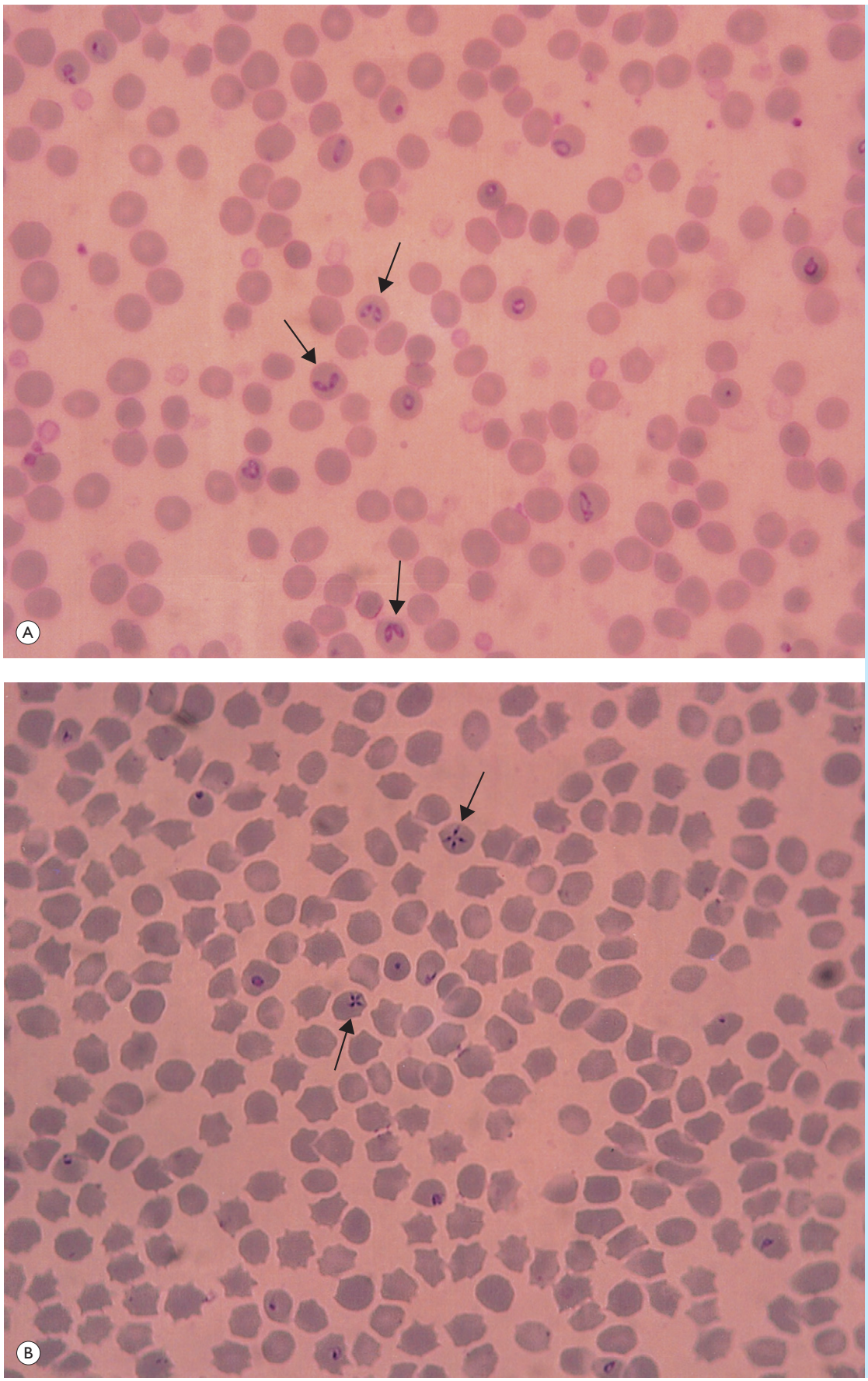


Fig. 44.5
Blood smears of horses with piroplasmosis. (A) *Babesia caballi* is characterized by paired intraerythrocytic merozoites (arrows). (B) *Theileria equi* is characterized by four smaller merozoites forming a 'Maltese cross' (arrows). (Courtesy of Dr Heinz Sager, Institute of Parasitology, University of Berne, Switzerland.)

detection on routine blood smears is usually not possible.[120] A quantitative buffy coat analysis technique using microhematocrit tubes and acridine orange staining (QBC® Malaria) is a simple, rapid, and more sensitive method for detection of blood parasites in all mammal species, but is not specific for piroplasmosis.[122,123] The use of polymerase chain reaction (PCR)[124–126] and in vitro culture[125] have been described for diagnosis of piroplasmosis in horses and, if available, may be useful for detection of carrier animals.[122]

Indirect tests are used for diagnosis of latent or chronic infections. Antibody titers become detectable between 2 and 20 days after infection, depending on the type of assay used. Several serologic tests are available for diagnosis of piroplasmosis in horses.[119,120,122] The complement fixation test (CFT) is frequently used for qualifying horses for international import/export. However, the CFT has technical drawbacks, is characterized by low sensitivity and specificity, and is not able to detect latent infections.[119,122,127–129] Indirect fluorescent antibody test (IFAT) has proven more sensitive and specific and can be used to distinguish between *B. caballi* and *T. equi* infections. Antibody titers remain positive during the latent phase of infection.[119,122,127–129] Western blot and ELISA techniques are considered very sensitive and specific for detection of carrier horses.[119,122,127] Competitive ELISA assays using monoclonal antibodies may be used in the future as screening tests for equine piroplasmosis and may replace CFT and IFAT assays.

Necropsy examination Gross pathological findings include generalized pallor or icterus, subcutaneous and subserosal edema, emaciation, hepato- and splenomegaly, enlarged kidneys, ascites, hydrothorax, pericardial effusion, pulmonary edema, and lymphadenopathy. Histopathological examination reveals pulmonary edema, liver necrosis, renal tubular degeneration, tubular protein and hemoglobin casts, proliferation of reticuloendothelial cells in liver, kidneys, lungs, and lymph nodes.[117]

Diagnostic confirmation The detection of intraerythrocytic parasites or positive direct or indirect tests in an animal with clinical signs of piroplasmosis is diagnostic.

Therapeutic aims The first goal of treatment is resolution of the clinical signs. The second goal is elimination of the parasites from affected horses. *T. equi* is less susceptible to treatment than *B. caballi*. Clinical recovery is usually achieved but infections with *T. equi* are difficult to eliminate with the currently available drugs. Horses recovered from clinical disease usually remain carriers, probably for life.[118–120] Elimination of *B. caballi* infections is rarely recommended in endemic areas.[120]

Therapy Imidocarb is the drug of choice for treatment of piroplasmosis. For *B. caballi*, two doses of 2.2 mg/kg i.m. at 24-h intervals are recommended; *T. equi* may be treated with four doses of 4 mg/kg i.m. at 72-h intervals.[117,120,130] This dose, however, is near toxic levels and may be detrimental to the animal itself. The drug should only be administered intramuscularly. Cholinergic adverse effects can be treated with atropine sulfate. Combined treatment with buparvaquone (4 mg/kg i.v.) and imidocarb (4 mg/kg i.m.) has been suggested for elimination of *T. equi*.[131,132]

Administration of polyionic electrolyte solutions is indicated to prevent or treat acute renal failure due to pigmenturia. Colic, enteritis, and pneumonia should be treated as necessary. Blood transfusions are indicated if signs of tissue hypoxia are present (see the section 'Acute blood loss').

Prognosis Early treatment is effective even without completely eliminating the etiologic agent. Chronic carriers are resistant to new infections.

Etiology and pathophysiology During the life cycle of *B. caballi* and *T. equi* ticks (*Dermacentor, Hyalomma*, and *Rhipicephalus* spp.) serve as vectors for transmission of the disease between host animals;[120,133] the incubation period varies from 5 to 30 days.[117,120,131] Erythrocyte destruction is related to the reproduction of merozoites in the erythrocytes,[133] and is primarily caused by intravascular hemolysis, mediated by antibodies against epitopes of the infectious agent, complexes of erythrocyte membrane and microbial proteins, and exposed erythrocyte membrane epitopes.[121] All mammalian hosts are able to develop immunity to the parasites after infection.[133] Development of an immunity without expression of clinical signs is common in endemic areas.[117,133] Acute infections are followed by a chronic carrier state that leads to persistent anemia and can result in decreased performance in race horses.[133]

Epidemiology Piroplasmosis occurs most commonly in subtropic and tropic regions in South and Central America, Africa, Asia, the Middle East, and Eastern and Southern Europe. It is, however, not strictly confined to these areas. The United States, Canada, Australia, Japan, Germany, England, and Ireland are considered non-endemic areas, although epidemic foci and introduction of the disease by imported horses have been reported.[119,120] The worldwide distribution is related to the presence of tick vectors.[117,120]

The infectious reservoir for *B. caballi* is the tick vectors. The parasites are transmitted transovarially (vertically) and trans-stadially (horizontally) within the tick population; *T. equi* is only transmitted trans-stadially (horizontally) and the reservoir is therefore considered to be the horse population. Unlike horses infected with *B. caballi*, those infected with *T. equi* are likely to remain lifelong carriers, even after treatment and resolution of the clinical signs.[117,118]

Prevention Tick control by regular application of an acaricide is the cornerstone for prevention of equine piroplasmosis. Currently, vaccines for equine piroplasmosis are not available.

Immune-mediated hemolytic anemia

- True autoimmune hemolytic anemia is uncommon in horses. Secondary IMHA has been reported secondary to infections, administration of certain drugs, and neoplasia, or in association with other immunologic diseases.
- Immune-mediated erythrocyte destruction leads to intravascular or extravascular hemolysis.
- The primary disease often predominates the clinical picture.
- Typical laboratory findings are autoagglutination of the blood and the presence of spherocytes. Coombs' test and direct immunofluorescence flow cytometry tests can confirm the diagnosis.

- Therapy consists of elimination of the primary cause, administration of corticosteroids, and supportive treatment.
- The prognosis depends on the underlying disease.

History and presenting complaint Lethargy, depression, weight loss, anorexia, and tachypnea are frequent presenting complaints. A history of recent drug administration or infectious disease may be obtained.

Physical examination Hemolysis can be acute and severe or chronic and insidious.[108] Clinical signs depend on the severity of the anemia, the rate of erythrocyte destruction, and the underlying disease process. Often, the clinical signs of the primary disease predominate the clinical picture. Lethargy, depression, pyrexia, tachycardia, tachypnea, icterus, and hemoglobinuria are found. Pallor of the mucous membranes can occur but is not a consistent finding.[103,108]

Special examination Ultrasonographic examination of abscesses and local swellings (myositis, cellulitis) can be useful to detect clostridial infections (gas and fluid accumulation). Rectal examination, and ultrasonographic examination of abdominal and thoracic cavity should be performed to detect possible neoplasia. Splenomegaly is occasionally found, and is likely caused by splenic hypertrophy or an underlying disease (neoplasia).

Laboratory examination Complete blood count and bone marrow analysis reveal signs for regenerative anemia within days after onset of hemolysis.[30] Serial measurements of hematocrit are helpful to detect ongoing hemolysis or regenerative response. Occasionally, the immune reaction also affects red blood cell precursors in the bone marrow, leading to non-regenerative anemia.[29,30] The presence of spherocytes is highly suggestive for immune-mediated hemolytic anemia.[29] Autoagglutination of red blood cells (Fig. 44.6) is a consistent finding in immune-mediated hemolytic anemia and should be distinguished from normal rouleaux formation (see above).[21,29,30]

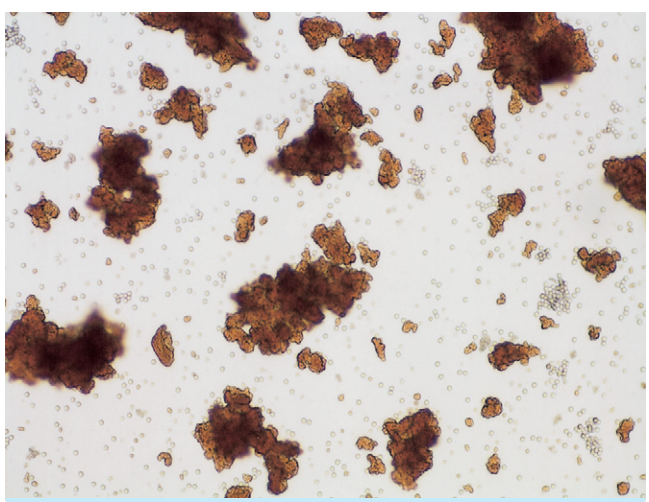


Fig. 44.6
Autoagglutination of erythrocytes in a horse with immune-mediated hemolytic anemia secondary to clostridial myositis.

Moderate neutrophilic leukocytosis is a common feature[134] and, occasionally, immune- mediated hemolytic anemia is associated with thrombocytopenia.[21,135,136] Red discoloration of the plasma after centrifugation indicates hemoglobinemia. The plasma protein concentration is typically normal. Hyperbilirubinemia may be present.[103]

The direct antiglobulin test (Coombs' test) using multivalent, species-specific reagent detects IgM (cold agglutinin) and IgG (warm agglutinin) anti-erythrocyte antibodies as well as complement protein C3 on the erythrocyte surface.[30] Although the specificity of the Coombs' test is very high, its sensitivity is low and a negative test does not rule out immune hemolytic anemia.[29] Previous corticosteroid treatment may lead to false-negative test results.[134] Direct immunofluorescence flow cytometry has recently been described for diagnosis of immune-mediated hemolytic anemia in horses.[137,138] This method allows the detection, differentiation, and quantification of cell-bound IgG-, IgM-, and IgA-antibodies. The sensitivity of the test is thought to be very high, whereas its specificity is somewhat lower than in the Coombs' test, occasionally leading to false-positive results. However, test characteristics have not yet been determined in horses.

Agar gel immunodiffusion for EIA (Coggins') should be submitted in all cases of hemolytic anemia. If the horse is living in or was imported from an area in which piroplasmosis is endemic, blood smears should be evaluated for presence of intraerythrocytic parasites, and appropriate further diagnostic should be performed. Determination of anti-penicillin IgG antibodies may be performed when penicillin-associated hemolytic anemia is suspected.[139–141] Clostridial infection (myositis or cellulitis) can be diagnosed by fine-needle aspirate, cytologic examination, Gram stains, and bacterial culture. Cytologic evaluation of abdominal or pleural fluid is recommended in cases with detectable effusion. Fine-needle aspiration of mass lesions is indicated to diagnose neoplasia.

Necropsy examination Generalized pallor or icterus is present on post-mortem examination. Lesions of primary disease may be found predominantly. Hemosiderosis of liver and kidneys, bone marrow erythroid hyperplasia, and extramedullary hematopoiesis are present.[46]

Diagnostic confirmation Diagnosis of immune-mediated hemolytic anemia is confirmed by ruling out other causes of hemolytic anemia, positive Coombs' test, positive flow cytometry test, and response to treatment with corticosteroids.

Therapeutic aims Treatment of the underlying disease, suppression of the abnormal immune response, and supportive care are the basic prerequisites for successful treatment of immune-mediated hemolytic anemia. Monitoring and support of renal function is important. If signs of tissue hypoxia and ischemia are present, increasing the hemoglobin concentration in the blood should be attempted.

Therapy The treatment depends on the severity and the primary cause of the anemia. Previously administered drugs should be discontinued. If antibiotic treatment is necessary, the class of the antimicrobial agent should be altered. Treatment with isotonic crystalloid solutions is crucial to avoid pigment nephropathy and acute renal failure in cases with severe hemolysis and hemoglobinuria.

Corticosteroids stabilize cell membranes, decrease the antibody production, decrease the affinity of the antibodies to the red blood cells, and decrease the rate of RBC destruction by macrophages of the reticuloendothelial system.[21,29,142] An initial daily dose of 0.05–0.1 mg/kg of dexamethasone i.m. or i.v. usually leads to a clinical and hematological response within 5–6 days. Alternatively, prednisolone can be administered orally at an initial dose of 1–1.5 mg/kg once daily. The dose should then be gradually reduced and continued for the total duration of 3 to 6 weeks, depending on the clinical response. Prior to initiation of corticosteroid treatment, possible infectious causes of immune hemolytic anemia should be precluded. In these cases, corticosteroids should be used with caution, as immune suppression can lead to exacerbation of the disease.[134]

Cytotoxic drugs including cyclophosphamide are recommended for severe therapy-resistant cases.[142] There is one report of treatment of a horse with cyclophosphamide and azathioprine.[46] Other therapies occasionally used in humans and dogs, including splenectomy, administration of intravenous immunoglobulins, and plasmapheresis, have not been described in horses.[29]

Clostridial myositis or cellulitis requires surgical debridement of necrotic tissue, analgesia, fluid therapy, and correction of electrolyte and acid–base disturbances.[143] Although penicillin is commonly recommended as the antimicrobial agent of choice, there is evidence that treatment with oxytetracycline and metronidazole may be more effective in decreasing toxin production and increasing the overall survival rate. [144,145]

If signs of tissue hypoxia and ischemia indicate the need to support the oxygen-carrying capacity of the blood, the use of whole-blood transfusions, packed red cells, or polymerized ultrapurified bovine hemoglobin (PUBH) should be considered (see the section 'Acute blood loss'). Transfusion of blood or erythrocyte concentrates may have limited benefits, as transfused cells are rapidly removed from the circulation and put additional workload on the reticuloendothelial system. Compatible donors often are not available, and cross-matching is usually positive. The absence of cell-surface antigens in PUBH solutions make them a useful agent for the treatment of severe immune-mediated hemolytic anemia, although costs are often prohibitive.[11,146, 147]

Prognosis The response to corticosteroid treatment is usually good in horses.[29] However, recurrence of the anemia after cessation of the treatment is possible, especially when the primary disease process is still present. The prognosis is best for patients with penicillin-associated anemia and primary idiopathic autoimmune hemolytic anemia. The prognosis for patients with neoplastic disease is usually poor.[29,134,148] Repeated monitoring of the hematologic parameters is recommended for 6 to 12 months after cessation of treatment.

Etiology and pathophysiology Immune-mediated hemolytic anemia is caused by antibodies directed against erythrocyte membrane proteins or membrane-bound antigens. Initiating factors are thought to be alterations of the erythrocyte membrane, alterations in immune regulation, or stimulation by other antigens, leading to the production of cross-reacting antibodies.[29,30] Erythrocyte destruction is the result of complement-mediated intravascular hemolysis or, more commonly, phagocytosis of antibody-coated erythrocytes by the macrophages of the reticuloendothelial system in liver and spleen (extravascular hemolysis).[29,30]

Occasionally, autoantibodies are also directed against bone marrow erythroid precursors, thereby interfering with erythropoiesis and leading to acquired pure red cell aplasia.[29,30] In patients in which no demonstrable underlying disease is present, the anemia is referred to as primary idiopathic autoimmune hemolytic anemia.[21,148] More commonly, immune-mediated hemolytic anemia occurs in association with other disease processes (secondary immune-mediated hemolytic anemia). A variety of causes has been described in association with immune-mediated hemolytic anemia in horses.

Immune-mediated hemolytic anemia secondary to clostridial myositis or cellulitis is not uncommon in horses. Autoagglutination can occur without clinically detectable hemolysis. Clostridial myositis or cellulitis is most commonly caused iatrogenically as a result of intramuscular injections of nonantibiotic drugs (flunixin meglumine, ivermectin, antihistamines, B-complex vitamins, prostaglandins, dipyrone, phenylbutazone).[143,149] Although *Clostridium perfringens* alpha toxin has a direct hemolytic effect resulting from massive acute destruction of the red cell membranes,[143,149,150] clinical and laboratory findings (delayed onset hemolysis, autoagglutination) suggest an immune-mediated cause of the anemia.[149] The pathomechanism may be related to bacterial synthesis of neuraminidase and subsequent enzyme-mediated exposure of a membrane-bound antigen (Thomsen–Friedenreich cryptantigen).[143,151] However, the contribution of this mechanism to the hemolytic process is unknown.

Immune-mediated hemolytic anemia is a rare complication after administration of penicillin[139–141,152] and possibly trimethoprim–sulfamethoxazole[153] in horses. Presumably the drugs act as haptens. They bind to erythrocyte membrane proteins and plasma proteins, and induce production of anti-penicillin IgG antibodies. Binding of the antibodies to the erythrocyte-bound penicillin leads predominantly to extravascular hemolysis, and to a lesser extent to complement-mediated intravascular hemolysis.[139,141] In part, the anemia may also result from pooling of red blood cells in the microcirculation or in the spleen, which would explain the rapid rise in hematocrit seen in some horses after cessation of penicillin treatment and initiation of corticosteroid treatment.[140]

Lymphosarcoma and other neoplasms are commonly associated with anemia of chronic disease and blood loss anemia. Occasionally, immune-mediated hemolytic anemia (and thrombocytopenia) may be found.[21,135,154]

Other primary disorders which may be associated with immune-mediated hemolytic anemia are purpura hemorrhagica and systemic lupus erythematosus, inflammatory bowel disease, and chronic bacterial infections or abscesses.[21,155,156] The etiology and pathogenesis of equine infectious anemia and piroplasmosis were described above.

Prevention Administration of drugs that are known to cause immune-mediated hemolytic anemia in an individual horse, and injection of irritating drugs (flunixin meglumine, ivermectin) that could cause clostridial myositis or cellulitis, should be avoided.

Heinz body hemolytic anemia

- Heinz body anemia results from toxic effects of maple leaves, wild onions, phenothiazines, or methylene blue.
- Oxidative damage to erythrocytes leads to hemolytic anemia characterized by the presence of Heinz bodies and eccentrocytes on the blood smear.
- Maple leaf toxicity also leads to methemoglobinemia and brown discoloration of mucous membranes, urine, and blood.
- Prognosis with rapidly developing severe anemia is poor.

History and presenting complaint Clinical signs vary depending on type and amount of toxin, time since exposure, and occurrence of complicating factors like pigment nephrosis and acute renal failure. Horses usually present with weakness, depression, anorexia, exercise intolerance, and signs of hematuria. Colic, ataxia, or acute death may occur.[108,157,158]

Physical examination Tachycardia, tachypnea and icterus are common findings. Brown discoloration of the mucous membranes, blood, and urine indicate methemoglobinuria, commonly found with maple leaf toxicity (Figs 44.7 and 44.8).[108,157]

Laboratory examination Moderate to severe anemia, hyperbilirubinemia, hemoglobinemia, and hemoglobinuria are present. Heinz bodies and eccentrocytes can be detected on blood smears (Fig. 44.9).[108,157] Measured blood methemoglobin concentration is increased in cases with maple leaf toxicity and can exceed 50% of total cellular hemoglobin concentration (normal methemoglobin fraction is less than 2% of total hemoglobin).[108] Serum biochemistry and urinalysis should be performed to monitor liver and kidney function. Blood gas analysis and serum lactate measurements may be used to assess severity and metabolic consequences of the anemia.

Diagnostic confirmation Clinical diagnosis is established based on history, clinical signs, specific laboratory findings, negative Coombs' test, and exclusion of other causes of anemia.

Treatment and prognosis Treatment consists of removal of the source of the toxin, administration of activated charcoal via nasogastric tube to decrease toxin absorption, intravenous fluid therapy to support renal function, and administration of high doses of vitamin C (30 mg/kg i.v. twice daily) as an antioxidant agent.[157,159,160] Whole-blood transfusion may be necessary when the hematocrit is less than 12% or if signs of tissue hypoxia are present (see the section 'Acute blood loss'). The use of a polymerized ultrapurified bovine hemoglobin solution (Oxyglobin®, Biopure Corporation, Cambridge, MA, USA) has been reported in horses for transient support of the oxygen-carrying capacity of the blood, providing a more optimal environment for a subsequent effective whole blood transfusion.[11,146] However, its use in adult horses is often limited by prohibitive costs.

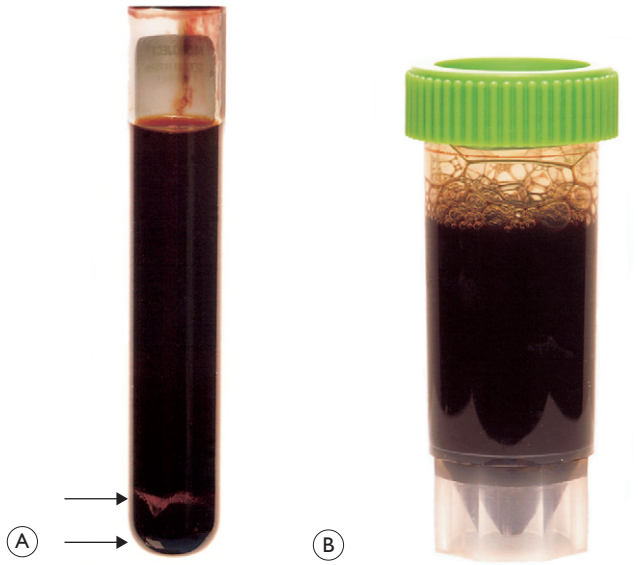


Fig. 44.8
(A) Blood sample of the same horse after complete sedimentation of the erythrocytes (arrows). Severe hemolysis and methemoglobinemia lead to a dark red-brown discoloration of the plasma. (B) Dark brown urine is consistent with hemoglobinuria and methemoglobinuria.

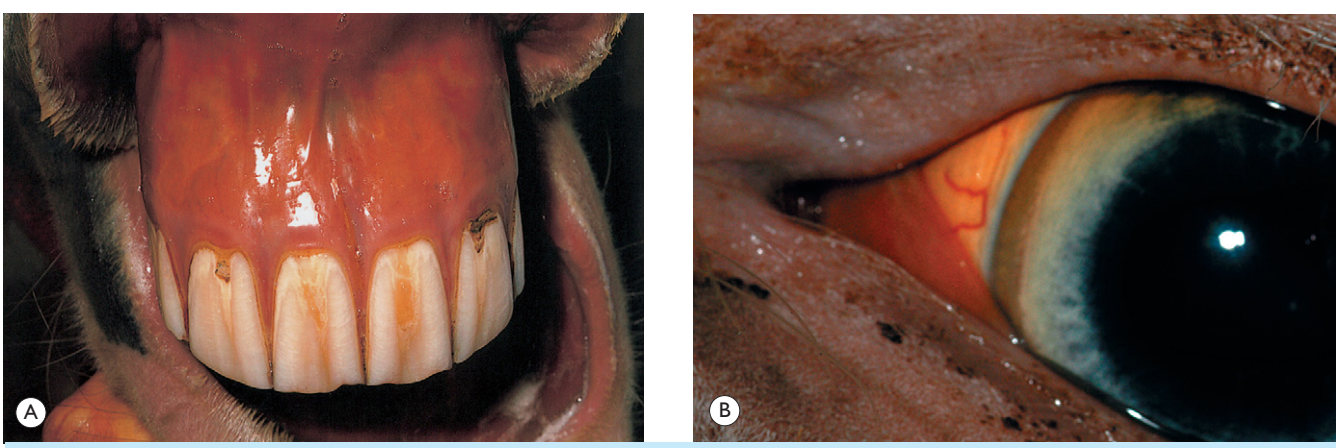


Fig. 44.7
Brown discoloration of mucous membranes (A) and conjunctivae (B) indicate severe methemoglobinemia associated with red maple leaf toxicity. The methemoglobin fraction in this horse was 44.3% of the total hemoglobin.

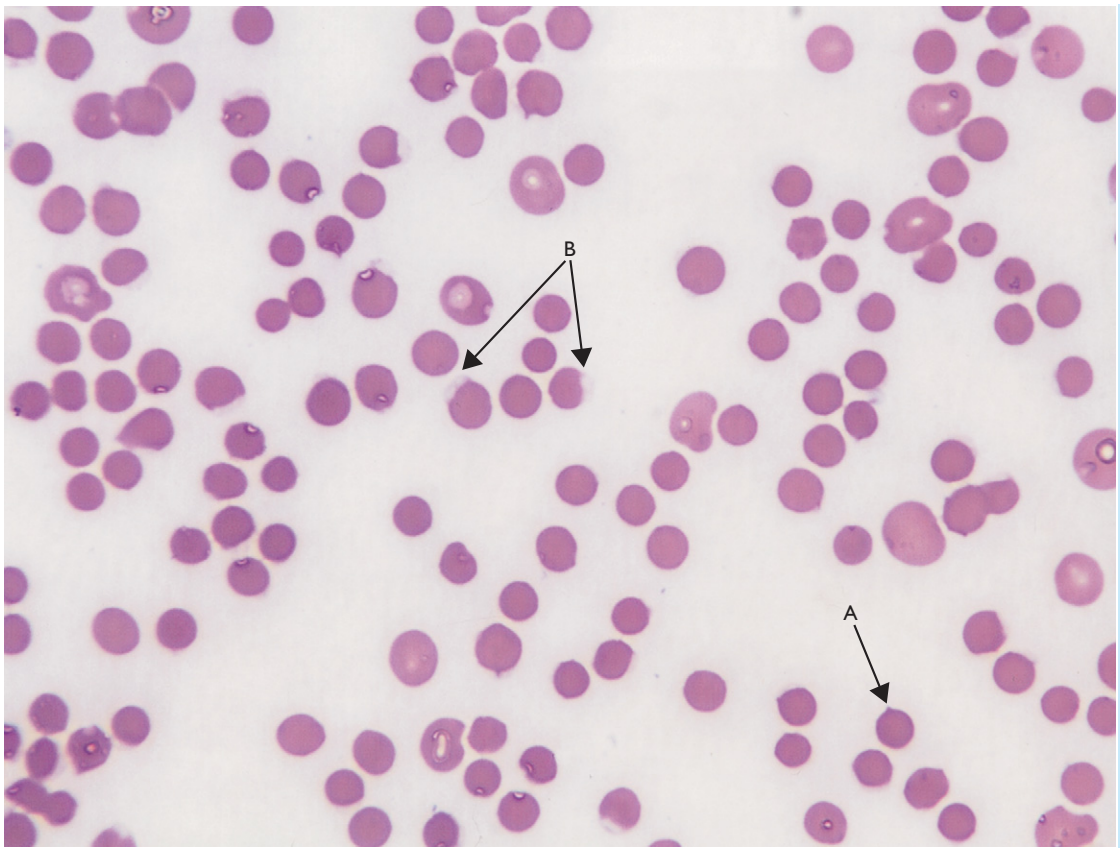


Fig. 44.9 Heinz bodies (A) and eccentrocytes (B) in a blood smear of a horse with hemolytic anemia due to red maple leaf toxicity.

The prognosis depends on the amount of the ingested toxin, occurrence of complicating factors, and the response to treatment. With rapidly progressive severe anemia, the prognosis is poor. The mortality rate with maple leaf toxicity is 60 to 65%.[157]

Etiology and pathophysiology Heinz body hemolytic anemia results from acute oxidative damage to the erythrocytes, caused by ingestion of maple leaves (red maple, *Acer rubrum)* and potentially, sugar maple (*A. saccharum)* and silver maple (*A. saccharinum*), wild onions (*Allium canadense*), or certain drugs including phenothiazines or methylene blue.[108,157,158,161]

Oxidative denaturation and aggregation of hemoglobin results in development of typical Heinz body inclusions, increased osmotic fragility of the erythrocytes, and enhanced cell clearance by mononuclear phagocytes, leading to intravascular and extravascular hemolysis. Maple leaf toxicity is also associated with formation of methemoglobin, which is incapable of carrying oxygen to the tissue.[108,157]

Hypoproliferative anemia

Anemia of inflammatory disease (AID)

- Non-regenerative anemia secondary to inflammatory or chronic disease is the most common type of anemia in horses.
- It is characterized by moderate anemia associated with normal or decreased serum iron concentration and total iron-binding capacity, and normal or increased serum ferritin and bone marrow iron stores.
- The pathogenesis is multifactorial, including sequestration of iron, decreased erythrocyte survival, and decreased bone marrow response to anemia.
- Treatment is directed against the primary disease process.
- The prognosis depends on the underlying problem.

Anemia of inflammatory disease (AID) is a mild to moderate, non-regenerative anemia associated with inflammatory disease, chronic infections, traumatic conditions, and neoplastic disorders.[37] It is also commonly referred to as anemia of chronic disease, although the syndrome may include anemias associated with diseases that are not chronic.[37,162] Anemia of inflammatory disease is considered the most common type of anemia in veterinary medicine, but it is usually a secondary finding of little clinical significance.[37]

History and presenting complaint The presenting complaints usually result from the primary underlying disease. Often, a history of poor performance, chronic weight loss, long-lasting disease processes and infectious conditions may be obtained.

Physical examination Signs of the primary disorder usually predominate the clinical picture. Weight loss and fever are often present. Pale mucous membranes are not consistently found, due to the mild to moderate character of the anemia.

Laboratory examination Laboratory findings include slightly to moderately decreased PCV and erythrocyte counts,

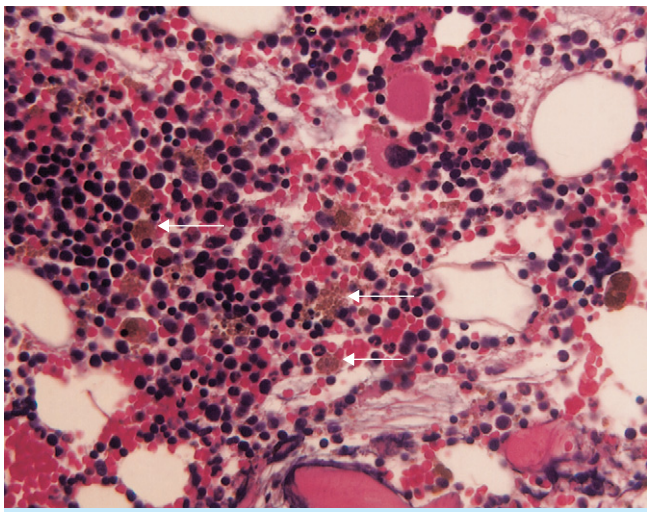


Fig. 44.10
Sternal bone marrow biopsy of a horse with anemia of inflammatory disease. Using conventional staining, increased hemosiderin deposits appear as brown aggregates (arrows). The cellular pattern is normal (hematoxylin–eosin staining).

and a low–normal or decreased MCV. Neutrophilic leukocytosis, monocytosis, and increased plasma fibrinogen and globulin concentrations usually indicate chronic inflammation.[163] Serum iron concentration and TIBC are normal or decreased, whereas serum ferritin and bone marrow stainable iron are normal or increased.[47,162] Bone marrow evaluation reveals increased stainable iron deposits with a nearly normal cellular pattern (Fig. 44.10).[37]

Diagnostic confirmation The presence of chronic inflammatory or neoplastic disease associated with mild to moderate non-regenerative anemia is highly suggestive for AID. Diagnostic confirmation of AID can be achieved by evaluation of the body iron status.[37]

Therapeutic aims Treatment is directed against the primary disease process. The anemia is rarely severe enough to require treatment.

Therapy Supplementation of iron is not useful, as the body is not iron deficient.

Prognosis The prognosis depends on the primary disease. The anemia usually resolves within weeks or months after resolution of the primary disease.

Etiology and pathophysiology The conditions leading to AID are inflammatory diseases, chronic infections, traumatic injuries, or neoplastic disorders. The anemia usually develops slowly to reach a plateau after the first 1 or 2 months of illness, but initial changes in hematocrit and hemoglobin concentration may occur after 3 to 10 days. There is no correlation between the duration of the disease and the severity of the anemia.[37]

The pathogenesis of AID is multifactorial, including sequestration of iron into storage forms in liver and bone marrow, decreased erythrocyte survival, and decreased bone marrow response to anemia.[37,162]

Increased sequestration of iron in macrophages and decreased absorption of iron from the intestinal tract is part of the acute-phase reaction, mediated by inflammatory mediators (interleukin-1, tumor necrosis factor α). This is considered to be part of a non-specific antibacterial immune response, reducing the availability of iron for bacterial growth. Increased erythrocyte destruction may be a major factor in the early stage of AID, presumably due to alterations in the red cell membrane, binding of IgG, and activation of the macrophages leading to a more efficient clearing of senescent and IgG-coated red blood cells from the circulation. Finally, decreased erythropoiesis results from blunted erythropoietin release in response to anemia, diminished bone marrow response to erythropoietin, and limited availability of iron.

Some chronic diseases and organ dysfunctions (chronic renal disease, hepatic disease, endocrine disease, and gastrointestinal disease) are associated with anemia that differs from AID in regards to pathophysiologic mechanism and iron metabolism.[162,163] However, no difference exists regarding treatment and prognosis of this type of anemia.

Iron-deficiency anemia

- Iron-deficiency anemia is rare in adult horses. It usually occurs secondary to chronic blood loss.
- The primary disease may predominate the clinical picture.
- Iron-deficiency anemia is characterized by microcytic non-regenerative anemia with low serum iron and serum ferritin concentrations, low bone marrow iron stores, and normal or increased iron-binding capacity.
- Treatment consists of elimination of the underlying disease process and iron supplementation.
- The prognosis depends on the primary cause of iron deficiency.
- Prevention should focus on potential causes of iron deficiency rather than daily supplementation of iron.

History and presenting complaint Clinical signs vary depending on cause and severity of the anemia and the presence of other concomitant disorders.[47] Poor performance, depression, weakness, and weight loss are common, as are unspecific features of iron-deficiency anemia.[47]

Physical examination Physical examination usually reveals signs of mild to moderate anemia. Pale mucous membranes, diarrhea, hematuria, hematochezia, melena, and epistaxis may be found in affected horses.[47] The primary disease may predominate the clinical picture.

Special examination Gastroscopy, fecal parasite egg counts, fecal occult blood test, urinalysis, and bronchoalveolar lavage may be performed in order to identify the underlying process leading to chronic blood loss and iron deficiency.

Laboratory examination Anemia due to chronic blood loss is initially macrocytic and regenerative. Only after weeks or months, in very late stages of severe iron depletion, does microcytic non-regenerative anemia develop.[47,48] The RDW may be increased because of the presence of microcytes together with normocytic cells. Hypochromasia is rarely apparent in horses with iron-deficiency anemia.[47] Hypoproteinemia is often associated when substantial recent or ongoing blood loss is present.[47]

Evaluation of the body iron status typically reveals low serum iron concentrations and increased TIBC. Serum

Table 44.8 Differentiation between anemia of inflammatory disease and iron-deficiency anemia[37,47,48]

	Iron-deficiency anemia	Anemia of inflammatory disease
Mean corpuscular volume (MCV)	⇓	Normal or ⇓
Red blood cell distribution width (RDW)	Normal or ⇑	Normal
Serum iron	⇓	⇓ or normal
Serum ferritin	⇓	Normal or ⇑
Total iron-binding capacity	Normal or ⇑	⇓ or normal
Bone marrow stainable iron	⇓ or absent	Normal or ⇑

ferritin concentration correlates directly with body iron stores and is usually low in iron-deficiency anemia.[47,48,53,54] Bone marrow evaluation is the most sensitive method for detection of iron deficiency, prior to development of microcytic anemia.[47,48,164] Typically, erythroid hyperplasia and ineffective erythropoiesis with asynchrony and shift to later rubricytes are found. Reduced erythropoiesis is apparent at later stages. Stainable iron in the bone marrow is minimal or absent.

Diagnostic confirmation Primary differential diagnosis in cases with mild to moderate non-regenerative anemia is anemia of inflammatory disease. Diagnostic confirmation of iron-deficiency anemia can be achieved by evaluation of the body iron status (Table 44.8).

Therapeutic aims Treatment should be directed towards elimination of the underlying process which causes the chronic blood loss.

Therapy Besides treatment of the primary disease process, iron supplementation is recommended. Oral supplementation of iron compounds is safe and can be achieved by administration of commercially available hematinics containing ferrous sulfate, copper, and various B-vitamins.[54] Parenteral iron dextran preparations should not be used due to severe tissue irritation (thrombophlebitis, myositis), possible related anaphylaxis, and fatal reactions.[47,54]

Prognosis The prognosis largely depends on the underlying disease causing the iron deficiency. Several months may be required to replenish body iron stores and to normalize hematocrit and red cell indices.

Etiology and pathophysiology Iron-deficiency anemia is rare in adult horses.[17,47,48,55] It usually occurs secondary to chronic blood loss due to gastrointestinal ulcers, parasites, neoplasia, and urinary or pulmonary hemorrhage. Dietary causes are rare. Unless the anemia is severe, clinical signs of iron deficiency are more likely the result of the underlying disease and the impaired function of iron-containing enzymes rather than the reduction of the oxygen-carrying capacity of the blood.[59]

Prevention The administration of hematinics (iron and B-vitamin-containing compounds) to horses is common practice, although efficacy of these treatments to enhance performance has not been proven.[48,54,59,165] Current recommendations suggest that the iron requirements vary between 500 and 1200 mg/day for a 500-kg horse, depending on work intensity.[165] Although exact iron requirements for athletic horses in training are not known, the usual dietary sources are considered adequate to maintain a sufficient supply of iron for hemoglobin synthesis and function of iron-dependent enzymes.[53,54,165,166] Prevention should therefore focus on potentially underlying disease processes rather than iron supplementation.

Other nutritional deficiency anemias Deficiencies of copper, folic acid, vitamin B_{12} (cobalamin), and cobalt can potentially lead to hypoproliferative anemia in humans and animals. However, reports on anemias due to nutritional deficiencies are often based on response to supplementation or treatment rather than demonstration of deficiency of a defined nutrient.[164] The true incidence of this type of anemias is therefore often unknown. Copper, folic acid, and cobalamin are common ingredients of modern horse feed and hematinic preparations, which are used empirically in horses.[54]

Copper Copper, as part of a copper-containing plasma protein (ceruloplasmin), plays an important role for transmembranous iron transport and transfer of iron from ferritin (ferrous form) to transferrin (ferric form). Although not well defined, daily copper requirements are currently estimated to be 131 to 187 mg/day for a 500-kg horse.[69,165] Copper deficiency can lead to impaired iron metabolism and accumulation of iron stores with signs of functional iron deficiency.[47,53] There is evidence of a relationship between developmental orthopedic disease and dietary copper intake in foals.[69,71] However, adult horses are usually not affected by copper deficiency.

Folic acid, vitamin B_{12}, and cobalt Folic acid and vitamin B_{12} (cobalamin) belong to the group of water-soluble vitamins (B vitamins). Interactive reactions of folic acid and vitamin B_{12} are involved in DNA synthesis and amino acid metabolism. These two vitamins are therefore essential for cell division and proliferation, especially in rapidly dividing cells such as the hematopoietic cells and the gastrointestinal endothelium.[77,167]

Requirements for vitamin B_{12} and folic acid are likely to be met by microbial synthesis within the large intestine of horses. Intake of folic acid is further provided by oral dietary intake.[54,71,167–169] Cobalt is essential for vitamin B_{12} synthesis.

Macrocytic or normocytic normochromic non-regenerative anemia caused by folate or vitamin B_{12} deficiency occurs in humans and ruminants. Although cases of poor performance and anemia have occasionally been associated with folate deficiency,[75] it seems to occur rarely in horses.[18,71,164,167] Horses also appear to be unaffected by vitamin B_{12} and cobalt deficiency.[71,168] However, serum folate concentrations in stabled, intensively training Thoroughbred and Standardbred horses are generally lower than in pastured horses,[73–76] and additional dietary folic acid may be indicated for some horses in training.

Administration of sulfadiazine and pyrimethamine to treat equine protozoal myeloencephalitis requires special consideration regarding folate metabolism. Both drugs sequentially limit folate synthesis by inhibition of protozoal enzymes and competition with para-amino benzoic acid, which is a precursor of folic acid.[77] Mammals are less sensi-

tive to these effects but intestinal uptake of folic acid may be inhibited. A rapid and significant reduction of serum folate concentrations occurs after administration of sulfadiazine and pyrimethamine to horses.[73]

Anemia, leukopenia, glossitis, oral ulcerations, and bone marrow hypoplasia have been reported in a horse during long-term treatment with orally administered folic acid, sulfadiazine, and pyrimethamine.[77] Experimental evidence from other species suggests that concomitant oral administration of folic acid and pyrimethamine may result in decline, rather than an increase, in plasma folate concentrations. This paradoxical effect is likely due to competition of the orally administered inactive form with endogenous folates for intestinal absorption and interruption of the enterohepatic circulation of folic acid.[77,170] Monitoring of serum or erythrocyte folate concentrations and hemograms may therefore be indicated in horses treated with sulfadiazine and pyrimethamine. However, against common recommendations, the use of folic acid as a dietary supplement with sulfadiazine/pyrimethamine treatment may be contraindicated.

Pure red cell aplasia secondary to treatment with recombinant human erythropoietin (rhEPO)

- Recombinant human erythropoietin is sometimes used as a supposed performance-enhancing agent.
- This form of doping is dangerous and can lead to severe pure red cell aplasia.
- The proposed underlying pathophysiologic mechanism is the production of anti-rhEPO antibodies that cross-react with endogenous erythropoietin and thereby suppress erythropoiesis.
- Diagnosis is based on exclusion of other causes for hypoproliferative anemia, bone marrow examination, and a history of rhEPO administration.
- The prognosis is guarded.
- Administration of rhEPO to horses is not recommended.

Recombinant human erythropoietin (rhEPO) is commonly used to treat human patients, dogs, and cats with chronic renal failure or other chronic or neoplastic desease.[171,172] Although rhEPO is not routinely used for therapeutic purposes in anemic horses, there seems to be an increasing tendency to administer rhEPO to equine athletes, as a performance-enhancing agent, to increase the total red cell mass and oxygen-carrying capacity of the blood.[173,174] However, this form of doping is dangerous. Similar to dogs, cats, and some people,[171,172,175,176] multiple administrations of rhEPO to horses can cause erythroid hypoplasia and severe non-regenerative anemia.[177,178]

History and presenting complaint Affected horses usually present with a history of poor performance, depression, anorexia, and weight loss.[177] Detailed information about previous administration of rhEPO is sometimes not readily available from trainers or owners.

Physical examination Poor body condition, lethargy, weakness, tachycardia, tachypnea, and pale mucous membranes are found in cases of severe anemia. Cardiac arrhythmia may indicate hypoxic myocardial damage. Earlier in the course of the disease, the anemia may be less profound and the clinical signs mild. Due to the slow development, the chronicity of the anemia, and effective compensating mechanisms (see above), most horses can tolerate even severe anemia.

Laboratory examination Laboratory evaluation usually reveals profound anemia without any signs of regenerative response. The severity of the anemia varies between individual horses and depends on the time since administration of the drug.[178] The PCV decreases continuously and can reach values as low as 5%. White blood cell counts, leukocyte differential, and platelet counts are usually within normal limits. Mild elevations of liver enzyme activities and cardiac troponin I serum concentrations may occur, most likely due to tissue hypoxia secondary to severe anemia.[178] Measurements of serum urea nitrogen, serum creatinine concentration, and urinalysis should be performed to rule out primary kidney disease and chronic renal failure.

Coombs' test and Coggins' test are negative. Evaluation of the serum iron concentration, percentage saturation of transferrin, ferritin concentration, and total iron-binding capacity indicates adequate iron supply and precludes iron-deficiency anemia.[177] Bone marrow evaluation typically reveals generalized hypocellularity with markedly decreased numbers or complete absence of erythroid precursors and increased M:E ratio (Fig. 44.11). The myeloid series appears normal and the number of megakaryocytes seems adequate. There is no evidence for a myelophthisic process. The findings are consistent with erythroid hypoplasia or pure red cell aplasia.[177,178]

Measurements of serum erythropoietin concentrations are of limited value for the diagnosis of rhEPO-associated anemia. Clearance of rhEPO from plasma in horses is rapid,[179,180] which precludes the possibility of detection of rhEPO at the time of onset of clinical signs. Furthermore, measurements of endogenous serum erythropoietin concentrations in affected horses are known to be inconsistent and

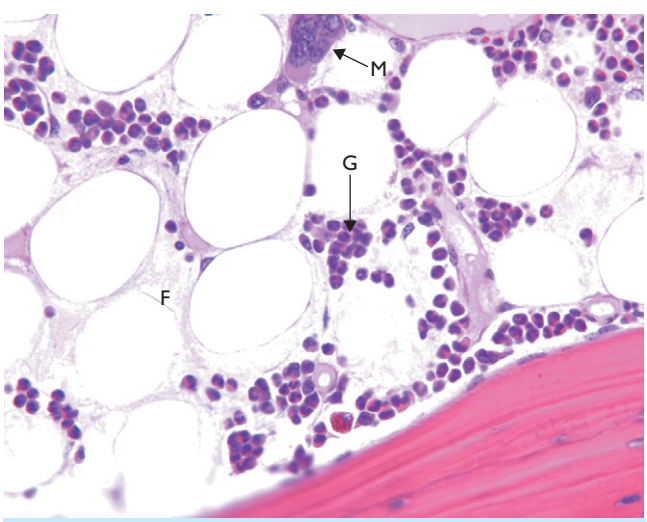


Fig. 44.11
Histologic preparation of a bone marrow biopsy taken from the sternum of a horse with rhEPO-induced pure red cell aplasia (PCV 5%). The bone marrow appears hypocellular. Cells of the granulocytic series (G), megakaryocytes (M), and fat (F), but no cells of the erythroid series are present.

Fig. 44.12
Diaphyseal bone marrow of the tibia in a horse with rhEPO-induced pure red cell aplasia. The yellow fatty appearance of the marrow indicates absence of hematopoietic tissue. Although this would be expected for diaphyseal marrow in normal horses, there should be a hematopoietic response given this horse's severe anemia (PCV 5%).

results vary considerably between different assays, possibly due to interference by anti-EPO antibodies.[178]

Clonogenic assays can be performed to determine whether the serum of affected horses contains substances inhibiting erythroid development. Positive results suggest presence of anti-rhEPO antibodies.[177] However, currently established methods for specific detection of anti-rhEPO antibodies in horses are not routinely available.

Necropsy examination The bone marrow found on necropsy has a markedly pale appearance, due to the lack of erythropoiesis (Fig. 44.12). Histopathology shows generalized hypocellularity with severe erythroid hypoplasia, normal myeloid series, and adequate numbers of megakaryocytes. There is no evidence of myelophthisic disease. Evidence for hypoxic damage of kidneys, liver, myocardium, and other organs may be present.

Diagnostic confirmation Exclusion of other causes for non-regenerative anemia, together with a history of rhEPO administration, strongly suggest rhEPO-associated anemia.

Therapeutic aims The initial goal of treatment is to provide adequate oxygen-carrying capacity to avoid hypoxic organ damage and sudden death. The second therapeutic aim is suppression of the immune response against erythropoietin.

Therapy Administration of rhEPO should be discontinued immediately. Blood transfusions should be performed when the PCV is below 10% or if signs of severe tissue hypoxia are present (see the section 'Acute blood loss'). Experience has shown that even large volumes of blood transfusions are not able to increase the PCV significantly and persistently, although clinical signs may improve.[178]

Dexamethasone or prednisolone have been used to attempt to suppress the hypothesized immune response that is causing the anemia.[77,178] The dose should be adjusted according to clinical response and considering possible adverse effects. The efficacy of corticosteroid treatment is unknown. In addition to corticosteroids, treatment with immunoglobulins, plasmapheresis, cyclophosphamide, and cyclosporine has been described in humans.[172,175]

Prognosis Erythropoietin-induced anemia may be reversible in some cases after cessation of treatment and decline in circulating anti-rhEPO antibodies.[77,171,176] However, the overall prognosis in horses is guarded. Potential recovery may take several months or years,[172,175] and acute death due to chronic hypoxia and organ failure is possible if the anemia remains untreated.

Etiology and pathophysiology The anemia is most likely the result of production of anti-rhEPO antibodies that cross-react with endogenous erythropoietin and inhibit its effect on bone marrow erythroid precursors.[171,172,175,177,178] Twenty to thirty percent of cats and dogs treated with rhEPO develop anti-rhEPO antibodies.[171,176] The susceptibility for rhEPO-induced anemia and the severity of the anemia seems to vary considerably between individual horses.[178]

Development of anemia is probably dose independent but may require repeated exposure to the antigen.[177] Equine erythrocytes have a long half-life and thus the development of the anemia is slow and clinical signs of anemia may occur with a delay of 2 to 6 months after administration of the drug and onset of the adverse reaction.[177,178,181] The clinical signs result directly from a reduced oxygen-carrying capacity of the blood and related compensatory mechanisms.

Prevention Administration of recombinant human erythropoietin to horses should be strictly avoided.

Other causes of hypoproliferative anemia Other very rare types of hypoproliferative anemia in horses are anemia secondary to organ dysfunction, aplastic anemia, myelophthisic disorders, and myelodysplastic syndromes.

Mild to moderate hypoproliferative anemia can occur in association with chronic renal failure, liver disease, gastrointestinal disease, or chronic endocrine disorders, which suppress hematopoiesis independent of alterations in iron metabolism that characterize anemia of inflammatory disease.[163]

Aplastic anemia is characterized by pancytopenia in peripheral blood, bone marrow panhypoplasia with fatty replacement, and the absence of primary disease processes infiltrating the bone marrow or suppressing hematopoiesis.[38,182] Clinical signs include hemorrhagic diathesis due to severe thrombocytopenia, increased susceptibility to infections due to neutropenia, and non-regenerative anemia.[183] The cause usually remains undetermined.[184–186] An association with administration of phenylbutazone has been suspected, but not conclusively proven, in some cases.[187] The underlying pathophysiologic mechanism of aplastic anemia may be immune-mediated in most cases.[182,186] Infectious agents, drugs, and toxins may also be responsible for development of aplastic anemia.[38]

Myelophthisis is characterized by normo- or hypercellular bone marrow and replacement of normal hematopoietic cells by neoplastic cells[188] or proliferating fibroblasts (myelofibrosis).[189]

Myelodysplastic syndromes are a heterogeneous group of disorders characterized by peripheral cytopenias and

normocellular or hypercellular bone marrow with abnormal morphology.[182,190] Refractory, severe anemia is usually accompanied by leukopenia and thrombocytopenia in variable degrees.

Anemia associated with administration of heparin

A distinct type of apparent anemia in horses cannot be categorized in the classical groups of regenerative and non-regenerative anemias. Anticoagulatory treatment with unfractioned heparin (sodium or calcium heparin) has been reported to decrease hematocrit, hemoglobin concentration, and erythrocyte concentration by as much as 50%.[191–194] This adverse effect of heparin is unique to horses. It is associated with erythrocyte agglutination and is thought to occur secondary to sequestration of the red cell agglutinates in the microcirculation, potentially leading to impairment of microvascular blood flow. The effect is reversible and resolves within 3–4 days of discontinuation of heparin therapy. Similar adverse effects are not encountered with use of low-molecular-weight heparin.[195,196]

Red cell hypervolemia in Standardbred Trotters

- Occurs predominantly in well-performing Standardbred Trotters, mainly stallions and geldings, 5–6 years of age.
- Initially good race horses gradually start to deteriorate in performance, after a long, often successful, racing career.
- Horses diagnosed as having red cell hypervolemia generally show no specific findings upon clinical examination.
- Diagnosis is based on history of impaired performance and determination of the total blood and red cell volume.
- Horses with this condition have an increased red cell volume compared to normovolemic horses of corresponding age and sex.
- Affected horses show decreased resting plasma cortisol concentrations and a decreased response to exogenous ACTH, suggesting a chronic stress syndrome.
- During exercise, these horses have higher pulmonary artery pressure and a higher pulmonary vascular resistance than normovolemic trotters.
- The pulmonary hypertension seen in horses with this condition is speculated to lead to a low-grade pulmonary edema and epistaxis.
- Red cell hypervolemic horses exhibit a more marked hypoxemia during exercise compared to normovolemic horses.
- The treatment is aimed towards eliminating stress factors in the environment and by changing the training regime.

Recognition of disease

History and presenting complaint

Red cell hypervolemia, or 'polycythemia' is reported to be a common finding in Standardbred Trotters in Sweden that are presented with a complaint of impaired performance capacity.[14,197,198] The Standardbred population in Sweden consists mainly of French and American Trotters and a mixture of these bloodlines. Red cell hypervolemia has been diagnosed in Standardbred Trotters both with American and French origin. The condition is mainly found in middle-aged (5–7 years) race horses, predominantly in stallions or geldings, that have recently experienced a gradual decline in performance.[199] The decline in performance is reflected in the marked drop in individual performance index, in earnings, and finishing status.[199] Generally, affected horses have initially been very successful on the race tracks in comparison to the contemporary average population. To enable the horse to remain competitive, trainers often train these horses very hard with a lot of high-speed interval training. A common complaint from trainers of affected horses is that such horses perform well during the major part of the race but are unable to increase speed during the final 400–500 m of the race. Many of these horses also have a history of epistaxis in association with intense exercise.[198,200,201] Another frequent observation by the trainers of these horses is a change in behavior of the horse. From previously having shown no remarkable signs of becoming easily excited before exercise, these horses gradually show more and more signs of apparent anxiety in connection with racing or training, the most common signs described being muscle

Table 44.9 Reference values (mean ± SD) for bodyweight (BW, kg), total red cell (CV/BW, mL/kg), total blood (TBV/BW, mL/kg), plasma (PV/BW, mL/kg) volumes relative to BW, and packed cell volume (PCV, L/L) in different age and sex groups in normally performing Standardbred Trotters

Age (years)	Sex	*n*	BW	CV/BW	TBV/BW	PV/BW	PCV
2		30	416 ± 38	52.2 ± 6.8	102.1 ± 7.6	49.9 ± 3.1	0.510 ± 0.035
3		45	437 ± 40	66.3 ± 8.6	118.0 ± 10.0	51.7 ± 3.4	0.560 ± 0.032
≥ 4	Fillies	45	429 ± 42	68.5 ± 8.3	119.6 ± 10.4	51.2 ± 4.3	0.571 ± 0.030
	Geldings	44	455 ± 39	74.4 ± 6.5	129.4 ± 8.4	55.0 ± 3.3	0.574 ± 0.021
	Colts	41	451 ± 46	79.6 ± 7.3	133.4 ± 9.2	53.7 ± 4.2	0.597 ± 0.026
All	Horses	205	439 ± 43	69.1 ± 11.3	121.5 ± 13.6	52.4 ± 4.1	0.566 ± 0.039

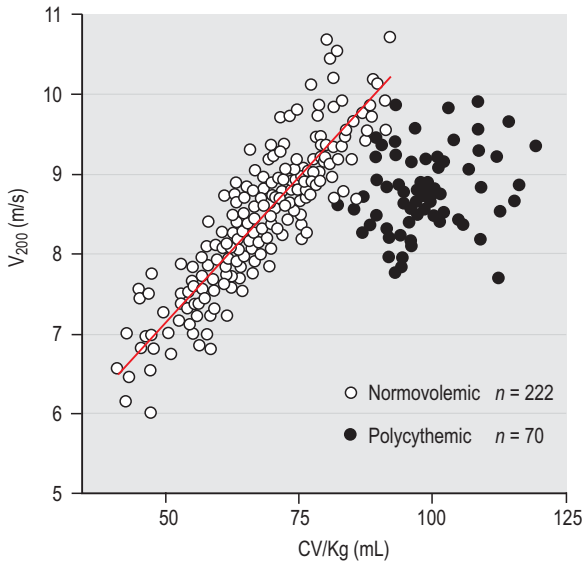


Fig. 44.13
The relationship between speed at a heart rate of 200 bpm (m/s) and the red cell volume in relation to body weight (mL/kg) in normovolemic (○) and polycythemic (●) horses.

tremor, tachycardia, excessive pulling during the race, sweating, and sometimes loose feces.

Physical examination

Generally, horses diagnosed to have red cell hypervolemia show no specific findings upon physical examination but in some cases this condition is associated with other clinical disorders such as small airway disease.[200,202–204] However, as already mentioned, many of these horses appear to be very nervous upon examination and handling.

Special examination

Hematocrit Previous studies have shown that there is a strong relationship between the red cell volume and total hemoglobin concentration and the aerobic metabolic capacity of horses.[14,16,198] Consequently, the estimation of total blood volume and red cell volume is useful in the evaluation of the exercise capacity in horses as well as evaluation of horses with impaired performance.[14,15,202,203,205] Horses with red cell hypervolemia have a significantly increased red cell volume and higher maximal hematocrit in comparison to normovolemic horses of corresponding age and sex.[14,206] One screening method to determine if a horse suffers from red cell hypervolemia is to measure the maximal hematocrit after exercise. The easiest way to do this is by having the horse exercise at a level that induces a pulse rate that exceeds 200 bpm, which induces a complete emptying of the splenic red cell reservoir.[14,198] This is preferably done on a track using a heart rate meter to assess the heart rate during exercise. The blood sample for measurement of hematocrit should be collected within 1 min of the end of exercise.[207] The measured hematocrit could then be compared to the hematocrit values from horses of the same age and sex. If the horse has a maximal hematocrit above 2 standard deviations of what is expected considering its age and sex, the horse can be suspected to have red cell hypervolemia. If, on the above screening testing, the horse is shown to have a high hematocrit value suggesting red cell hypervolemia then the total red cell volume and total blood volume should be determined to confirm the diagnosis. This is done using the Evans Blue dye dilution technique to measure plasma volume, and determination of the maximal hematocrit after exercise, which then allows calculation of the total blood volume and red cell volume.[14,207]

Red cell volume To standardize the exercise conditions, the exercise test is often done on a treadmill. The horse performs a standardized submaximal incremental exercise test on an inclined (3.6° [6.25%]) treadmill.[14,198] During the standardized submaximal exercise test the heart rate is recorded and mixed-venous blood samples are drawn at the end of each speed step. The blood samples are then analyzed for the concentration of blood lactate. This makes it possible to calculate the individual values for $\dot{V}La_4$ and $\dot{V}_{200}$. Red cell hypervolemic horses have an abnormally high heart rate in relation to their red cell volume during submaximal exercise. [14,198] Despite this, the values for $\dot{V}_{200}$ do not seem to differ between red cell hypervolemic and normovolemic horses during submaximal exercise.[208,209] However, nothing is known about the relationship between pulse rate and red cell volume during intensive exercise to fatigue in red cell hypervolemic horses. Red cell hypervolemic horses also have a tendency to have lower blood lactate concentrations immediately postexercise than normovolemic horses.[205] The clinical impression is also that horses with red cell hypervolemia tend to reach the lactate threshold of 4 mmol/L later during exercise than well-trained normovolemic horses. There is, however, no scientific evidence to support this opinion.

Endoscopy Endoscopy of the respiratory tract within 90 min of performing the submaximal exercise test often reveals blood in the trachea in these horses. Although the prevalence of EIPH after racing is reported to be lower in Standardbred Trotters (23–45%) than in Thoroughbreds (over 90%), there are indications that Standardbred Trotters with red cell hypervolemia have an increased incidence of exercise-induced pulmonary hemorrhage (EIPH) (92%) than normovolemic Standardbred Trotters[198,201,210,211] (Adehed & Funkquist, unpublished data). The reason for this increased incidence of EIPH may be related to stress failure of the capillary endothelial layers.[201,212]

Laboratory examination

Bronchoalveolar lavage often reveals hemosiderophages, which is interpreted as evidence of previous EIPH, but is a common finding in almost all actively racing horses.[213–215] Consequently these horses frequently exhibit hemosiderosis on bronchoalveolar lavage.[201] The clinical impression is also that some horses with red cell hypervolemia have signs of a subclinical bronchiolitis on bronchoalveolar lavage.

Histochemical analysis of muscle biopsies collected from the gluteus medius muscle from horses with red cell hypervolemia reveals that the muscle fiber composition and fiber area do not differ from normovolemic horses.[216,217] However, a higher percentage of type IIB fibers shows a high oxidative capacity on the NADH-stain than in normovolemic horses.[216] A recent study using the immunohistochemical technique has shown that horses with red cell hypervolemia express less of the isoform of myosin heavy-chain MHCIIX in comparison to well-trained normovolemic horses.[218] There are three different isoforms of myosin heavy chains (MHC) MHCI, MHCIIA, MHCIIX, and the oxidative capacity is highest in the type I and lowest in the type IIX fibers. Training has been shown to cause a transformation of IIX to IIA fibers.

Measurement of maximal hematocrit, as well as determination of the total blood volume, are common methods used in clinical practice to diagnose this condition. However, research on red cell hypervolemic horses have shown that they have an altered physiological response to exercise in comparison to normovolemic horses. The methods used in research are often too complicated or too expensive to be used in practice. However, research on horses with this condition has shown that:

- Red cell hypervolemic horses appear to have an adrenocortical malfunction with decreased resting plasma cortisol concentrations and a decreased response to exogenous ACTH.[197]
- During exercise, red cell hypervolemic horses have higher pulmonary artery pressure (PAP) and systemic artery pressure (SAP) than normovolemic Trotters and also a higher pulmonary vascular resistance.[200] There is also an increasing difference in vascular resistance between hypervolemic and normovolemic horses as exercise intensity increases.
- Red cell hypervolemic horses have a more marked hypoxemia during exercise in comparison to normovolemic horses.[202,204] This is mainly a result of an increase in inequality of the ventilation–perfusion distribution ($\dot{V}_A/\dot{Q}$). This has been found in studies using the multiple inert gas elimination technique described by Wagner et al.[219–221] The mismatch in $\dot{V}_A/\dot{Q}$ is likely caused by a mild interstitial pulmonary edema that occurs as a result of an increased fluid transudation secondary to the pulmonary hypertension.[212,222]
- Unpublished data indicate that blood viscosity is higher in red cell hypervolemic horses than in normovolemic horses (P. Funkquist, unpublished data: 6.67 ± 0.37 mPa × s, range 6.27–7.19, at maximal exercise to fatigue).
- Horses with red cell hypervolemia have also been found to have a lower capillary supply in muscle compared to well-trained, normovolemic horses.[209] Moreover, the activities of muscle enzymes such as citrate synthase (CS), lactate dehydrogenase (LDH), or 3-hydroxy acyl CoA dehydrogenase (HAD) in horses with this condition are unaltered in comparison to normovolemic horses.[208,209,216,217]

Necropsy examination

Generally, horses with red cell hypervolemia are not euthanized so little is known regarding specific findings on necropsy.

Diagnostic confirmation

Differential diagnoses to red cell hypervolemia are other clinical disorders that cause an impaired performance capacity in horses that have previously performed well. As red cell hypervolemia can sometimes be secondary to other diseases, such as small airway disease or myocardial disease causing hypoxia, it is important to eliminate these disorders as a cause of the increase in red cell volume. The diagnosis of red cell hypervolemia is confirmed by the finding of abnormally high total blood volume and maximal hematocrit values in a horse without any other clinical findings that could explain the onset of poor performance.

Treatment and prognosis

Therapeutic aims

Occasionally, the red cell hypervolemia is associated with another clinical disorder,[203,223] for instance chronic small airway disease, that could be the primary cause for the development of an increased production of erythrocytes. The therapy is thus directed towards treating the primary disorder. However, many horses diagnosed with red cell hypervolemia have no detectable underlying disease as an explanation for the development of this condition. The pathophysiology behind red cell hypervolemia is incompletely understood but there are indications that these horses could suffer from a chronic stress syndrome.[197] The therapeutic aim is therefore oriented towards diminishing the stress factors for the horse. Excessive training is thought to be an important reason for the development of red cell hypervolemia and consequently an alteration in training regimen is often indicated.

Therapy

Alterations in training regimens Despite some minor differences in training regimens between different trainers, Standardbred Trotters in Sweden are trained in a similar manner. The normal training regimens for a Standardbred Trotter often consist of 2 or 3 days of interval training (6–7 intervals) on a straight or round course for 600–700 m. The last interval is often performed at near to, or maximal speed; the speed is dependent on the age and training status of the horse. Between the days of interval training there are often 1 or 2 days of slow aerobic exercise (driven or ridden), and 2 days of rest in the paddock. Horses with red cell hypervolemia often have a history of very intense training with a lot of interval training at high speed. It is recommended that horses with red cell hypervolemia rest completely from training for a period of 3–6 months, depending on the severity of the condition. However, some trainers choose to continue the training without any resting period as they find it difficult to

get these horses back in condition again. After the initial period of rest, training intensity should be reduced by leaving out the interval training and using races as speed training. An additional recommendation is also to reduce the frequency of racing and to choose races with a less intense competition.

It is also recommended to move these horses from busy large training camps to smaller and quieter stables. All these recommendations are given with the purpose to reduce the stress connected with training and stabling for these horses.

Phlebotomy There is evidence that phlebotomy of horses with red cell hypervolemia decreases both the maximal hematocrit as well as maximal hemoglobin concentration.[201] Phlebotomy also decreases the pulmonary artery blood pressure, blood viscosity, and incidence of pulmonary hemorrhage. The duration of this effect has not been determined. In the study by Funkquist et al[201] the run time to fatigue during submaximal exercise on a treadmill was decreased by phlebotomy. Conversely, clinical experience suggests that phlebotomy could have a positive effect on performance. However, the study by Funkquist and colleagues found that the plasma volume was not restored after phlebotomy. This could be one explanation for the decrease seen in performance after phlebotomy.

Castration The prevalence of red cell hypervolemia is higher in stallions compared to mares. This may be because stallions have been shown to have a larger red cell volume and total blood volume in relation to bodyweight than both mares and geldings, probably due to the erythropoietic effect of testosterone.[14] Thus one therapeutic method that has been used in stallions in order to decrease the erythrocyte production is castration. However, no studies regarding the effect of castration on the red cell volume support castration as a treatment for horses with this condition.

Prognosis

Although a slight improvement can be seen after a longer period of rest and alterations in training regimes, there are indications that horses with red cell hypervolemia seldom reach their previous racing capacity.[199] Thus it is common for red cell hypervolemia to denote the end of a successful racing career.

Prevention

As the pathophysiology of red cell hypervolemia is unclear, it is difficult to give recommendations for prevention of this condition. Given that these horses often have a history of a long period of intensive training before the development of the condition, and show signs of chronic physical and environmental stress, it is likely that they have reached their genetic limit of performance. The prevention of excessive training could be a factor of importance in trying to prevent the condition from occurring. However, as there is a great genetic variability in the exercise capacity of individual horses, it is difficult to determine when the training is overly intense. Further studies are needed to find different markers for this.

Etiology and pathophysiology

The exact cause of the development of red cell hypervolemia is still unclear. The prolonged and excessive training is, however, thought to be an important factor for the development of this condition. Red cell hypervolemia is likely a result of a decreased peripheral oxygen utilization, either depending on a peripheral circulatory insufficiency and tissue hypoxia during intensive exercise or a decreased oxygen uptake by the muscle cell.[14,197] The former has similarities to a condition called vasoregulatory asthenia, which is seen in man after excessive physical training.[224] The decreased uptake of oxygen could be a result of a reduced diffusion of oxygen to mitochondria. The hypoxia is thought to cause a compensatory increase in plasma erythropoietin that results in an absolute secondary erythrocytosis. The mobilization of red blood cells from the spleen during exercise has been reported to contribute to the exercise-induced hypoxemia seen in normal horses during exercise.[202] In horses with red cell hypervolemia this hypoxia is likely exaggerated because of an increase in blood viscosity, a higher pulmonary vascular resistance and an inequality in ventilation–perfusion distribution. Little is known about the plasma erythropoietin concentrations in horses with red cell hypervolemia and further studies are needed to establish if horses with this condition show alterations in the concentrations of plasma erythropoietin in comparison to normovolemic horses.

References

1. Marino PL. Erythrocyte transfusions. In: Marino PL, ed. The ICU book, 2nd edn. Philadelphia: Lippincott Williams and Wilkins; 1998:691–708.
2. Aird B. Clinical and hematologic manifestations of anemia. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:140–142.
3. Mellema M. Cardiac output, wedge pressure, and oxygen delivery. Vet Clin North Am: Small Anim Pract 2001; 31(6):1175–1205.
4. Marino PL. Respiratory gas transport. In: Marino PL, ed. The ICU book, 2nd edn. Philadelphia: Lippincott Williams and Wilkins; 1998:19–31.
5. Guyton AC, Hall JE. Transport of oxygen and carbon dioxide in the blood and body fluids. In: Guyton AC, Hall JE, eds. Textbook of medical physiology, 10th edn. Philadelphia: WB Saunders; 2000:463–473.
6. Guyton AC, Hall JE. Red blood cells, anemia, and polycythemia. In: Guyton AC, Hall JE, eds. Textbook of medical physiology, 10th edn. Philadelphia: WB Saunders; 2000:382–391.
7. Guyton AC, Hall JE. Overview of the circulation: medical physics of pressure, flow, and resistance. In: Guyton AC, Hall JE, eds. Textbook of medical physiology, 10th edn. Philadelphia: WB Saunders; 2000:144–151.
8. Guyton AC, Hall JE. Local control of blood flow by the tissues; and humoral regulation. In: Guyton AC, Hall JE, eds. Textbook of medical physiology, 10th edn. Philadelphia: WB Saunders; 2000:175–183.

9. Guyton AC, Hall JE. Cardiac output, venous return, and their regulation. In: Guyton AC, Hall JE, eds. Textbook of medical physiology, 10th edn. Philadelphia: WB Saunders; 2000:210–222.
10. Meyer R. Current topics in fluid therapy: oxyglobin. In: Gleed RD, Ludders JW, eds. Recent advances in veterinary anesthesia and analgesia: companion animals. Ithaca, NY: International Veterinary Information Service; 2001:online. available: www.ivis.org; Document No. A1407.0501
11. Rentko VT, Sharpe TA. Red blood cell substitutes. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:874–878.
12. Moore KE, Murtaugh RJ. Pathophysiologic characteristics of hypovolemic shock. Vet Clin North Am: Small Anim Pract 2001; 31(6):1115–1128.
13. Kumar A, Parrillo JE. Shock: Classification, pathophysiology, and approach to management. In: Parrillo JE, Dellinger RP, eds. Critical care medicine: principles of diagnosis and management in the adult, 2nd edn. St Louis: Mosby; 2001:371–420.
14. Persson S. On blood volume and working capacity in horses: studies of methodology and physiological and pathological variations. Acta Vet Scand 1967; Suppl 19:1–189.
15. Persson SGB. Blood volume, state of training and working capacity of race horses. Equine Vet J 1968; 1:52–62.
16. Persson SG. Heart rate and blood lactate responses to submaximal treadmill exercise in the normally performing standardbred trotter – age and sex variations and predictability from the total red blood cell volume. Zentralbl Veterinarmed A 1997; 44(3):125–132.
17. Lassen ED, Swardson CJ. Hematology and hemostasis in the horse: normal functions and common abnormalities. Vet Clin North Am: Equine Pract 1995; 11(3):351–389.
18. Tvedten H, Weiss DJ. Classification and laboratory evaluation of anemia. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:143–150.
19. Radin MJ, Eubank MC, Weiser MG. Electronic measurement of erythrocyte volume and volume heterogeneity in horses during erythrocyte regeneration associated with experimental anemias. Vet Pathol 1986; 23(6):656–660.
20. Smith JE, Agar NS. Studies on erythrocyte metabolism following acute blood loss in the horse. Equine Vet J 1976; 8(1):34–37.
21. Mair TS, Taylor FG, Hillyer MH. Autoimmune haemolytic anaemia in eight horses. Vet Rec 1990; 126(3):51–53.
22. Weiser MG. Erythrocyte volume distribution analysis in healthy dogs, cats, horses, and dairy cows. Am J Vet Res 1982; 43(1):163–166.
23. Easley JR. Erythrogram and red cell distribution width of Equidae with experimentally induced anemia. Am J Vet Res 1985; 46(11):2378–2384.
24. Lumsden JH, Valli VE, McSherry BJ, et al. The kinetics of hematopoiesis in the light horse II. The hematological response to hemorrhagic anemia. Can J Comp Med 1975; 39(3):324–331.
25. Lumsden HJ, Valli VE, McSherry BJ, et al. The kinetics of hematopoiesis in the light horse III. The hematological response to hemolytic anemia. Can J Comp Med 1975; 39(3):332–339.
26. Fernandez FR, Grindem CB. Reticulocyte response. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:110–116.
27. Weiser G, Kohn C, Vachon A. Erythrocyte volume distribution analysis and hematologic changes in two horses with immune-mediated hemolytic anemia. Vet Pathol 1983; 20(4):424–433.
28. Latimer KS, Rakich PM. Peripheral blood smears. In: Cowell RL, Tyler RD, eds. Diagnostic cytology and hematology of the horse, 2nd edn. St Louis: Mosby; 2002:200–216.
29. Barker RN. Anemia associated with immune response. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:169–177.
30. Day MJ. Immune-mediated hemolytic anemia. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:799–806.
31. Malikides N, Kessell A, Hodgson JL, et al. Bone marrow response to large volume blood collection in the horse. Res Vet Sci 1999; 67(3):285–293.
32. Freeman KP. Bone marrow evaluation. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:29–32.
33. Russell KE, Sellon DC, Grindem CB. Bone marrow in horses: indications, sample handling, and complications. Compend Contin Educ Pract Vet 1994; 16(10):1359–1365.
34. Taylor FGR, Hillyer MH. Blood disorders. In: Taylor FGR, Hillyer MH, eds. Diagnostic techniques in equine medicine. London: WB Saunders; 1997:137–158.
35. Latimer KS, Andreasen CB. Bone marrow. In: Cowell RL, Tyler RD, eds. Diagnostic cytology and hematology of the horse, 2nd edn. St Louis: Mosby; 2002:217–226.
36. Steiger R, Geyer H, Provencher A, et al. Equine bone core biopsy: evaluation of collection sites using a new electric drilling machine. Equine Prac 1999; 21(7):14–21.
37. Waner T, Harrus S. Anemia of inflammatory disease. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:205–209.
38. Weiss DJ. Aplastic anemia. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:212–215.
39. Tschudi P, Archer RK, Gerber H. The cells of equine blood and their development. Equine Vet J 1975; 7(3):141–147.
40. Franken P, Wensing T, Schotman AJH. The bone-marrow of the horse I. The techniques of sampling and examination and values of normal warm-blooded horses. Zentralbl Veterinarmed A 1982; 29(1):16–22.
41. Franken P, Wensing T, Schotman AJH. The bone-marrow of the horse II. Warm-blooded horses with anemia. Zentralbl Veterinarmed A 1982; 29(1):23–27.
42. Schalm OW. Bone marrow erythroid cytology in anemias of the horse. In: Kitchen H, Krehbiel JD, eds. First international symposium on equine hematology. Michigan State University; 1975:17–25.
43. Schalm OW. Equine hematology: Part IV – erythroid marrow cytology in response to anemia. Equine Prac 1980; 2(5):35–40.
44. Tablin F, Weiss L. Equine bone marrow: a quantitative analysis of erythroid maturation. Anat Rec 1985; 213(Oct):202–206.
45. Tschudi P, Archer RK, Gerber H. Cytochemical staining of equine blood and bone marrow cells. Equine Vet J 1977; 9:205–207.
46. Messer NT, Arnold K. Immune-mediated hemolytic anemia in a horse. J Am Vet Med Assoc 1991; 198(8):1415–1416.
47. Harvey JW. Microcytic anemias. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn.

Philadelphia: Lippincott Williams and Wilkins; 2000:200–204.
48. Carlson G. A survey of the iron status of thoroughbred horses in race training. In: Proceedings of the 10th annual ACVIM forum. San Diego: American College of Veterinary Internal Medicine; 1992:448–449.
49. Carlson G. Clinical chemistry tests. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:389–412.
50. Schott II HC, Van Metre DC, Divers TJ. Diseases of the renal system. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:824–872.
51. Pearson EG. Diseases of the hepatobiliary system. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:790–823.
52. Klein HG, Higgins MJ. Use of blood components in the intensive care unit. In: Parrillo JE, Dellinger RP, eds. Critical care medicine: principles of diagnosis and management in the adult, 2nd edn. St Louis: Mosby; 2001:1416–1438.
53. Andrews GA, Smith JE. Iron metabolism. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:129–134.
54. Geor RJ, Weiss DJ. Drugs affecting the hematologic system of the performance horse. Vet Clin North Am Equine Pract 1993; 9(3):649–667.
55. Smith JE, Cipriano JE, DeBowes R, et al. Iron deficiency and pseudo-iron deficiency in hospitalized horses. J Am Vet Med Assoc 1986; 188(3):285–287.
56. Smith JE, Moore K, Cipriano JE, et al. Serum ferritin as a measure of stored iron in horses. J Nutr 1984; 114(4):677–681.
57. Smith JE, Cipriano JE. Inflammation-induced changes in serum iron analytes and ceruloplasmin of Shetland ponies. Vet Pathol 1987; 24(4):354–356.
58. Franken P, Wensing T, Schotman AJ. The concentration of iron in the liver, spleen and plasma, and the amount of iron in bone marrow of horses. Zentralbl Veterinarmed A 1981; 28:381–389.
59. Mills PC, Marlin DJ. Plasma iron in elite horses at rest and after transport. Vet Rec 1996; 139(9):215–217.
60. Kaneko JJ, Harvey JW, Bruss ML. Blood analyte reference values in large animals. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. San Diego: Academic Press; 1997:890–894.
61. Osbaldiston GW, Griffith PR. Serum iron levels in normal and anemic horses. Can Vet J 1972; 13:105–108.
62. Kohn CW, Jacobs RM, Knight D, et al. Microcytosis, hypoferremia, hypoferritemia, and hypertransferrinemia in standardbred foals from birth to 4 months of age. Am J Vet Res 1990; 51(8):1198–1205.
63. Suttle N, Small J, Jones D. Overestimation of copper deficiency in horses? Vet Rec 1995; 136(5):131.
64. Auer DE, Ng JC, Seawright AA. Assessment of copper and zinc status of farm horses and training thoroughbreds in south-east Queensland. Aust Vet J 1988; 65(10):317–320.
65. Cymbaluk NF, Bristol FM, Christensen DA. Influence of age and breed of equid on plasma copper and zinc concentrations. Am J Vet Res 1986; 47(1):192–195.
66. Stubley D, Campbell C, Dant C, et al. Copper and zinc levels in the blood of thoroughbreds in training in the United Kingdom. Equine Vet J 1983; 15(3):253–256.
67. Mee JF, McLaughlin J. 'Normal' blood copper levels in horses. Vet Rec 1995; 136(11):275.
68. Suttle NF, Small JN, Collins EA, et al. Serum and hepatic copper concentrations used to define normal, marginal and deficient copper status in horses. Equine Vet J 1996; 28(6):497–499.
69. Pearce SG, Grace ND, Firth EC, et al. Effect of copper supplementation on the copper status of pasture-fed young thoroughbreds. Equine Vet J 1998; 30(3):204–210.
70. Pearce SG, Firth EC, Grace ND, et al. Liver biopsy techniques for adult horses and neonatal foals to assess copper status. Aust Vet J 1997; 75(3):194–198.
71. Radostits OM, Gay CC, Blood DC, et al. Diseases caused by nutritional deficiencies. In: Radostits OM, Gay CC, Blood DC, et al., eds. Veterinary medicine: a textbook of the diseases of cattle, sheep, pigs, goats and horses. London: WB Saunders; 2000:1477–1560.
72. Okumura M, Fujinaga T, Yamashita K, et al. Isolation, characterization, and quantitative analysis of ceruloplasmin from horses. Am J Vet Res 1991; 52(12): 1979–1985.
73. Colahan PT, Bailey JE, Johnson M, et al. Effect of sulfadiazine and pyrimethamine on selected physiologic and performance parameters in athletically conditioned thoroughbred horses during an incremental exercise stress test. Vet Ther 2002; 3(1):49–63.
74. Allen BV. Serum folate levels in horses, with particular reference to the English thoroughbred. Vet Rec 1978; 103(12):257–259.
75. Seckington IM, Huntsman RG, Jenkins GC. The serum folic acid levels of grass-fed and stabled horses. Vet Rec 1967; 81:158–161.
76. Roberts MC. Serum and red cell folate and serum vitamin B12 levels in horses. Aust Vet J 1983; 60(4):106–111.
77. Piercy RJ, Hinchcliff KW, Reed SM. Folate deficiency during treatment with orally administered folic acid, sulphadiazine and pyrimethamine in a horse with suspected equine protozoal myeloencephalitis (EPM). Equine Vet J 2002; 34(3):311–316.
78. Aird B. Acute blood loss anemia. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:151–153.
79. Moore RM. Pathophysiology of circulatory shock. In: Colahan PT, Merritt AM, Moore JN, et al., eds. Equine medicine and surgery, 5th edn. St Louis: Mosby; 1999:210–218.
80. Jeffrey SC. Managing hemoperitoneum in horses. Equine Prac 1996; 91(9):850–856.
81. Edens LM. Abdominal hemorrhage. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia: WB Saunders; 1997:211–214.
82. Morris DD. Diseases associated with blood loss or hemostatic dysfunction. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1039–1048.
83. McCarthy PF, Hooper RN, Carter GK, et al. Postparturient hemorrhage in the mare: managing ruptured arteries of the broad ligament. Equine Prac 1994; 89(2):147–152.
84. Collatos C. Blood loss anemia. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia: WB Saunders; 1997:276–277.
85. Muir WW. Small volume resuscitation using hypertonic saline. Cornell Vet 1990; 80(1):7–12.
86. Schmall LM, Muir WW, Robertson JT. Haemodynamic effects of small volume hypertonic saline in experimentally induced haemorrhagic shock. Equine Vet J 1990; 22(4):273–277.
87. Schmall LM, Muir WW, Robertson JT. Haematological, serum electrolyte and blood gas effects of small volume hypertonic saline in experimentally induced haemorrhagic shock. Equine Vet J 1990; 22(4):278–283.

88. Hermann M, Bretscher R, Thiebaud G, et al. [Preliminary experiences with the treatment of shock in horses with a plasma expander from a starch base]. Schweiz Arch Tierheilkd 1990; 132(1):5–12.
89. Jones PA, Bain FT, Byars TD, et al. Effect of hydroxyethyl starch infusion on colloid oncotic pressure in hypoproteinemic horses. J Am Vet Med Assoc 2001; 218(7):1130–1135.
90. Jones PA, Tomasic M, Gentry PA. Oncotic, hemodilutional, and hemostatic effects of isotonic saline and hydroxyethyl starch solutions in clinically normal ponies. Am J Vet Res 1997; 58(5):541–548.
91. Rudloff E, Kirby R. The critical need for colloids: administering colloids effectively. Compend Contin Educ Pract Vet 1997; 20(1):27–43.
92. Rudloff E, Kirby R. The critical need for colloids: selecting the right colloid. Compend Contin Educ Pract Vet 1997; 19(7):811–825.
93. Capone AC, Safar P, Stezoski W, et al. Improved outcome with fluid restriction in treatment of uncontrolled hemorrhagic shock. J Am Coll Surg 1995; 180(1):49–56.
94. Stern SA. Low-volume fluid resuscitation for presumed hemorrhagic shock: helpful or harmful? Curr Opin Crit Care 2001; 7(6):422–430.
95. Roberts SJ. The effects of various intravenous injections on the horse. Am J Vet Res 1943; 4(12):226–239.
96. Jones W. IV formalin to control hemorrhage. J Equine Vet Sci 1998; 18(9):581.
97. Taylor EL, Sellon DC, Wardrop KJ, et al. Effects of intravenous administration of formaldehyde on platelet and coagulation variables in healthy horses. Am J Vet Res 2000; 61(10):1191–1196.
98. Maxson AD, Giger U, Sweeney CR, et al. Use of a bovine hemoglobin preparation in the treatment of cyclic ovarian hemorrhage in a miniature horse. J Am Vet Med Assoc 1993; 203(9):1308–1311.
99. Belgrave RL, Hines MT, Keegan RD, et al. Effects of a polymerized ultrapurified bovine hemoglobin blood substitute administered to ponies with normovolemic anemia. J Vet Intern Med 2002; 16(4):396–403.
100. Collatos C. Blood and blood component treatment. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia: WB Saunders; 1997:290–292.
101. Divers TJ. Liver failure and hemolytic anemia. In: Orsini JA, Divers TJ, eds. Manual of equine emergencies, 2nd edn. Philadelphia: WB Saunders; 2003:315–338.
102. Hohenhaus AE. Oxyglobin: a transfusion solution? J Vet Intern Med 2002; 16(4):394–395.
103. Morris DD. Review of anemia in horses. Part II: pathophysiologic mechanisms, specific diseases and treatment. Equine Prac 1989; 11(5):34–46.
104. Sellon DC. Equine infectious anemia. Vet Clin North Am: Equine Pract 1993; 9(2):321–336.
105. Coggins L, Auchnie JA. Control of equine infectious anemia in horses in Hong Kong. J Am Vet Med Assoc 1977; 170(11):1299–1301.
106. Anonymous. OIE classification of disease. Paris: World Organization for Animal Health (OIE); 2002:Online. Available: www.oie.int/eng/maladies/en_classification.htm
107. Carlson G. Equine infectious anemia. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1056–1058.
108. Sellon DC. Hemolytic anemia. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia: WB Saunders; 1997:278–282.
109. Sellon DC. Coggins positive: an owner's nightmare. In: Proceedings of the 14th ACVIM Forum. St. Antonio: American College of Veterinary Internal Medicine; 1996:413–415.
110. Anonymous. Manual of standards for diagnostic tests and vaccines, 4th edn. Paris: World Organization for Animal Health (OIE); 2000.
111. McGuire TC, Henson JB, Quist SE. Impaired bone marrow response in equine infectious anemia. Am J Vet Res 1969; 30:2099–2104.
112. Sellon DC, Perry ST, Coggins L, et al. Wild-type equine infectious anemia virus replicates in vivo predominantly in tissue macrophages, not in peripheral blood monocytes. J Virol 1992; 66(10):5906–5913.
113. Swardson CJ, Lichtenstein DL, Wang S, et al. Infection of bone marrow macrophages by equine infectious anemia virus. Am J Vet Res 1997; 58:1402–1407.
114. Issel CJ, Foil LD. Studies on equine infectious anemia virus transmission by insects. J Am Vet Med Assoc 1984; 184(3):293–297.
115. Tashjian RJ. Transmission and clinical evaluation of an equine infectious anemia herd and their offspring over a 13-year period. J Am Vet Med Assoc 1984; 184(3):282–288.
116. Swardson CJ, Kociba GJ, Perryman LE. Effects of equine infectious anemia virus on hematopoietic progenitors in vitro. Am J Vet Res 1992; 53(7):1176–1179.
117. De Waal DT. Equine piroplasmosis: a review. Br Vet J 1992; 148(1):6–14.
118. Knowles D, Jr. Equine babesiosis (piroplasmosis): a problem in the international movement of horses. Br Vet J 1996; 152(2):123–126.
119. Bruning A. Equine piroplasmosis an update on diagnosis, treatment and prevention. Br Vet J 1996; 152(2):139–151.
120. Friedhoff KT, Soule C. An account on equine babesioses. Rev Sci Tech 1996; 15(3):1191–1201.
121. Gaunt SD. Hemolytic anemias caused by blood rickettsial agents and protozoa. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:154–162.
122. Böse R, Jorgensen WK, Dalgliesh RJ, et al. Current state and future trends in the diagnosis of babesiosis. Vet Parasitol 1995; 57(1–3):61–74.
123. Mattia AR, Waldron MA, Sierra LS. Use of the quantitative Buffy Coat system for detection of parasitemia in patients with babesiosis. J Clin Microbiol 1993; 31(10):2816–2818.
124. Sahagun-Ruiz A, Waghela SD, Holman PJ, et al. Biotin-labeled DNA probe in a PCR-based assay increases detection sensitivity for the equine hemoparasite *Babesia caballi*. Vet Parasitol 1997; 73(1–2):53–63.
125. Holman PJ, Hietala SK, Kayashima LR, et al. Case report: field-acquired subclinical *Babesia equi* infection confirmed by in vitro culture. J Clin Microbiol 1997; 35(2):474–476.
126. Nicolaiewsky TB, Richter MF, Lunge VR, et al. Detection of *Babesia equi* (Laveran, 1901) by nested polymerase chain reaction. Vet Parasitol 2001; 101(1):9–21.
127. Böse R, Peymann B. Diagnosis of *Babesia caballi* infections in horses by enzyme-linked immunosorbent assay (ELISA) and western blot. Int J Parasitol 1994; 24(3):341–346.
128. Weiland G. Species-specific serodiagnosis of equine piroplasma infections by means of complement fixation test (CFT), immunofluorescence (IIF), and enzyme-linked immunosorbent assay (ELISA). Vet Parasitol 1986; 20(1–3):43–48.
129. Tenter AM, Friedhoff KT. Serodiagnosis of experimental and natural *Babesia* equi and *B. caballi* infections. Vet Parasitol 1986; 20(1–3):49–61.
130. Belloli C, Crescenzo G, Lai O, et al. Pharmacokinetics of imidocarb dipropionate in horses after intramuscular administration. Equine Vet J 2002; 34(6):625–629.

131. Zaugg JL. Babesiosis. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1051–1055.
132. Zaugg JL, Lane VM. Efficacy of buparvaquone as a therapeutic and clearing agent of *Babesia equi* of European origin in horses. Am J Vet Res 1992; 53(8):1396–1399.
133. Homer MJ, Aguilar-Delfin I, Telford SR III et al. Babesiosis. Clin Microbiol Rev 2000; 13(3):451–469.
134. Carlson GP. Autoimmune hemolytic anemia. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1058–1059.
135. Reef VB, Dyson SS, Beech J. Lymphosarcoma and associated immune-mediated hemolytic anemia and thrombocytopenia in horses. J Am Vet Med Assoc 1984; 184(3):313–317.
136. Lubas G, Ciattini F, Gavazza A. Immune-mediated thrombocytopenia and hemolytic anemia (Evans' syndrome) in a horse. Equine Prac 1997; 19(4):27–32.
137. Davis EG, Wilkerson MJ, Rush BR. Flow cytometry: clinical applications in equine medicine. J Vet Intern Med 2002; 16(4):404–410.
138. Wilkerson MJ, Davis E, Shuman W, et al. Isotype-specific antibodies in horses and dogs with immune-mediated hemolytic anemia. J Vet Intern Med 2000; 14(2):190–196.
139. McConnico RS, Roberts MC, Tompkins M. Penicillin-induced immune-mediated hemolytic anemia in a horse. J Am Vet Med Assoc 1992; 201(9):1402–1403.
140. Step DL, Blue JT, Dill SG. Penicillin-induced hemolytic anemia and acute hepatic failure following treatment of tetanus in a horse. Cornell Vet 1991; 81(1):13–18.
141. Blue JT, Dinsmore RP, Anderson KL. Immune-mediated hemolytic anemia induced by penicillin in horses. Cornell Vet 1987; 77(3):263–276.
142. Tizard IR. Drugs and other agents that affect the immune system. In: Tizard IR, ed. Veterinary immunology – An introduction, 6th edn. Philadelphia: WB Saunders; 2000:426–433.
143. Jeanes LV, Magdesian KG, Madigan JE, et al. Clostridial myositis in horses. Compend Contin Educ Pract Vet 2001; 23(6):577–587.
144. Stevens DL, Maier KA, Laine BM, et al. Comparison of clindamycin, rifampin, tetracycline, metronidazole, and penicillin for efficacy in prevention of experimental gas gangrene due to *Clostridium perfringens*. J Infect Dis 1987; 155(2):220–228.
145. Stevens DL, Maier KA, Mitten JE. Effect of antibiotics on toxin production and viability of *Clostridium perfringens*. Antimicrob Agents Chemother 1987; 31(2):213–218.
146. Vin R, Bedenice D, Rentko VT, et al. The use of ultrapurified bovine hemoglobin solution in the treatment of two cases of presumed red maple toxicosis in a miniature horse and a pony. J Vet Emerg Crit Care 2002; 12(3):169–175.
147. Mullon J, Giacoppe G, Clagett C, et al. Transfusions of polymerized bovine hemoglobin in a patient with severe autoimmune hemolytic anemia. N Engl J Med 2000; 342(22):1638–1643.
148. Beck DJ. A case of primary autoimmune haemolytic anaemia in a pony. Equine Vet J 1990; 22(4):292–294.
149. Reef VB. *Clostridium perfringens* cellulitis and immune-mediated hemolytic anemia in a horse. J Am Vet Med Assoc 1983; 182(3):251–254.
150. Hübl W, Mostbeck B, Hartleb H, et al. Investigation of the pathogenesis of massive hemolysis in a case of *Clostridium perfringens* septicemia. Ann Hematol 1993; 67(3):145–147.
151. Batge B, Filejski W, Kurowski V, et al. Clostridial sepsis with massive intravascular hemolysis: rapid diagnosis and successful treatment. Intensive Care Med 1992; 18(8):488–490.
152. Robbins RL, Wallace SS, Brunner CJ, et al. Immune-mediated hemolytic disease after penicillin therapy in a horse. Equine Vet J 1993; 25(5):462–465.
153. Thomas HL, Livesey MA. Immune-mediated hemolytic anemia associated with trimethoprim-sulphamethoxazole administration in a horse. Can Vet J 1998; 39(3):171–173.
154. Ogilvie GK. Paraneoplastic syndromes. Vet Clin North Am Equine Pract 1998; 14(3):439–449.
155. Geor RJ, Clark EG, Haines DM, et al. Systemic lupus erythematosus in a filly. J Am Vet Med Assoc 1990; 197(11):1489–1492.
156. Collins JD. Autoimmune haemolytic anemia in the horse. In: Kitchen H, Krehbiel JD, eds. First international symposium on equine hematology. Michigan State University; 1975:342–348.
157. Corriher CA, Parviainen AKJ, Gibbons DS, et al. Equine red maple leaf toxicosis. Compend Contin Educ Pract Vet 1999; 21(1):74–80.
158. Carlson G. Heinz body hemolytic anemia. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1059–1061.
159. McConnico RS, Brownie CF. The use of ascorbic acid in the treatment of 2 cases of red maple (*Acer rubrum*)-poisoned horses. Cornell Vet 1992; 82(3):293–300.
160. Loscher W, Jaeschke G, Keller H. Pharmacokinetics of ascorbic acid in horses. Equine Vet J 1984; 16(1):59–65.
161. Boyer JD, Breeden DC, Brown DL. Isolation, identification, and characterization of compounds from *Acer rubrum* capable of oxidizing equine erythrocytes. Am J Vet Res 2002; 63(4):604–610.
162. Means RT, Jr, Krantz SB. Progress in understanding the pathogenesis of the anemia of chronic disease. Blood 1992; 80(7):1639–1647.
163. Carlson G. Depression anemia. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1063–1065.
164. Watson ADJ, Canfield PJ. Nutritional deficiency anemias. In: Feldman BF, Zinkl JG, Jain NC, eds. Schalm's veterinary hematology, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2000:190–195.
165. Jackson SG. Trace minerals for the performance horse: known biochemical roles and estimates of requirements. Irish Vet J 1997; 50(11):668–674.
166. Pearson EG, Andreasen CB. Effect of oral administration of excessive iron in adult ponies. J Am Vet Med Assoc 2001; 218(3):400–404.
167. Rucker RB, Morris JG. The vitamins. In: Kaneko JJ, Harvey JW, Bruss ML, eds. Clinical biochemistry of domestic animals, 5th edn. San Diego: Academic Press; 1997:703–739.
168. Alexander F, Davies ME. Studies on vitamin B12 in the horse. Br Vet J 1969; 125(4):169–176.
169. Salminen K. Cobalt metabolism in horse. Serum level and biosynthesis of vitamin B12. Acta Vet Scand 1975; 16(1):84–94.
170. Toribio RE, Bain FT, Mrad DR, et al. Congenital defects in newborn foals of mares treated for equine protozoal myeloencephalitis during pregnancy. J Am Vet Med Assoc 1998; 212(5):697–701.
171. Cowgill LD, James KM, Levy JK, et al. Use of recombinant human erythropoietin for management of anemia in dogs and cats with renal failure. J Am Vet Med Assoc 1998; 212(4):521–528.
172. Casadevall N, Nataf J, Viron B, et al. Pure red-cell aplasia and antierythropoietin antibodies in patients treated with

recombinant erythropoietin. N Engl J Med 2002; 346(7):469–475.
173. Barragry T. Drugs, doping and current sporting problems: 1. Irish Vet J 2000; 53(6):312–319.
174. Kearns CF, Lenhart JA, McKeever KH. Cross reactivity between human erythropoietin antibody and horse erythropoietin. Electrophoresis 2000; 21(8):1454–1457.
175. Casadevall N. Antibodies against rHuEPO: native and recombinant. Nephrol Dial Transplant 2002; 17 Suppl 5:42–47.
176. Giger U. Erythropoietin and its clinical use. Compend Contin Educ Pract Vet 1992; 14(1):25–34.
177. Piercy RJ, Swardson CJ, Hinchcliff KW. Erythroid hypoplasia and anemia following administration of recombinant human erythropoietin to two horses. J Am Vet Med Assoc 1998; 212(2):244–247.
178. Woods PR, Campbell G, Cowell RL. Nonregenerative anaemia associated with administration of recombinant human erythropoietin to a thoroughbred racehorse. Equine Vet J 1997; 29(4):326–328.
179. Souillard A, Audran M, Bressolle F, et al. Pharmacokinetics and haematological parameters of recombinant human erythropoietin after subcutaneous administrations in horses. Biopharm Drug Dispos 1996; 17(9):805–815.
180. Jaussaud P, Audran M, Gareau RL, et al. Kinetics and haematological effects of erythropoietin in horses. Vet Res 1994; 25(6):568–573.
181. Lappin TRJ, Maxwell AP. Recombinant human erythropoietin and the anaemic horse: flogging a dead horse? Equine Vet J 1997; 29(4):255–256.
182. Young NS, Maciejewski J. The pathophysiology of acquired aplastic anemia. N Engl J Med 1997; 336(19):1365–1372.
183. Morris DD. Aplastic anemia. In: Smith BP, ed. Large animal internal medicine, 3rd edn. St Louis: Mosby; 2002:1065–1066.
184. Ward MV, Mountan PC, Dodds WJ. Severe idiopathic refractory anemia and leukopenia in a horse. Calif Vet 1980; 12:19–22.
185. Berggren PC. Aplastic anemia in a horse. J Am Vet Med Assoc 1981; 179(12):1400–1402.
186. Lavoie JP, Morris DD, Zinkl JG, et al. Pancytopenia caused by bone marrow aplasia in a horse. J Am Vet Med Assoc 1987; 191(11):1462–1464.
187. Dunavant ML. Clinical evidence of phenylbutazone induced hypoplastic anemia. In: Kitchen H, Krehbiel JD, eds. First international symposium on equine hematology. Michigan State University; 1975:383–385.
188. Lester GD, Alleman AR, Raskin RE, et al. Pancytopenia secondary to lymphoid leukemia in three horses. J Vet Intern Med 1993; 7:360–363.
189. Angel KL, Spano JS, Schumacher J, et al. Myelophthisic pancytopenia in a pony mare. J Am Vet Med Assoc 1991; 198(6):1039–1042.
190. Durando MM, Alleman AR, Harvey JW. Myelodysplastic syndrome in a quarter horse gelding. Equine Vet J 1994; 26:83–85.
191. Moore JN, Mahaffey EA, Zboran M. Heparin-induced agglutination of erythrocytes in horses. Am J Vet Res 1987; 48(1):68–71.
192. Mahaffey EA, Moore JN. Erythrocyte agglutination associated with heparin treatment in three horses. J Am Vet Med Assoc 1986; 189(11):1478–1480.
193. Gerhards H. Low dose calcium heparin in horses: plasma heparin concentrations, effects on red blood cell mass and on coagulation variables. Equine Vet J 1991; 23(1):37–43.
194. Duncan SG, Meyers KM, Reed SM. Reduction of the red blood cell mass of horses: toxic effect of heparin anticoagulant therapy. Am J Vet Res 1983; 44(12):2271–2276.
195. Feige, K, Schwarzwald CC, Bombeli TH. Comparison of unfractioned low-molecular-weight heparin and heparin for prophylaxis of coagulopathies in 52 horses with colic: a randomized double-blind trial. Equine Vet J 2003; 35(5):506–513.
196. Monreal L, Villatoro AJ, Monreal M, et al. Comparison of the effects of low-molecular-weight and unfractioned heparin in horses. Am J Vet Res 1995; 56(10):1281–1285.
197. Persson SG, Larsson M, Lindholm A. Effects of training on adreno-cortical function and red-cell volume in trotters. Zentralbl Veterinarmed A 1980; 27(4):261–268.
198. Persson SGB. Evaluation of exercise tolerance and fitness in the performance horse. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology 1. Cambridge: Granta Publications; 1983:441–457.
199. Persson SG, Osterberg I. Racing performance in red blood cell hypervolaemic standardbred trotters. Equine Vet J 1999; Suppl 30:617–620.
200. Funkquist P, Nyman G, Persson SGB. Haemodynamic response to exercise in trotters with red cell hypervolaemia and exercise induced pulmonary haemorrhage. In: Kallings P, Bondesson U, Houghton E, eds. Proceedings of the 10th international conference of racing analysts and veterinarians. Newmarket: R and W Publications; 1994:165–167.
201. Funkquist P, Sandhagen B, Persson SG, et al. Effects of phlebotomy on haemodynamic characteristics during exercise in standardbred trotters with red cell hypervolaemia. Equine Vet J 2001; 33(4):417–424.
202. Persson SGB, Exercise tolerance in standardbred trotters with T-wave abnormalities in the electrocardiogram. In: Gillespie JR, Robinson NE, eds. Proceedings of the 2nd International Conference on Equine Exercise Physiology. San Diego: ICEEP Publications; 1986:772–780.
203. Persson SGB. Lung biopsy pathology and exercise intolerance in horses with chronic bronchiolitis. In: Persson SGB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications; 1991:457–464.
204. Funkquist P, Wagner PD, Hedenstierna G, et al. Ventilation–perfusion relationships during exercise in standardbred trotters with red cell hypervolaemia. Equine Vet J Suppl 1999; 30:107–113.
205. Persson SGB. Blood volume in relation to exercise tolerance in trotters. J S Afr Vet Med Assoc 1974; 45:293–299.
206. Persson SG, Funkquist P, Nyman G. Total blood volume in the normally performing standardbred trotter: age and sex variations. Zentralbl Veterinarmed A 1996; 43(1):57–64.
207. Persson SGB. Practical aspects of blood volume measurement. Procedure for determination of total red cell volume (CV) in the horse. Proc Int Conf Equine Sports Med 1986:51.
208. Pösö AR, Essén-Gustavsson B, Persson SG. Metabolic response to standardised exercise test in standardbred trotters with red cell hypervolaemia. Equine Vet J 1993; 25(6):527–531.
209. Karlström K, Essén-Gustavsson B, Persson SGB. Capillaries of muscle in red cell hypervolaemic versus normovolaemic standardbred horses. Equine Vet J 1995; Suppl 18:228–230.
210. Burrell MH. Endoscopic and virological observations on respiratory disease in a group of young thoroughbred horses in training. Equine Vet J 1985; 17(2):99–103.
211. Hed U, Aslin T. Blödning fran luftvägarna hos svenska travhästar i samband med tävlingsprestation (EIPH). Svensk Veterinärtidning 1986; 38:309–311.

212. West JB, Mathieu-Costello O, Jones JH, et al. Stress failure of pulmonary capillaries in racehorses with exercise-induced pulmonary hemorrhage. J Appl Physiol 1993; 75(3):1097–1109.
213. McKane SA, Canfield PJ, Rose RJ. Equine bronchoalveolar lavage cytology: survey of thoroughbred racehorses in training. Aust Vet J 1993; 70(11):401–404.
214. O'Callaghan MW, Pascoe JR, Tyler WS, et al. Exercise-induced pulmonary haemorrhage in the horse: results of a detailed clinical, post mortem and imaging study. VIII. Conclusions and implications. Equine Vet J 1987; 19(5):428–434.
215. Meyer TS, Fedde MR, Gaughan EM, et al. Quantification of exercise-induced pulmonary haemorrhage with bronchoalveolar lavage. Equine Vet J 1998; 30(4):284–288.
216. Roneus M, Persson SG, Essén-Gustavsson B, et al. Skeletal muscle characteristics in red blood cell normovolaemic and hypervolaemic standardbred racehorses. Equine Vet J 1994; 26(4):319–322.
217. Funkquist P, Essén-Gustavsson B, Nyman G. Muscle characteristics in standardbred trotters with red cell hypervolemia and pronounced hypertension during exercise. In: Proceedings of the Association of Equine Sports Medicine. San Antonio; 1997:31–34.
218. Karlstrom K, Essén-Gustavsson B. Myosin heavy chain-based fibre types in red cell hyper- and normovolaemic standardbred trotters. Equine Vet J 2002; Suppl 34:279–282.
219. Wagner PD, Laravuso RB, Uhl RR, et al. Continuous distributions of ventilation–perfusion ratios in normal subjects breathing air and 100 per cent O_2. J Clin Invest 1974; 54(1):54–68.
220. Wagner PD, Saltzman HA, West JB. Measurement of continuous distributions of ventilation–perfusion ratios: theory. J Appl Physiol 1974; 36(5):588–599.
221. Wagner PD, Naumann PF, Laravuso RB. Simultaneous measurement of eight foreign gases in blood by gas chromatography. J Appl Physiol 1974; 36(5):600–605.
222. Birks EK, Mathieu-Costello O, Fu Z, et al. Very high pressures are required to cause stress failure of pulmonary capillaries in thoroughbred racehorses. J Appl Physiol 1997; 82(5):1584–1592.
223. Nyman G, Bjork M, Funkquist P. Gas exchange during exercise in standardbred trotters with mild bronchiolitis. Equine Vet J Suppl 1999; 30:96–101.
224. Holmgren A, Jonsson B, Levander M, et al. Low physical working capacity in suspected heart cases due to inadequate adjustment of peripheral blood flow (vasoregulatory asthenia). Acta Med Scand 1957; 158:413.

CHAPTER 45

Immunological responses to exercise and training

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It is a common belief that habitual exercise provides an individual with enhanced protection from disease. A review of the scientific literature, however, reveals seemingly paradoxic reports on the effect of exercise on the immune system.[1–3] More than 30 years of research on this topic has made it clear that the effects of exercise on the immune system are complex and dependent upon multiple factors, including: (i) the immune function or characteristic being analyzed; (ii) the intensity and duration of exercise; and (iii) the timing of the measurement of immune function in relation to the exercise bout.[1,2,4] The underlying mechanisms whereby exercise alters immune responses are likewise multifactorial and likely include both neuroendocrine[5–7] and metabolic factors.[8–10] Although the clinical consequences of the exercise-induced immune changes have not formally been identified, there is evidence that high-intensity exercise in humans can lead to an overall impairment of the cellular immune system, resulting in low concentrations of lymphocytes, suppressed natural immunity, suppressed lymphocyte proliferation, suppressed levels of secretory IgA in saliva, and an increased incidence of upper respiratory tract infections.[8,11–16] By contrast, a regular routine of moderate exercise seems to improve immunological function and increase disease resistance, particularly in the elderly.[4,17]

The majority of the studies concerning the immunologic responses to exercise and training have focused on humans and laboratory animals. Although the horse provides an excellent opportunity for exercise-based studies, there is a limited amount of information available concerning the effect of exercise on the equine immune system.[18] Most of this review will therefore emphasize those results obtained from human and rodent exercise studies. When possible, specific information regarding equine exercise studies will also be included.

Immune responses

Most investigations on the effect of exercise on immune function have focused on the innate immune response in both horse and man.[1,18,19] This initial response to pathogens plays a central role in disease resistance and the development of subsequent adaptive or specific immune responses. The innate immune response includes both cellular and humoral components, although most studies on the effect of exercise on this response have focused on the cellular components, namely neutrophils, macrophages, and natural killer (NK) cells.[18,19] The essential characteristic of the innate immune response is that it does not exhibit specificity for the invading organism. Thus the induction of an innate immune response does not require prior exposure to the invading organism, nor is it augmented by repeated exposure to the same organism. The innate immune response plays an important role in prompting the adaptive immune response as well as providing valuable time for specific adaptive responses to develop.

The adaptive immune response is likewise mediated by both humoral and cellular components. The humoral response consists of antigen-specific antibodies produced by B cells and plasma cells. The cellular response is composed of effector T cells such as cytotoxic T-lymphocytes (CTLs) that exhibit both antigen specificity and the phenomena of immunological memory. The regulation of the adaptive immune response is mediated by T helper (Th) cells that produce various cytokines, small hormone-like proteins that control the growth, differentiation, and activation state of various cells of the immune system.[20] Together, these responses provide the functional capacity to completely protect an animal against a particular pathogen.

Functionality of the innate immune response is assessed in vitro by measuring the phagocytic or oxidative metabolic activity of macrophages and neutrophils[21–24] and the cytotoxic activity of NK cells.[25–28] The adaptive immune response is assessed in vitro by the ability of lymphocytes to proliferate[4,29–31] or produce cytokines in response to various mitogens and specific antigens;[4,30,32] and in vivo by measuring antibody responses.[30,33–35]

Exercise intensity and immune function

An acute exercise bout or test is the most frequently used method for exercise immunology studies.[3,36,37] Even with this approach the overall response depends on many factors, including the intensity, duration, and mode of exercise; plasma concentrations of hormones and cytokines; physiologic changes in the body including temperature, blood flow, and hydration status; and the overall fitness of the subject.[36] In general, acute exercise bouts of moderate duration (< 60 min) and intensity (< 60% $\dot{V}O_{2max}$) are associated with fewer perturbations to the immune system than prolonged, high-intensity sessions in humans[36,38,39] and horses (Table 45.1).[23,24,40] Conditioning of elite human athletes may or may not alter exercise-induced changes in immune function, and may be sport dependent.[41,42] Studies of unconditioned horses have shown decreased immune responses after a single[43,44] and multiple bouts of intensive exercise.[30] Other studies involving conditioned horses found decreased lymphoproliferative responses following treadmill exercise[45] or racing[29] and impaired neutrophil function after endurance riding.[46,47] Long-term exercise training of low intensity appears to improve some measures of human immune function,[48] whereas overtraining is associated with decrements in some immune measures (granulocyte oxidative burst, NK cell activity, lymphocyte proliferation, the production of cytokines in response to mitogens, nasal and salivary immunoglobulin A levels) and increases in others (granulocyte and monocyte phagocytosis, and inflammatory cytokine production).[8,13–16] Interestingly, overtraining in humans is associated with a decrease in maximum exercise-induced adrenocorticotropin hormone (ACTH) and, to a lesser degree, cortisol and free plasma catecholamines.[49] No similar alterations in stress hormone production have been seen in overtrained horses,[50,51] although the possibility of immunological alterations in overtrained horses has not been addressed.[18]

Table 45.1 Summary of exercise intensity effects on immune functions[18]

Immune function	Moderate exercise	Intense exercise
LAK/NK lysis	↑	↓
Lymphoproliferation	↓	↓
Neutrophil function	↓	↓
Macrophage function	↓	↓
Proinflammatory cytokines	↑	↑
Antibody levels	↕	↓

The stress response

The physiologic and immunologic consequences of intensive exercise parallel the effect of other physical and psychological stressors.[52–54] It should be noted that exercise stress is not a single homogeneous stressor. Rather, it is actually a culmination of several different stressors, including physiologic, environmental, social, and psychological stressors.[53–55] Stress has been defined, in general, as an abnormal or extreme adjustment in the physiology of the animal to cope with adverse effects of its environment or management.[56,57] Initial theories attempting to identify a common non-specific stress response pathway (e.g. Hans Seyles' General Adaptation syndrome) have been discounted and instead four separate pathways have been identified: the hypothalamic–pituitary–adrenal (HPA) axis, the autonomic nervous system, extra-adrenal pathways, and extra-neuronal production of cytokine mediators (Fig. 45.1).[58] Although products of each of the pathways appear to be involved in stress-induced immunomodulation, the HPA axis and its production of cortisol and catecholamines has been the most intensively studied stress pathway in terms of exercise-induced immune modulation (Fig. 45.2).[54,59]

Cortisol represents the chronic response to stress whereas catecholamines represent the acute stress response.[60,61] Cortisol, the primary biologically relevant corticosteroid of humans and horses, is a cholesterol derivative produced by the adrenal cortex under the direction of ACTH produced by the pituitary.[62] Production of ACTH is regulated by corticotropin-releasing factor (CRF), which is produced by the hypothalamus.[63] Cortisol production in humans and horses has an ACTH-dependent circadian rhythm with peak levels in the early morning and a nadir in the evening.[64–66] This rhythm can be disrupted by physical and psychological stress.[65,66] Intensive exercise is likewise associated with an increase in plasma cortisol in both man and horse.[54,67,68] Therefore it is tempting to

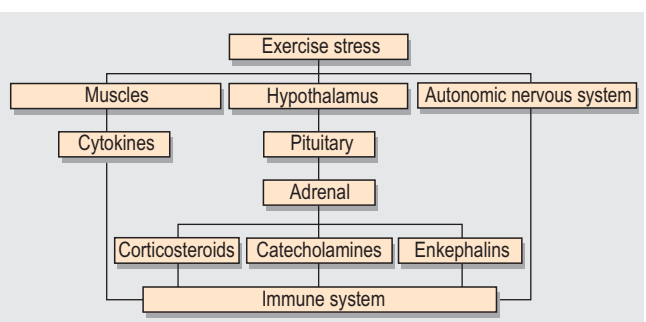

Fig. 45.1
Exercise effects on the immune system. Exercise can affect the immune response either directly via the production of various cytokines by muscle cells or via hormone produced via the hypothalamus–pituitary–adrenal axis.

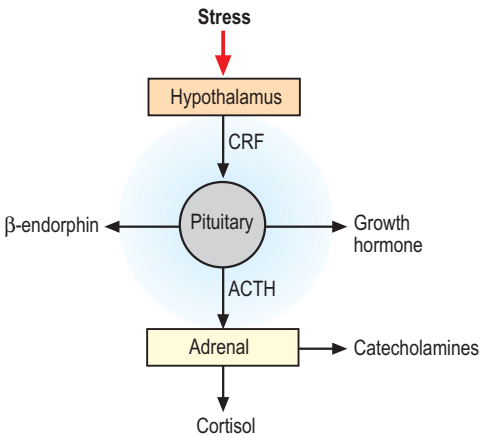

Fig. 45.2
Hypothalamus–pituitary–adrenal (HPA) axis. The perception of the stressor signals corticotropic-releasing factor (CRF) production by the hypothalamus, which causes the pituitary to produce adrenocorticotrophic hormone (ACTH) and β-endorphin. ACTH stimulates cortisol production by the adrenal glands, which also produce catecholamines.

ascribe exercise-induced changes in immune function to increases in plasma cortisol, because corticosteroids are known to be potent anti-inflammatory agents and to have dramatic effects on immune cell function (see below).[69]

Catecholamine production by the nervous system is another important component of the stress response.[59,70] Catecholamines, such as epinephrine (adrenaline) and norepinephrine (noradrenaline), are derivatives of tyrosine produced by sympathetic nerve endings and the adrenal medulla.[71] They mediate a multitude of physiologic changes that broadly encompass the 'fight or flight' response to stressors.[57,72] Catecholamines exert their effects within minutes of their induction and are considered to represent the active response to stress.[73] Catecholamines mediate their effect through the interaction with adrenergic receptors found on the surface of various cells, including lymphocytes.[74–76] A number of immunomodulatory effects of catecholamines has been described (see below).

It has been suggested that stress-induced impairment of either innate or specific immune responses opens a 'window of susceptibility' to infectious agents.[77] This is likely due to subtler changes in immune function rather than complete immune suppression.[78–85] These subtle changes in lymphocyte function could account for aberrant responses to vaccination seen in stressed individuals[86,87] and the increased incidence of upper respiratory tract infections in human athletes.[88–91] Although the precise mechanism responsible for the increase in disease remains uncertain, a number of in vitro correlates have been identified.

Exercise-induced leukocytosis

One of the most consistent effects of exercise on the immune system is the leukocytosis seen after strenuous exercise in humans,[21,92–95] as well as horses.[96–98] As with the other effects of exercise on immune function, the magnitude of the leukocytosis increases as the intensity and duration of exercise increases.[94] The leukocytosis observed following acute intense exercise is biphasic in nature, characterized by an initial increase in lymphocyte numbers followed by an increase in neutrophil and monocyte numbers.[93,95,99] Lymphocyte numbers have been shown to return to resting levels in as short as 1 h after exercise, whereas neutrophils are slower in returning to resting values and, considering the fact that lymphocyte numbers decline rapidly, are responsible for the increased neutrophil to lymphocyte ratio reported in most studies.[95,96] Lymphocyte numbers have been shown to drop below baseline values in human and equine subjects during the recovery phase following intense exercise creating a lymphopenia,[61,100] and this effect has been attributed to post-exercise production of cortisol.[77]

In addition to the increase in lymphocyte numbers in response to exercise, it has been shown that exercise has an effect on lymphocyte subpopulations. The majority of the work has concentrated on the changes in circulating numbers of $CD4^+$ and $CD8^+$ T-lymphocytes.[39,101–105] Most Th cells are $CD4^+$ while CTLs are $CD8^+$. In one study with a limited number of horses, $CD4^+$ T cell numbers were shown to decline following intense exercise, with no change in $CD8^+$ numbers.[18] In related studies using human subjects, $CD4^+$ and $CD8^+$ T cell numbers have been shown to increase, decrease, or remain stable following exercise.[39,103–105] In general, these results indicate that exercise-induced lymphocyte subset reduction is transient and dependent upon exercise intensity and duration with high-intensity exercise tending to decrease the number of $CD4^+$ T cells.[12,39,103]

The number of circulating NK cells, identified by the presence of the CD16 cell-surface antigen, has been shown to increase following exercise in humans.[12,28,39,106–108] The effect of exercise on NK cells in the horse is unknown, because equine NK cells are difficult to identify. Several markers that selectively bind to the equine NK cell have been identified and may provide the answer to this and many other questions regarding equine NK cells.[109,110] Equine lymphokine-activated killer (LAK) cell activity, which appears to be distinct from NK cell activity,[111,112] has been shown to increase following exercise,[113] although the circulating numbers of these cells remain stable following exercise.[27]

There are three likely mechanisms to explain the exercise-induced leukocytosis. The first mechanism involves hemoconcentration resulting from shifts in fluid balance with the overall effect of decreasing the extracellular fluid compartment.[102,114,115] The increase in the packed cell volume and total protein concentration due to intense exercise are partially due to this mechanism as well.[116,117] The second mechanism involves catecholamine levels, which have been shown to rise in response to exercise and are known to mobilize leukocytes from the marginal pool.[95] The third mechanism that may play a role in the leukocytosis of exercise involves the mobilization of granulocytes from the marrow pool caused by exercise-induced increases in cortisol

concentration.[102,118–120] It is believed that this latter mechanism is responsible for the previously mentioned biphasic nature of exercise-induced leukocytosis.[77,93,95,99,120,121]

Exercise and leukocyte function

Single bouts of moderate to intensive exercise are associated with an initial increase in NK or LAK cell function in humans[26,28,107,122] and horses[27] but severe exercise is followed by depression of NK function.[122] Single bouts of moderate to intensive exercise transiently impair neutrophil antimicrobial functions in both horse and man.[21,98] High-intensity exercise on a treadmill has been associated with a general reduction in neutrophil function in both species.[44,123] Endurance racing is likewise associated with negative changes in neutrophil function in both man and horse.[46,47] Similar effects of intensive exercise on bronchoalveolar macrophage function are also seen in horses,[23,24] although in mice there appears to be an enhancement of macrophage function following an exercise challenge.[22] As such, these studies indicate that equine innate immune functions, like those of humans, can be adversely affected by intensive exercise.

There are relatively few reports of exercise-induced changes in antigen-specific lymphoproliferation as the majority of the work on exercise-induced changes in lymphocyte function has concentrated on the mitogen-specific response. In general, intense exercise leads to decreased lymphoproliferation to both mitogens and antigens.[11,12,124] The magnitude of this effect has been shown to increase with increases in exercise intensity and duration.[36,38,39] In one study in horses, there was no change in the lymphoproliferative response to the various mitogens.[24] In contrast, other studies have shown that unconditioned horses exhibit decreased lymphoproliferative responses to both mitogens and equine influenza virus in response to a single bout[43,44] and multiple bouts of intensive exercise.[30] Studies involving conditioned horses found decreased lymphoproliferative responses to mitogens in response to treadmill-based exercise challenge[45] and racing.[29] While positive training effects have been observed on human basal immune responses,[4,17] exercise-conditioned horses do not appear to have a similar increase in their basal immune responses (Table 45.2).

More recently it has been suggested that strenuous exercise might also alter patterns of cytokine gene expression, though the absolute effect varied.[32,33,125] Production of the proinflammatory cytokines interleukin (IL)-1, IL-6, IL-8, IL-12, granulocyte/macrophage-colony stimulating factor (GM-CSF), and tumor necrosis factor (TNF)-α is enhanced by intensive exercise,[126–128] suggesting that exercise is a form of limited inflammatory response.[129] IL-6 is thought to play a central role in this process as it is produced in large quantities in response to exercise and locally in skeletal muscle in response to exercise.[130] From these results, it has thus been proposed that skeletal muscle damage during physical exercise results in an inflammatory response.[131,132] It has recently been reported that multiple bouts of high-intensity exercise may be more potent inducers of this inflammatory response.[133,134] Although the overall significance of these results remains controversial,[135] it is becoming increasingly apparent that exercise is associated with a proinflammatory cytokine response. Whereas these cytokines themselves have immunoregulatory functions, their production may also have a role in post-exercise immune suppression.[136,137] The theory is that the counter-regulation of the initial inflammatory immune response involves the production of cortisol, prostaglandins, and IL-10 (an anti-inflammatory cytokine), all of which contribute to the post-exercise immune suppression.[130,137] This mechanism is also consistent with reports that exercise may enhance Th2 immune responses at the expense of Th1 responses.[32] IL-10 and corticosteroids suppresses Th1 responses and favor Th2 development.[137] Intensive exercise-induced inhibition of Th1 cytokine production also occurs in horses,[30] although the role of IL-10 in this process is unknown. Clearly the effect of exercise on cytokine production in the horse needs further work.

The effects of exercise on humoral immunity are conflicting at best. Prolonged periods of intense training lead to an impairment of mucosal immunoglobulin levels in humans.[2,138–140] Exercise appears to have little effect on immunoglobulin concentrations or antibody production in horses.[30,98] Actively exercising horses and humans produce similar levels of antibodies following vaccination as unexercised controls,[34,141] however, cell-mediated immunity following vaccination may be impaired.[30,142,143] The possibility of altered patterns of immunoglobulin isotype production in response to exercise has not been addressed, although such alterations have been described in other stress models.[86,87] Additional work needs to be done to elucidate the effect of exercise on immunoglobulin levels and isotype production in both horse and man.

Table 45.2 Basal immune responses of trained and untrained horses[43]

Immune response	Untrained horses	Trained horses
Mitogen proliferation	68 266 ± 2082 cpm	68 066 ± 5428 cpm
Influenza proliferation	7358 ± 426 cpm	8480 ± 1494 cpm
LAK cytotoxicity	16.2 ± 1.8 lytic units	12.8 ± 3.1 lytic units

LAK, lymphokine-activated killer.

Mechanisms of exercise-induced changes in immune function

The mechanisms responsible for changes in immune function are unknown, although much of the data seem to implicate a

central role for cortisol and/or catecholamines. Exercise has been shown to significantly increase the plasma concentration of cortisol and catecholamines and the magnitude of this response is directly related to the intensity and duration of exercise.[54,77] Hormonal responses of the horse to exercise have been shown to mimic the response of humans and other mammals in which both cortisol and catecholamine levels have been shown to significantly increase in response to high-intensity exercise.[68,100,144–146] Again, the general consensus is that cortisol mediates the later changes following exercise while the early or immediate effects of exercise are due to the catecholamines (Fig. 45.3).

Production of cortisol, the primary secretory glucocorticoid, in the horse has been well studied but the actual physiological significance of the changes that occur following exercise are far from being understood. Plasma cortisol in the horse has a half-life of 70–100 min and has been shown to peak 20–30 min after the cessation of exercise.[145] It has been determined that plasma cortisol levels do not increase due to exercise until the work load reaches the 60% maximum oxygen uptake ($\dot{V}O_{2max}$).[30,147–149] The increase in plasma cortisol concentration is the result of a change in the balance between the combined increased secretion of cortisol and increased clearance rate in response to exercise, with the secretion rate showing the greater increase.[67] Exercise training is associated with an adaptation of the HPA axis leading to decreased pituitary sensitivity to corticosteroids and increased plasma cortisol levels.[150,151] Exercise-induced alterations in glucocorticoid receptor expression and signaling in lymphocytes have also been reported in human athletes,[152,153] and this can lead to decreased sensitivity of corticosteroid suppression of immune function.[154] No similar information is available for the horse.

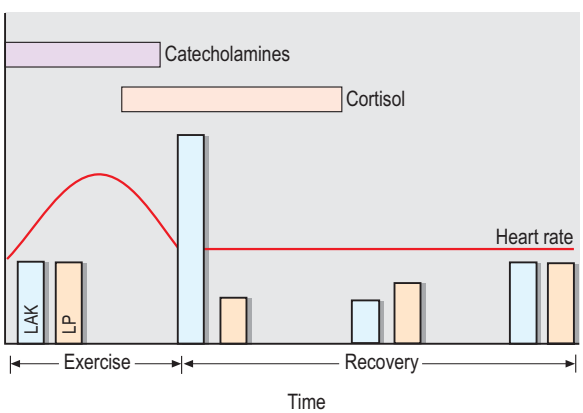

Fig. 45.3
Equine exercise–immunology model. Exercise is associated with the early production of catecholamines and an increase in heart rate. Cortisol production occurs later and is intensity dependent. Lymphokine-activated killer (LAK) cell activity and the lymphoproliferative (LP) response to mitogens are at a baseline level prior to exercise. Upon completion of exercise, LAK activity increases with a concomitant decrease in the LP response. Later in the recovery period, both LAK and LP responses are suppressed, although eventually they will return to baseline levels. The magnitude and duration of the effect on LAK and LP is also intensity dependent.

Because corticosteroids are known to be potent anti-inflammatory agents and to have dramatic effects on immune cell function,[69] it is tempting to attribute exercise-induced changes in immune function to increases in plasma cortisol. Thus corticosteroids inhibit synthesis of various cytokines such as IL-1, IL-2, IL-3, IL-6, interferon gamma (IFN-γ), GM-CSF, and TNF-α.[69,155,156] Likewise, the production or release of lymphotoxin, monocyte chemotactic factors, vasoactive amines, prostaglandins, and plasminogen activator are diminished in the presence of corticosteroids.[69,155,156] Indirect corticosteroid effects on in vitro lymphoid cell function have likewise been reported, presumably resulting from altered regulation of cytokine production and activity and/or antigen-presenting cell function.[157] Thus a variety of research has demonstrated corticosteroid-related decreases in mitogen responses, LAK cell activity, CTL function, NK cell-mediated cytotoxicity, and lymphocyte proliferative responses to specific antigens.[54,158–160] Although the magnitude of the cellular response to glucocorticoid depends upon the hormone level to which it is exposed, the relationship between corticosteroids and the immune system is complex and may be obscured by factors such as steroid preparation and species sensitivity to corticosteroids.[161] Studies that demonstrate corticosteroid-associated immune suppression in vitro often utilize synthetic preparations and/or non-physiologic concentrations of the steroid. Synthetic hormones such as dexamethasone or prednisolone have a longer half-life in circulation, bind less strongly to cortisol-binding globulin, and have a higher affinity for the corticosteroid receptor and are thus more potent than cortisol.[162,163] Pharmacologic concentrations of cortisol that are immunosuppressive are not relevant to the in vivo situation.[163] Finally, it should be noted that most studies on the effects of corticosteroids have been performed on corticosteroid-sensitive species such as rats and mice.[164] In these animals, relatively small amounts of corticosteroids have dramatic suppressive effects on immune function, including thymic involution and lymphoid cell death.[164] In corticosteroid-resistant species such as the horse, immune suppression by corticosteroids may be absent or else require even higher doses and prolonged exposure to corticosteroids for expression.[165] It is important to keep these caveats in mind when considering the role that cortisol may play in exercise-induced immune modulation. To address some of these issues we have tested equine peripheral blood mononuclear cells in vitro for the effect of cortisol on lymphoproliferative and LAK cell function (Fig. 45.4). Significant effects were only observed at the highest (10^{-6} M) concentrations. Likewise, injection of a single bolus of cortisol at physiologic concentrations failed to alter immune cell function, although hematologic responses were observed (Table 45.3). Together, these results indicate that cortisol alone may not account for exercise-induced changes in immune cell function in the horse.

Catecholamines have also been shown to significantly increase in response to exercise in the horse.[146,166] Epinephrine (adrenaline) and norepinephrine (noradrenaline) are the major secretory catecholamines and have similar

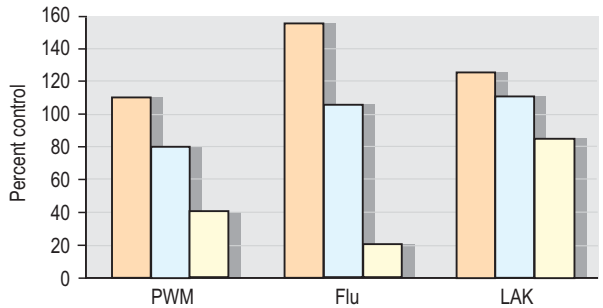

Fig. 45.4
The effect of cortisol on equine proliferation and lymphokine-activated killer (LAK) cell activity. Peripheral blood mononuclear cells were incubated with increasing concentrations of cortisol (10^{-10}, 10^{-8}, and 10^{-6} M, orange, blue and yellow bars, respectively) and either equine influenza virus antigens (Flu) or pokeweed mitogen (PWM) and the proliferative response determined by ^{3}H-thymidine incorporation on days 5 and 3, respectively. Cortisol was added to equine LAK cell cultures at the same doses and cytotoxic activity assayed as previously described (see Table 45.3). Data are presented as the average ± SE of the percentage of the response of cultures not receiving any cortisol.

functions including enhancement of cardiac contraction, blood flow to the heart and skeletal muscle, blood glucose, lipolysis, and oxygen consumption.[57,72] The plasma half-life of both epinephrine (adrenaline) and norepinephrine (noradrenaline) is less than 30 s in the horse.[166] As is the case for cortisol, catecholamine secretion has been shown to increase as the intensity of exercise increases.[166–168]

Catecholamines exert some of their effects on immune responses indirectly by causing the redistribution of the blood cells leading to leukocytosis, lymphocytosis, neutrophilia, decreases in the CD4:CD8 ratio, and increases in NK cell numbers.[25,75,95,169] Catecholamines also directly influence antigen-specific antibody responses, mitogen-stimulated lymphocyte blastogenesis, and natural cytotoxicity.[170–172]

Table 45.3 Hematologic results from an intravenous injection of cortisol or vehicle[43]

	Cortisol			Vehicle		
	–60	+20	+120	–60	+20	+120
WBC	8.4	7.7*	8.5	10.9	11.0	11.2
Neuts	5.1	4.9*	6.0	6.8	6.6	6.7
Lymphs	2.8	2.5	2.0*	3.0	3.2	2.8
N/L	1.8	2.0	3.0*	2.3	2.1	2.4
LAK	62.3	53.2	108.9	52.9	58.2	58.5
PWM	35.3	35.0	33.4	28.4	31.5	35.7
Flu	4.3	1.9	3.6	3.4	2.3	4.1

Flu, proliferative response to influenza virus (× 10^3 net cpm); LAK, lymphokine-activated killer – cell activity as lytic units per 10^6 cells; Neuts, neutrophils; lymphs, lymphocytes × 10^3/μL; N/L, neutrophil/lymphocyte; PWM, proliferative response to pokeweed mitogen (× 10^3 net cpm); WBC, white blood cells.
* Significantly different from – 60 timepoint ($P < 0.01$, RMANOVA).

In addition to the effects of cortisol and catecholamines on the immune system, several other mediators have been implicated as having a potential role in the changes seen following exercise. These include β-endorphin, growth hormone, prolactin, and enkephalin.[126,149,173,174] Among these, β-endorphin has been the most extensively studied in terms of its effect on immune cell function. β-Endorphin release has been shown to increase following intense exercise requiring intensity in excess of 60% $\dot{V}O_{2max}$.[149,173,174] β-Endorphin has been shown to be generally immunosuppressive.[54,126]

Exercise and infectious disease

The central question remains, does exercise lead to increased susceptibility of horses to bacterial and viral infections? Although the physiologic and immunologic consequences of intensive exercise parallel the effect of other physical and psychological stressors,[53,54] do these changes in immunologic function measured in vitro correlate with increased susceptibility to disease in vivo? Epidemiologic surveys have confirmed an increased incidence of upper respiratory tract infection symptoms in human athletes following participation in high-intensity events, such as marathon races,[89–91] although the precise mechanism responsible for this increase remains uncertain.[175–177]

The marked susceptibility of race horses to respiratory infections is widely recognized.[178–180] The reasons for this remain unknown, although they are likely to include the immune status of the susceptible population as well as exposure to infected individuals.[181,182] Interestingly, a recent history of vaccination is not necessarily associated with a reduction in disease risk.[182] The possibility of training or racing schedules affecting the incidence of disease has not been widely considered.[181] In a recent study using a treadmill-based exercise protocol it was shown that vaccinated ponies subjected to repeated bouts of high-intensity exercise were susceptible to influenza virus infection, whereas non-exercised controls were protected.[30] This increased susceptibility was associated with alterations in the in vitro cell-mediated immune response to the virus.[30] Could a similar exercise (stress)-induced alteration in immune function account for influenza infections in vaccinated race horses? Do exercise-induced alterations in neutrophil function likewise leave endurance and race horses susceptible to bacterial infections? Although there is little information currently available to support these concerns, the experience from human sports medicine does suggest that there could be a similar 'window of vulnerability' in our equine athletes.

Assuming that there is an association between exercise-induced immune suppression and increased incidence of respiratory disease in the horse, what can be done? Some attempts have been made through chemical or nutritional means (e.g. indometacin, glutamine, vitamin C, and carbohydrate supplementation) to attenuate immune changes after intensive exercise,[9,183,184] although no consistent relationship

between nutritional interventions, exercise immunology, and upper respiratory tract infection risk has yet been established.[183] Increased carbohydrate ingestion was associated with an attenuated cortisol, growth hormone, and epinephrine (adrenaline) response and fewer perturbations in immune function.[9] Whereas dietary manipulation has been widely recognized as a means to meet the energetic needs of the equine athlete,[185,186] the possible effect of diet on immunocompetency in the exercising horse has not yet been addressed.

Conclusions

Our understanding of the effect of exercise on the immune system is improving, although a number of issues remain unresolved, including the in vivo significance of some of the in vitro findings. Further work defining the mechanisms and long-term consequences of exercise-induced immune modulation is needed before specific changes in current training or vaccination programs can be contemplated. Nevertheless, evidence from the human literature indicates that such efforts could prove useful in protecting the health and welfare of the equine athlete.

References

1. Woods JA, Davis JM, Smith JA, Nieman DC. Exercise and cellular innate immune function. Med Sci Sports Exerc 1999; 31:57–66.
2. Mackinnon LT. Chronic exercise training effects on immune function. Med Sci Sports Exerc 2000; 32:S369–S376.
3. Rowbottom DG, Green KJ. Acute exercise effects on the immune system. Med Sci Sports Exerc 2000; 32:S396–S405.
4. Pedersen BK, Toft AD. Effects of exercise on lymphocytes and cytokines. Br J Sports Med 2000; 34:246–251.
5. Jonsdottir IH. Special feature for the Olympics. Effects of exercise on the immune system: neuropeptides and their interaction with exercise and immune function. Immunol Cell Biol 2000; 78:562–570.
6. Woods JA. Exercise and neuroendocrine modulation of macrophage function. Int J Sports Med 2000; 21 Suppl 1:S24–S30.
7. Fleshner M. Exercise and neuroendocrine regulation of antibody production: protective effect of physical activity on stress-induced suppression of the specific antibody response. Int J Sports Med 2000; 21 Suppl 1:S14–19.
8. Venkatraman JT, Pendergast DR. Effect of dietary intake on immune function in athletes. Sports Med 2002; 32:323–337.
9. Nieman DC. Exercise immunology: nutritional countermeasures. Can J Appl Physiol 2001; 26 Suppl:S45–S55.
10. Gleeson M, Lancaster GI, Bishop NC. Nutritional strategies to minimise exercise-induced immunosuppression in athletes. Can J Appl Physiol 2001; 26 Suppl:S23–S35.
11. Fitzgerald L. Exercise and the immune system. Immunol Today 1988; 9:337–339.
12. Field CJ, Gougeon R, Marliss EB. Circulating mononuclear cell numbers and function during intense exercise and recovery. J Appl Physiol 1991; 71:1089–1097.
13. MacKinnon LT. Special feature for the Olympics. Effects of exercise on the immune system: overtraining effects on immunity and performance in athletes. Immunol Cell Biol 2000; 78:502–509.
14. McKenzie DC. Markers of excessive exercise. Can J Appl Physiol 1999; 24:66–73.
15. Gabriel HH, Urhausen A, Valet G et al. Overtraining and immune system: a prospective longitudinal study in endurance athletes. Med Sci Sports Exerc 1998; 30:1151–1157.
16. Fitzgerald L. Overtraining increases the susceptibility to infection. Int J Sports Med 1991; 12 Suppl 1:S5–S8.
17. Bruunsgaard H, Pedersen BK. Special feature for the Olympics. Effects of exercise on the immune system: effects of exercise on the immune system in the elderly population. Immunol Cell Biol 2000; 78:523–531.
18. Hines MT, Schott HC II, Bayly WM, Leroux AJ. Exercise and immunity: a review with emphasis on the horse. J Vet Intern Med 1996; 10:280–289.
19. Nieman DC, Pedersen BK. Exercise and immune function. Recent developments. Sports Med 1999; 27:73–80.
20. Horohov DW. Equine T-cell cytokines. Protection and pathology. Vet Clin North Am Equine Pract 2000; 16:1–14.
21. Pyne DB. Regulation of neutrophil function during exercise. Sports Med 1994; 17:245–258.
22. Su SH, Chen HI, Jen CJ. Severe exercise enhances phagocytosis by murine bronchoalveolar macrophages. J Leukoc Biol 2001; 69:75–80.
23. Raidal SL, Love DN, Bailey GD, Rose RJ. The effect of high intensity exercise on the functional capacity of equine pulmonary alveolar macrophages and BAL-derived lymphocytes. Res Vet Sci 2000; 68:249–253.
24. Wong CW, Thompson HL, Thong YH, Thornton JR. Effect of strenuous exercise stress on chemiluminescence response of equine alveolar macrophages. Equine Vet J 1990; 22:33–35.
25. Jonsdottir IH. Exercise immunology: neuroendocrine regulation of NK-cells. Int J Sports Med 2000; 21 Suppl 1:S20–S23.
26. Hoffman-Goetz L, May KM, Arumugam Y. Exercise training and mouse mammary tumour metastasis. Anticancer Res 1994; 14:2627–2631.
27. Horohov DW, Keadle TL, Pourciau SS, et al. Mechanism of exercise-induced augmentation of lymphokine activated killer (LAK) cell activity in the horse. Vet Immunol Immunopathol 1996; 53:221–233.
28. Nielsen HB, Secher NH, Kappel M et al. Lymphocyte, NK and LAK cell responses to maximal exercise. Int J Sports Med 1996; 17:60–65.
29. Nesse LL, Johansen GI, Blom AK. Effects of racing on lymphocyte proliferation in horses. Am J Vet Res 2002; 63:528–530.
30. Folsom RW, Littlefield-Chabaud MA, French DD et al. Exercise alters the immune response to equine influenza virus and increases susceptibility to infection. Equine Vet J 2001; 33:664–669.
31. Dohi K, Mastro AM, Miles MP, et al. Lymphocyte proliferation in response to acute heavy resistance exercise in women: influence of muscle strength and total work. Eur J Appl Physiol 2001; 85:367–373.
32. Steensberg A, Toft AD, Bruunsgaard H et al. Strenuous exercise decreases the percentage of type 1 T cells in the circulation. J Appl Physiol 2001; 91:1708–1712.

33. Kohut ML, Boehm GW, Moynihan JA. Moderate exercise is associated with enhanced antigen-specific cytokine, but not IgM antibody production in aged mice. Mech Ageing Dev 2001; 122:1135–1150.
34. Lunn DP, Hussey S, Sebing R, et al. Safety, efficacy, and immunogenicity of a modified-live equine influenza virus vaccine in ponies after induction of exercise-induced immunosuppression. J Am Vet Med Assoc 2001; 218:900–906.
35. Gleeson M, Pyne DB. Special feature for the Olympics. Effects of exercise on the immune system: exercise effects on mucosal immunity. Immunol Cell Biol 2000; 78:536–544.
36. Nieman DC. Exercise immunology: practical applications. Int J Sports Med 1997; 18 Suppl 1:S91–S100.
37. Nash MS. Exercise and immunology. Med Sci Sports Exerc 1994; 26:125–127.
38. Robson PJ, Blannin AK, Walsh NP et al. Effects of exercise intensity, duration and recovery on in vitro neutrophil function in male athletes. Int J Sports Med 1999; 20:128–135.
39. Tvede N, Kappel M, Halkjaer-Kristensen J et al. The effect of light, moderate and severe bicycle exercise on lymphocyte subsets, natural and lymphokine activated killer cells, lymphocyte proliferative response and interleukin 2 production. Int J Sports Med 1993; 14:275–282.
40. Horohov DW, Dimock A, Guirnalda P et al. Effect of exercise on the immune response of young and old horses. Am J Vet Res 1999; 60:643–647.
41. Hanson PG, Flaherty DK. Immunological responses to training in conditioned runners. Clin Sci (Lond) 1981; 60:225–228.
42. Espersen GT, Elbaek A, Schmidt-Olsen S et al. Short-term changes in the immune system of elite swimmers under competition conditions. Different immunomodulation induced by various types of sport. Scand J Med Sci Sports 1996; 6:156–163.
43. Keadle TL. The effect of exercise stress on equine immune funtion. PhD dissertation. Baton Rouge: Louisiana State University, 1992.
44. Raidal SL, Love DN, Bailey GD, Rose RJ. Effect of single bouts of moderate and high intensity exercise and training on equine peripheral blood neutrophil function. Res Vet Sci 2000; 68:141–146.
45. Kurcz EV, Lawrence LM, Kelley KW, Miller PA. The effect of intense exercise on the cell-mediated immune response of horses. Eq Nutr Physiol Soc 1988; 8:237–239.
46. Jensen-Waern M, Lindberg A, Johannisson A et al. The effect of an endurance ride on metabolism and neutrophil function. Eq Vet J Suppl 1999; 30:605–609.
47. Robson P, Alston T, Myburgh K. Prolonged suppression of the innate immune system in the horse following an 80 km endurance race. Eq Vet J 2003; 35(2): 133–137.
48. Shore S, Shinkai S, Rhind S, Shephard RJ. Immune responses to training: how critical is training volume? J Sports Med Phys Fitness 1999; 39:1–11.
49. Urhausen A, Kindermann W. Diagnosis of overtraining: what tools do we have? Sports Med 2002; 32:95–102.
50. Bruin G, Kuipers H, Keizer HA, Vander Vusse GJ. Adaptation and overtraining in horses subjected to increasing training loads. J Appl Physiol 1994; 76:1908–1913.
51. Tyler-McGowan CM, Golland LC, Evans DL et al. Haematological and biochemical responses to training and overtraining. Equine Vet J Suppl 1999; 30: 621–625.
52. Hoffman-Goetz L, Pedersen BK. Exercise and the immune system: a model of the stress response? Immunol Today 1994; 15:382–387.
53. Clow A, Hucklebridge F. The impact of psychological stress on immune function in the athletic population. Exerc Immunol Rev 2001; 7:5–17.
54. Pedersen BK, Hoffman-Goetz L. Exercise and the immune system: regulation, integration, and adaptation. Physiol Rev 2000; 80:1055–1081.
55. Cannon JG. Exercise and resistance to infection. J Appl Physiol 1993; 74:973–981.
56. Fraser SB, Richie JSD, Fraser AF. The term "stress" in the veterinary context. Br Vet J 1975; 131:653–662.
57. Dienstbier RA. Arousal and physiological toughness: implications for mental and physical health. Psychol Rev 1989; 96:84–100.
58. Griffin T, Frank J. Stress and immunity: a unifying concept. Vet Immunol Immunopath 1989; 20:263–312.
59. Nagatomi R, Kaifu T, Okutsu M et al. Modulation of the immune system by the autonomic nervous system and its implication in immunological changes after training. Exerc Immunol Rev 2000; 6:54–74.
60. Ursin H, Olff M. Psychobiology of coping and defence strategies. Neuropsychobiology 1993; 28:66–71.
61. Pedersen BK, Bruunsgaard H, Klokker M et al. Exercise-induced immunomodulation – possible roles of neuroendocrine and metabolic factors. Int J Sports Med 1997; 18(Suppl 1):S2–S7.
62. Delbende C, Delarue C, Lefebvre H et al. Glucocorticoids, transmitters and stress. Br J Psychiatry 1992; 160:24–34.
63. Berkenbosch F, Wolvers DA, Derijk R. Neuroendocrine and immunological mechanisms in stress-induced immunomodulation. J Steroid Biochem Mol Biol 1991; 40:639–647.
64. Czeisler CA, Klerman EB. Circadian and sleep-dependent regulation of hormone release in humans. Recent Prog Horm Res 1999; 54:97–130.
65. DeRijk R, Michelson D, Karp B et al. Exercise and circadian rhythm-induced variations in plasma cortisol differentially regulate interleukin-1 beta (IL-1 beta), IL-6, and tumor necrosis factor-alpha (TNF alpha) production in humans: high sensitivity of TNF alpha and resistance of IL-6. J Clin Endocrinol Metab 1997; 82:2182–2191.
66. Irvine CH, Alexander SL. Factors affecting the circadian rhythm in plasma cortisol concentrations in the horse. Domest Anim Endocrinol 1994; 11:227–238.
67. Lassourd V, Gayrard V, Laroute V et al. Cortisol disposition and production rate in horses during rest and exercise. Am J Physiol 1996; 271:R25–R33.
68. Snow DH, Rose RJ. Hormonal changes associated with long distance exercise. Equine Vet J 1981; 13:195–197.
69. Derijk R, Sternberg EM. Corticosteroid action and neuroendocrine–immune interactions. Ann N Y Acad Sci 1994; 746:33–41.
70. Black PH. Central nervous system–immune system interactions: psychoneuroendocrinology of stress and its immune consequences. Antimicrob Agents Chemother 1994; 38:1–6.
71. Wan W, Vriend CY, Wetmore L et al. The effects of stress on splenic immune function are mediated by the splenic nerve. Brain Res Bull 1993; 30:101–105.
72. Kusnecov AW, Rabin BS. Stressor-induced alterations of immune function: mechanisms and issues. Int Arch Allergy Immunol 1994; 105:107–121.
73. Cacioppo JT, Berntson GG, Malarkey WB et al. Autonomic, neuroendocrine, and immune responses to psychological

stress: the reactivity hypothesis. Ann N Y Acad Sci 1998; 840:664–673.
74. Landmann R. Beta-adrenergic receptors in human leukocyte subpopulations. Eur J Clin Invest 1992; 22 Suppl 1:30–36.
75. Chambers DA, Cohen RL, Perlman RL. Neuroimmune modulation: signal transduction and catecholamines. Neurochem Int 1993; 22:95–110.
76. Madden KS, Sanders VM, Felten DL. Catecholamine influences and sympathetic neural modulation of immune responsiveness. Annu Rev Pharmacol Toxicol 1995; 35:417–448.
77. Perna FM, Schneiderman N, LaPerriere A. Psychological stress, exercise and immunity. Int J Sports Med 1997; 18 Suppl 1:S78–S83.
78. Zwilling BS. Stress affects disease outcomes. Confronted with infectious disease agents, the nervous and immune systems interact in complex ways. ASM News 1992; 58:23–25.
79. Young RA, Elliot TJ. Stress proteins, infection, and immune surveillance. Cell 1989; 59:5–8.
80. Fleshner M, Nguyen KT, Cotter CS et al. Acute stressor exposure both suppresses acquired immunity and potentiates innate immunity. Am J Physiol 1998; 275:R870–R878.
81. Decker D, Schondorf M, Bidlingmaier F et al. Surgical stress induces a shift in the type-1/type-2 T-helper cell balance, suggesting down-regulation of cell-mediated and up-regulation of antibody-mediated immunity commensurate to the trauma. Surgery 1996; 119:316–325.
82. Moynihan JA, Callahan TA, Kelley SP, Campbell LM. Adrenal hormone modulation of type 1 and type 2 cytokine production by spleen cells: dexamethasone and dehydroepiandrosterone suppress interleukin-2, interleukin-4, and interferon-gamma production in vitro. Cell Immunol 1998; 184:58–64.
83. Webster EL, Elenkov IJ, Chrousos GP. The role of corticotropin-releasing hormone in neuroendocrine-immune interactions. Mol Psychiatry 1997; 2:368–372.
84. Milburn HJ, Poulter LW, Dilmec A et al. Corticosteroids restore the balance between locally produced Th1 and Th2 cytokines and immunoglobulin isotypes to normal in sarcoid lung. Clin Exp Immunol 1997; 108:105–113.
85. Sanders VM. The role of norepinephrine and beta-2-adrenergic receptor stimulation in the modulation of Th1, Th2, and B lymphocyte function. Adv Exp Med Biol 1998; 437:269–278.
86. Kiecolt-Glaser JK, Glaser R, Gravenstein S, Malarkey WB. Chronic stress alters the immune response to influenza virus vaccine in older adults. Proc Natl Acad Sci USA 1996; 93:3043.
87. Glaser R, Kiecolt-Glaser JK, Malarkey WB, Sheridan JF. The influence of psychological stress on the immune response to vaccines. Ann N Y Acad Sci 1998; 840:649–655.
88. Brenner IK, Shek PN, Shephard RJ. Infection in athletes. Sports Med 1994; 17:86–107.
89. Nieman DC. Exercise, upper respiratory tract infection, and the immune system. Med Sci Sports Exerc 1994; 26:128–139.
90. Peters EM. Exercise, immunology and upper respiratory tract infections. Int J Sports Med 1997; 18 Suppl 1:S69–S77.
91. Kohut ML, Boehm GW, Moynihan JA. Prolonged exercise suppresses antigen-specific cytokine response to upper respiratory infection. J Appl Physiol 2001; 90:678–684.
92. Keast D, Cameron K, Morton AR. Exercise and the immune response. Sports Med 1988; 5:248–267.
93. Gabriel H, Kindermann W. The acute immune response to exercise: what does it mean? Int J Sports Med 1997; 18 Suppl 1:S28–S45.
94. Brenner I, Shek PN, Zamecnik J, Shephard RJ. Stress hormones and the immunological responses to heat and exercise. Int J Sports Med 1998; 19:130–143.
95. Benschop RJ, Rodriguez-Feuerhahn M, Schedlowski M. Catecholamine-induced leukocytosis: early observations, current research, and future directions. Brain Behav Immun 1996; 10:77–91.
96. Snow DH, Ricketts SW, Mason DK. Haematological response to racing and training exercise in thoroughbred horses, with particular reference to the leucocyte response. Equine Vet J 1983; 15:149–154.
97. Rose R, Allen J. Hematologic responses to exercise and training. Vet Clin North Am: Equine Prac 1985; 1:461–476.
98. Wong CW, Smith SE, Thong YH et al. Effects of exercise stress on various immune functions in horses. Am J Vet Res 1992; 53:1414–1417.
99. Ceddia MA, Price EA, Kohlmeier CK et al. Differential leukocytosis and lymphocyte mitogenic response to acute maximal exercise in the young and old. Med Sci Sports Exerc 1999; 31:829–836.
100. Rossdale PD, Burguez PN, Cash RS. Changes in blood neutrophil/lymphocyte ratio related to adrenocortical function in the horse. Equine Vet J 1982; 14:293–298.
101. Ricken KH, Rieder T, Hauck G, Kindermann W. Changes in lymphocyte subpopulations after prolonged exercise. Int J Sports Med 1990; 11:132–135.
102. Haq A, al-Hussein K, Lee J, al-Sedairy S. Changes in peripheral blood lymphocyte subsets associated with marathon running. Med Sci Sports Exerc 1993; 25:186–190.
103. Kajiura JS, MacDougall JD, Ernst PB, Younglai EV. Immune response to changes in training intensity and volume in runners. Med Sci Sports Exerc 1995; 27:1111–1117.
104. Ronsen O, Pedersen BK, Oritsland TR et al. Leukocyte counts and lymphocyte responsiveness associated with repeated bouts of strenuous endurance exercise. J Appl Physiol 2001; 91:425–434.
105. Shek PN, Sabiston BH, Buguet A, Radomski MW. Strenuous exercise and immunological changes: a multiple-time-point analysis of leukocyte subsets, CD4/CD8 ratio, immunoglobulin production and NK cell response. Int J Sports Med 1995; 16:466–474.
106. Espersen GT, Elbaek A, Ernst E et al. Effect of physical exercise on cytokines and lymphocyte subpopulations in human peripheral blood. Apmis 1990; 98:395–400.
107. Shephard RJ, Rhind S, Shek PN. Exercise and the immune system. Natural killer cells, interleukins and related responses. Sports Med 1994; 18:340–369.
108. Ullum H, Palmo J, Halkjaer-Kristensen J et al. The effect of acute exercise on lymphocyte subsets, natural killer cells, proliferative responses, and cytokines in HIV-seropositive persons. J Acquir Immune Defic Syndr 1994; 7:1122–1133.
109. Shirai K, Watanabe H, Weerasinghe A et al. A monoclonal antibody, DL10, which recognizes a sugar moiety of MHC class I antigens expressed on NK cells, NK+ T cells, and granulocytes in humans. J Clin Immunol 1997; 17:510–523.
110. Harris DT, Camenisch TD, Jaso-Friedmann L, Evans DL. Expression of an evolutionarily conserved function associated molecule on sheep, horse and cattle natural killer cells. Vet Immunol Immunopathol 1993; 38:273–282.
111. Lunn DP, Schram BR, Vagnoni KE et al. Positive selection of EqCD8+ precursors increases equine lymphokine-activated killing. Vet Immunol Immunopathol 1996; 53:1–13.
112. Viveiros MM, Antczak DF. Characterization of equine natural killer and IL-2 stimulated lymphokine activated

killer cell populations. Dev Comp Immunol 1999; 23:521–532.
113. Keadle TL, Pourciau SS, Melrose PA et al. Acute exercise stress modulates immune function in unfit horses. J Eq Vet Sci 1993; 13:4–9.
114. Dickson DN, Wilkinson RL, Noakes TD. Effects of ultra-marathon training and racing on hematologic parameters and serum ferritin levels in well-trained athletes. Int J Sports Med 1982; 3:111–117.
115. Greenleaf JE, Jackson CG, Lawless D. CD4+/CD8+ T-lymphocyte ratio: effects of rehydration before exercise in dehydrated men. Med Sci Sports Exerc 1995; 27:194–199.
116. Novosadova J. The changes in hematocrit, hemoglobin, plasma volume and proteins during and after different types of exercise. Eur J Appl Physiol Occup Physiol 1977; 36:223–230.
117. Wilkerson JE, Gutin B, Horvath SM. Exercise-induced changes in blood, red cell, and plasma volumes in man. Med Sci Sports 1977; 9:155–158.
118. Nieman DC, Berk LS, Simpson-Westerberg M et al. Effects of long-endurance running on immune system parameters and lymphocyte function in experienced marathoners. Int J Sports Med 1989; 10:317–323.
119. McCarthy DA, Macdonald I, Grant M et al. Studies on the immediate and delayed leucocytosis elicited by brief (30-min) strenuous exercise. Eur J Appl Physiol Occup Physiol 1992; 64:513–517.
120. McCarthy DA, Grant M, Marbut M et al. Brief exercise induces an immediate and a delayed leucocytosis. Br J Sports Med 1991; 25:191–195.
121. Shinkai S, Shore S, Shek PN, Shephard RJ. Acute exercise and immune function. Relationship between lymphocyte activity and changes in subset counts. Int J Sports Med 1992; 13:452–461.
122. Pedersen BK, Ullum H. NK cell response to physical activity: possible mechanisms of action. Med Sci Sports Exerc 1994; 26:140–146.
123. Smith JA, Pyne DB. Exercise, training, and neutrophil function. Exerc Immunol Rev 1997; 3:96–116.
124. Nieman DC. Exercise, infection, and immunity. Int J Sports Med 1994; 15 Suppl 3:S131–S141.
125. Goebel MU, Mills PJ, Irwin MR, Ziegler MG. Interleukin-6 and tumor necrosis factor-alpha production after acute psychological stress, exercise, and infused isoproterenol: differential effects and pathways. Psychosom Med 2000; 62:591–598.
126. Suzuki K, Yamada M, Kurakake S et al. Circulating cytokines and hormones with immunosuppressive but neutrophil-priming potentials rise after endurance exercise in humans. Eur J Appl Physiol 2000; 81:281–287.
127. Pedersen BK, Rohde T, Ostrowski K. Recovery of the immune system after exercise. Acta Physiol Scand 1998; 162:325–332.
128. Northoff H, Berg A. Immunologic mediators as parameters of the reaction to strenuous exercise. Int J Sports Med 1991; 12 Suppl 1:S9–S15.
129. Shek PN, Shephard RJ. Physical exercise as a human model of limited inflammatory response. Can J Physiol Pharmacol 1998; 76:589–597.
130. Pedersen BK. Special feature for the Olympics. Effects of exercise on the immune system: exercise and cytokines. Immunol Cell Biol 2000; 78:532–535.
131. Moldoveanu AI, Shephard RJ, Shek PN. The cytokine response to physical activity and training. Sports Med 2001; 31:115–144.
132. Brenner IK, Natale VM, Vasiliou P et al. Impact of three different types of exercise on components of the inflammatory response. Eur J Appl Physiol Occup Physiol 1999; 80:452–460.
133. Ronsen O, Haug E, Pedersen BK, Bahr R. Increased neuroendocrine response to a repeated bout of endurance exercise. Med Sci Sports Exerc 2001; 33:568–575.
134. Meyer T, Gabriel HH, Ratz M et al. Anaerobic exercise induces moderate acute phase response. Med Sci Sports Exerc 2001; 33:549–555.
135. Malm C. Exercise-induced muscle damage and inflammation: fact or fiction? Acta Physiol Scand 2001; 171:233–239.
136. Weinstock C, Konig D, Harnischmacher R et al. Effect of exhaustive exercise stress on the cytokine response. Med Sci Sports Exerc 1997; 29:345–354.
137. Elenkov IJ, Chrousos GP, Wilder RL. Neuroendocrine regulation of IL-12 and TNF-alpha/IL-10 balance. Clinical implications. Ann N Y Acad Sci 2000; 917:94–105.
138. Tomasi TB, Trudeau FB, Czerwinski D, Erredge S. Immune parameters in athletes before and after strenuous exercise. J Clin Immunol 1982; 2:173–178.
139. Pyne DB, Gleeson M. Effects of intensive exercise training on immunity in athletes. Int J Sports Med 1998; 19 Suppl 3:S183–191.
140. Gleeson M, McDonald WA, Pyne DB et al. Immune status and respiratory illness for elite swimmers during a 12-week training cycle. Int J Sports Med 2000; 21:302–307.
141. Gleeson M. Mucosal immune responses and risk of respiratory illness in elite athletes. Exerc Immunol Rev 2000; 6:5–42.
142. Nielsen HB, Pedersen BK. Lymphocyte proliferation in response to exercise. Eur J Appl Physiol Occup Physiol 1997; 75:375–379.
143. Bruunsgaard H, Hartkopp A, Mohr T et al. In vivo cell-mediated immunity and vaccination response following prolonged, intense exercise. Med Sci Sports Exerc 1997; 29:1176–1181.
144. Rose RJ, Hodgson DR, Sampson D, Chan W. Changes in plasma biochemistry in horses competing in a 160 km endurance ride. Aust Vet J 1983; 60:101–105.
145. Valberg S, Gustavsson BE, Lindholm A, Persson SG. Blood chemistry and skeletal muscle metabolic responses during and after different speeds and durations of trotting. Equine Vet J 1989; 21:91–95.
146. Nagata S, Takeda F, Kurosawa M et al. Plasma adrenocorticotropin, cortisol and catecholamines response to various exercises. Equine Vet J Suppl 1999; 30:570–574.
147. Kraemer RR, Acevedo EO, Synovitz LB et al. Glucoregulatory endocrine responses to intermittent exercise of different intensities: plasma changes in a pancreatic beta-cell peptide, amylin. Metabolism 2002; 51:657–663.
148. Thornton JR, Essen-Gustavsson B, Lindholm A et al. Effects of training and detraining on oxygen uptake, cardiac output, blood-gas tensions, pH and lactate concentrations during and after exercise in the horse. In: Snow DH, Persson SG, Rose RJ, eds. Equine exercise physiology, vol 1. Cambridge: Granta Editions, 1983:470–486.
149. Art T, Franchimont P, Lekeux P. Plasma beta-endorphin response of thoroughbred horses to maximal exercise. Vet Rec 1994; 135:499–503.
150. Duclos M, Corcuff JB, Pehourcq F, Tabarin A. Decreased pituitary sensitivity to glucocorticoids in endurance-trained men. Eur J Endocrinol 2001; 144:363–368.
151. Duclos M, Corcuff JB, Arsac L et al. Corticotroph axis sensitivity after exercise in endurance-trained athletes. Clin Endocrinol (Oxf) 1998; 48:493–501.

152. DeRijk RH, Petrides J, Deuster P et al. Changes in corticosteroid sensitivity of peripheral blood lymphocytes after strenuous exercise in humans. J Clin Endocrinol Metab 1996; 81:228–235.
153. Grasso G, Lodi L, Lupo C, Muscettola M. Glucocorticoid receptors in human peripheral blood mononuclear cells in relation to age and to sport activity. Life Sci 1997; 61:301–308.
154. Duclos M, Minkhar M, Sarrieau A et al. Reversibility of endurance training-induced changes on glucocorticoid sensitivity of monocytes by an acute exercise. Clin Endocrinol (Oxf) 1999; 51:749–756.
155. Wilder RL. Neuroendocrine–immune system interactions and autoimmunity. Annu Rev Immunol 1995; 13:307–338.
156. Wu CY, Gargeas C, Nakajima T, Delespesse G. Glucocortioids suppress the production of IL-4 by human lymphocytes. Eur J Immunol 1991; 21:2645–2647.
157. Visser J, van Boxel-Dezaire A, Methorst D et al. Differential regulation of interleukin-10 (IL-10) and IL-12 by glucocorticoids in vitro. Blood 1998; 91:4255–4264.
158. Webster JI, Tonelli L, Sternberg EM. Neuroendocrine regulation of immunity. Annu Rev Immunol 2002; 20:125–163.
159. Nieman DC. Special feature for the Olympics. Effects of exercise on the immune system: exercise effects on systemic immunity. Immunol Cell Biol 2000; 78:496–501.
160. Brattsand R, Linden M. Cytokine modulation by glucocorticoids: mechanisms and actions in cellular studies. Aliment Pharmacol Ther 1996; 10:81–90.
161. Bamberger C, Schulte H, Chrousos G. Molecular determinants of glucocorticoid receptor function and tissue sensitivity to glucocorticoids. Endocrinol Rev 1996; 17:245–261.
162. Munck A, Guyre PM. Glucocorticoid physiology, pharmacology and stress. Adv Exp Med Biol 1986; 196:81–96.
163. Jefferies WM. Cortisol and immunity. Med Hypotheses 1991; 34:198–208.
164. Garvy BA, Fraker PJ. Suppression of the antigenic response of murine bone marrow B cells by physiological concentrations of glucocorticoids. Immunology 1991; 74:519–523.
165. Magnuson NS, McGuire TC, Banks KL, Perryman LE. In vitro and in vivo effects of corticosteroids on peripheral blood lymphocytes from ponies. Am J Vet Res 1978; 39:393–398.
166. Snow DH, Harris RC, MacDonald IA et al. Effects of high-intensity exercise on plasma catecholamines in the thoroughbred horse. Equine Vet J 1992; 24:462–467.
167. Thornton JR. Hormonal responses to exercise and training. Vet Clin North Am: Equine Pract 1985; 1:477–496.
168. Mazzeo RS. Catecholamine responses to acute and chronic exercise. Med Sci Sports Exerc 1991; 23:839–845.
169. Friedman EM, Irwin MR. Modulation of immune cell function by the autonomic nervous system. Pharmacol Ther 1997; 74:27–38.
170. Dohms JE, Metz A. Stress – mechanisms of immunosuppression. Vet Immunol Immunopathol 1991; 30:89–109.
171. Rabin BS, Cohen S, Ganguli R et al. Bidirectional interaction between the central nervous system and the immune system. Crit Rev Immunol 1989; 9:279–312.
172. Kaufman JC, Harris TJ, Higgins J, Maisel AS. Exercise-induced enhancement of immune function in the rat. Circulation 1994; 90:525–532.
173. Jonsdottir IH, Hoffmann P, Thoren P. Physical exercise, endogenous opioids and immune function. Acta Physiol Scand Suppl 1997; 640:47–50.
174. Golland LC, Evans DL, Stone GM et al. Plasma cortisol and beta-endorphin concentrations in trained and over-trained standardbred racehorses. Pflugers Arch 1999; 439:11–17.
175. Bishop NC, Blannin AK, Walsh NP et al. Nutritional aspects of immunosuppression in athletes. Sports Med 1999; 28:151–176.
176. Ostrowski K, Rohde T, Asp S et al. Chemokines are elevated in plasma after strenuous exercise in humans. Eur J Appl Physiol 2001; 84:244–245.
177. Moseley PL. Exercise, stress, and the immune conversation. Exerc Sport Sci Rev 2000; 28:128–132.
178. Burrell MH, Wood JL, Whitwell KE et al. Respiratory disease in thoroughbred horses in training: the relationships between disease and viruses, bacteria and environment. Vet Rec 1996; 139:308–313.
179. Morley PS, Townsend HG, Bogdan JR, Haines DM. Descriptive epidemiologic study of disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216:535–544.
180. Racklyeft DJ, Raidal S, Love DN. Towards an understanding of equine pleuropneumonia: factors relevant for control. Aust Vet J 2000; 78:334–338.
181. Christley RM, Rose RJ, Hodgson DR et al. Attitudes of Australian veterinarians about the cause and treatment of lower-respiratory-tract disease in racehorses. Prev Vet Med 2000; 46:149–159.
182. Morley PS, Townsend HG, Bogdan JR, Haines DM. Risk factors for disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216:545–550.
183. Nieman DC. Is infection risk linked to exercise workload? Med Sci Sports Exerc 2000; 32:S406–S411.
184. Cynober LA. Do we have unrealistic expectations of the potential of immuno-nutrition? Can J Appl Physiol 2001; 26 Suppl:S36–S44.
185. Lawrence L, Soderholm LV, Roberts A et al. Feeding status affects glucose metabolism in exercising horses. J Nutr 1993; 123:2152–2157.
186. Hintz HF. Nutrition and equine performance. J Nutr 1994; 124:2723S–2729S.

CHAPTER 46

Effects of exercise on gastrointestinal function

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Background

Based upon the design of its gastrointestinal tract (GIT) alone, the horse would be an unlikely animal for humans to choose as their athletic alter ego. The very large cecum and folded large colon, normally filled with ingesta, must certainly not be the easiest structures to move around. Likewise, the anatomic arrangement and complexity of function of these fermentation vats could, theoretically at least, set the system up for any number of exercise-induced abnormalities. When left to their own devices in the wild, herbivores, whether they be the forestomach fermenters or the hind-gut fermenters which include the equidae, spend the large majority of their day quietly grazing or resting.[1] Instances of movement faster than a walk are usually brief and in response to attack by a predator or a rival.

'Domesticated' horses, on the other hand, are often subject to many situations that result in a greater percentage of their level of daily activity being much more vigorous than just walking and standing around grazing. While hard data concerning the effect of any form of exertion on the equine GIT, whether it be direct or indirect, are scarce, we have some results showing that even the anticipation of an upcoming training session on a treadmill, such as turning on the treadmill motor, will evoke an increase in intra-abdominal pressure, reflecting tensing of the abdominal muscles.[2] One outstanding effect this pressure increase, and that associated with subsequent trotting or galloping, has on the stomach, for example, will be discussed later in this chapter. The point is that the intra-abdominal pressure response could have far-reaching effects on abdominal viscera, and that the character of the response could vary depending upon the type and duration of the exertion. Galloping may have a different effect than trotting, while trotting may have a different effect than pacing. Jumping may have entirely unique consequences. Effects could include distortion and/or displacement of viscera, redirection of blood flow, and release of various regulatory peptides.

A study of human subjects that were 'encouraged to perform at near-maximal effort' indicated that runners have more complaints of gastro-esophageal reflux (GERD) than do cyclists.[3] Could this be because, in the bent over position in which they ride, cyclists create less abdominal muscle press than do runners? Or is it because, as one report has suggested, the physical displacement of the abdominal viscera associated with the 'pounding of the pavement' results in an irritation that produces symptoms – the so-called 'cecal slap syndrome'?[4] Or, could it be a question of experimental methodology, since two subsequent studies found that subjects asked to perform at up to 90% $\dot{V}o_{2\,max}$ on a stationary bicycle experienced GERD that was exercise intensity dependent?[5,6] That is, type, duration and intensity of exercise all need to be considered from the standpoint of potentially differential effects on the gut.

Finally, considering all of the things humans ask horses to do in the form of exertion, are some forms more stressful than others? In general, existent data indicate a direct relationship between plasma adrenocorticotrophin (ACTH) and cortisol concentrations and intensity and duration of exercise, respectively, in horses.[7] But in one study, for instance, galloping caused no significant increase in pituitary venous blood corticotrophin-releasing hormone (CRH), although ACTH concentration did increase significantly.[8] These issues must also be factored in with respect to the potential impact on the GIT. This chapter considers the potential effects of exercise on: (i) digestion; (ii) absorption; (iii) secretion; (iv) motility; (v) maintenance of mucosal barrier integrity, and (vi) liver-specific functions. These functions are directly influenced by blood flow status, and activity within the enteric nervous system (ENS), which may be strictly intrinsic or may be modified by input from the central nervous system (CNS). With respect to

horses, some special species-relevant aspects of these functions deserve note, and will be explained further below.

Digestion

Some fermentation of soluble carbohydrate occurs within the stomach, with the production of lactic and volatile fatty acids. Whether and to what extent these products are absorbed across the gastric wall and into the bloodstream is not known, though a large proportion should be in the non-ionized, diffusable form, given the acidic environment. Pancreatic secretion, on the other hand, while being large in volume, is very low in amylase and protease activity. The usual complement of small intestinal (brush border) disaccharide enzymes is present. However, small intestinal proteolytic enzymes have not been measured in horses. From a comparative perspective, the one thing that makes horses unique with respect to other domestic species is the degree of cecal and colonic digestion of dietary fiber; up to 35% of the animal's daily caloric needs may be derived from the volatile fatty acids (VFAs) produced from the fermentation of dietary fiber.[9]

Absorption

As indicated above, one of the most unique aspects of equine gut function is the fermentation of carbohydrates at both ends of the tract. While we still know little about where and how the products of gastric fermentation are absorbed, we do know that absorption of VFAs produced in the cecum and colon requires mucosal Na^+/H^+ exchange. A mole of water follows each mole of VFA to be absorbed. It follows that disruption of any of the mechanisms involved in support of normal mucosal function, because of an exercise-related event for example, could have major consequences on water and electrolyte balance, and nutrition. In addition, under conditions where the cecum and colon are presented with a large amount of fermentable carbohydrate over a short period of time, the production rate of the VFAs may initially outstrip absorption and, through the osmotic gradient created, pull water from plasma into the colonic lumen.

Secretion

Gastric acid secretion occurs in the horse even under fasting conditions.[10] The important role played by acid in gastric squamous mucosal ulcerogenesis has been demonstrated, especially as related to the high incidence of this form of gastric ulcer disease in horses under intensive training conditions.[2,11–13] This association probably provides one of the clearest representations to date of how exertion can affect the equine GIT (see below). As mentioned above, from a comparative perspective, pancreatic secretion in horses is very high in daily volume – estimated at 50–60 L/day – but is relatively low in bicarbonate and amylase and protease enzyme concentration.[14] At least when the stomach is empty, large volumes of small intestinal contents, made up primarily of pancreatic juice, periodically reflux into the stomach, providing some buffering of the acid present.[15] The effect of exercise, if any, on this process still needs to be investigated. Finally, the horse undoubtedly possesses all the intestinal secretory mechanisms that have been described in other species, but to what degree needs to be defined. What must be remembered is that, in contrast to humans and animals with relatively simple colons, a hypersecretion of strictly small intestinal origin in the horse would not manifest as diarrhea because of the ability, from a water balance perspective, of the ceco-colon to compensate for that malfunction.[16] Thus, diarrhea in adult horses is indicative of a large bowel dysfunction, which could include hypersecretion at this level.

Motility

As an extension of the human experience, horse trainers often try to schedule the training sessions for a time when they think the horse has a relatively empty stomach. Humans in general do not feel that they can perform maximally on a 'full stomach.' It has been shown that pedaling exercise slows gastric emptying rate in humans, though more runners than cyclists complain of GI problems.[17] The effects of exercise on gastric motility and emptying function in horses are not known and require study, as they may have important implications regarding squamous mucosal ulcerogenesis. As in other species, the proximal stomach relaxes in response to active ingestion (receptive relaxation), and the degree of this relaxation is directly related to the amount of feed ingested.[18] A more sustained, but less profound, postingestion proximal relaxation (accommodation) then occurs, along with peristaltic-like contractions that begin in the middle of the gastric body and traverse through the antrum and promote emptying of gastric contents into the duodenum. The presence of those contents within the duodenum will, in turn, have modulatory effects on the rate of gastric emptying, the degree of which will depend upon their specific composition.[19] This complex regulatory process could be affected by exertion. As indicated earlier, intragastric fermentation of ingested soluble carbohydrates occurs to a considerable degree in horses, and this implies gas production as a result. It follows that this gas must also be moved aborally into the duodenum, since horses do not normally eructate. Likewise, the large amount of gas that is generated from hindgut fermentation must be moved aborally, along with the contents, to be expelled via the anus. Thus, any condition that could adversely reduce the delivery of gas and/or contents, such as an exercise-induced dysmotility, could result in notable abdominal discomfort and/or diarrhea.

Maintenance of mucosal barrier integrity

Normal gut function is dependent upon a reasonably intact barrier between luminal contents and the submucosa.[20–22] Maintenance of barrier integrity is dependent upon numerous factors that include blood flow, mucosal cell turnover rate, and immunologic tolerance to luminal antigens. Methods for experimentally evaluating the 'leakiness' of GI mucosa are discussed below. From the few in vivo and in vitro studies done to date, it appears that horses probably will not differ fundamentally from other species with respect to regional mucosal barrier characteristics, though this needs much more investigation.[23–28]

Liver specific functions

Irrespective of species, normal liver function is critical to good health, and this is highly dependent upon adequate blood supply from both arterial and portal venous sources. Blood supply is emphasized here because it is probably the aspect of liver function most prone to modification by exercise. From a species-specific perspective, it should also be kept in mind that certain detoxifying and conjugative functions of the equine liver might be prone to modulation by fasting and fever, as is the case for endogenously generated bilirubin.[29]

Available methodologies to document the effects of exercise on the equine gastrointestinal system

Methods that have been used in horses

Transit markers

Gastrointestinal transit time can be measured by the use of indigestible, non-absorbable markers. The rate of passage is normally expressed as mean retention time (amount of marker excreted at a certain time after administration of the marker), cumulative excretion, or percentage recovery rate.

Comparison of rate of digesta passage during rest and light to moderate exercise has been evaluated in horses and donkeys. Some of the markers used in these studies were cobalt-EDTA, for liquid phase, chromium-mordanted fiber, for solid phase, and ruthenium-phenanthroline and ytterbium chloride, for particulates passage.[30–32] Non-absorbable markers, such as phenol red in man[17,33,34] and horse,[35] and polyethylene glycol in dog,[36] have been used to measure the effect of different levels of exercise on gastric emptying (GE) of liquid meals. After ingestion of a labeled meal, gastric contents are aspirated through a nasogastric tube or recovered by drainage through a gastric cannula. The amount of marker remaining in the stomach after exercise will depend on the rate of GE of the labeled meal. However, repeated nasogastric intubation per se may affect gastric emptying rate.

Apparent digestibility of diet

Changes in efficiency of dietary fiber utilization in response to exercise may reflect changes in the passage rate of digesta, the activity or population of microbes within the gut, or mucosal integrity.[37] Apparent digestibility is calculated as the

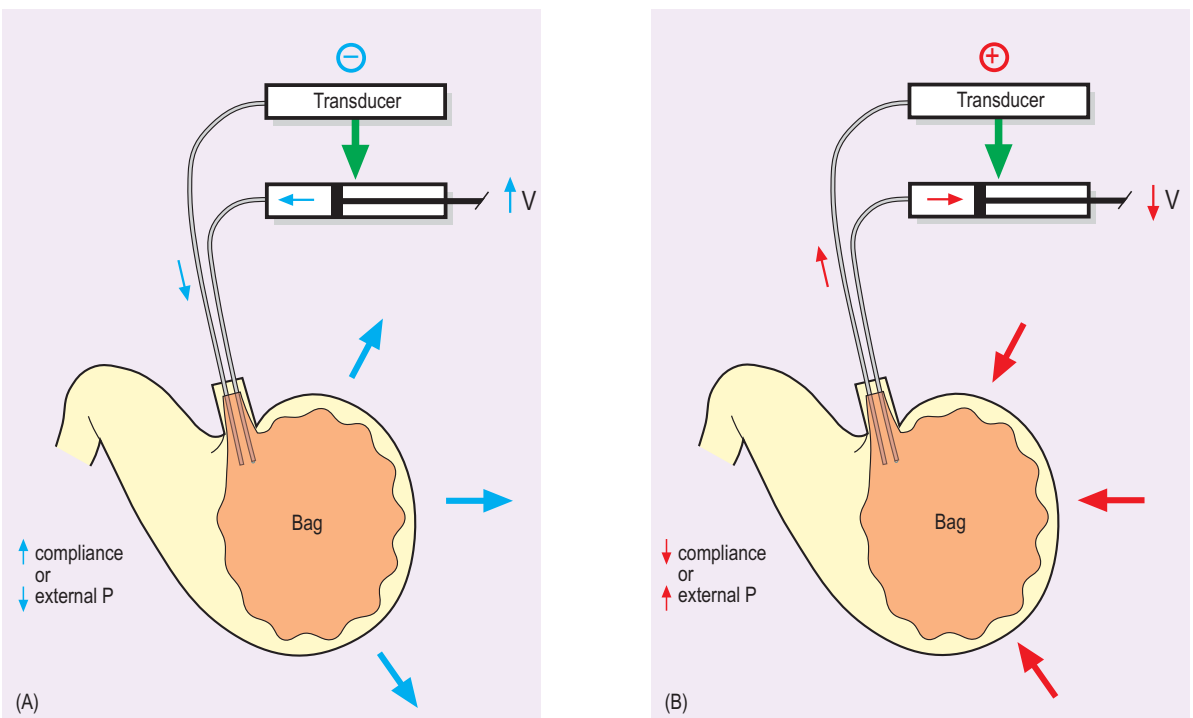


Fig. 46.1
Motility of the stomach can be indirectly measured by an electronic barostat. The barostat maintains a constant pressure (P) within an intra-gastric bag. When the stomach relaxes or the gastric wall becomes more compliant, the system injects air into the bag (panel A). Conversely, when the stomach contracts or the gastric wall becomes less compliant, air is aspirated from the bag (panel B). Changes in bag volume can also reflect changes in pressure exerted extraluminally upon the stomach. The same method could be applied to study motility at any site of the intestine.

difference between specific components of the diet and those found in feces, expressed as percent utilization. The effect of exercise on diet digestibility has been studied in horses.[30–32]

Barostat

The electronic barostat has been extensively used to document gastrointestinal motility in many species, including horses.[2,38–40] Unlike other methods, this system is more useful for recording changes in smooth muscle tone than active, phasic contractions. The principle of the barostat is to maintain a constant pressure within a plastic bag of infinite compliance, positioned within the lumen of the segment to be studied. When the internal pressure of the organ increases for any reason (e.g. contraction, increased mural tone), the barostat aspirates air from the bag to maintain the intrabag pressure constant. Conversely, when the internal pressure decreases, air is injected into the bag. Therefore, as the bag follows the movement of the visceral walls, changes in bag volume are an indirect measurement of changes in tone of the organ (Fig. 46.1).[41]

In other instances, changes in bag volume reflect changes in external pressure exerted over the organ containing the bag. As we mentioned earlier, we observed such changes in the proximal stomach of horses under a training session[2] and related them to increased intra-abdominal pressure caused by tensing of the abdominal muscles during exercise. Interestingly, we also observed in some horses relaxation of the proximal stomach soon after exercise (unpublished data). What effect this might have on gastric emptying, for instance, could provide some useful information concerning optimal timing of feeding with respect to a given exercise schedule.

Blood flow measurement

Adequate local perfusion is necessary for normal gut tissue activity, which requires oxygen and nutrients supplied by peripheral blood. Exercise leads to blood flow diversion from the GIT to the working skeletal muscles and the skin.[42] Decreased perfusion or ischemic damage may result in impairment of normal function of the gastrointestinal tissues, including mechanisms of mucosal protection, membrane secretory and absorptive functions, and motility.

The effect of short-term exercise on blood flow of abdominal organs has been measured in the horse, using radionuclide-labeled microspheres.[43] Once injected into the general circulation, the distribution of microspheres is proportional to the blood flow during its first transit through the circulation.[44,45] Consequent quantification of radioactivity within tissue preparations from horses that have been exercised indicates the level of regional blood flow to those tissues.

Additionally, hepatic blood flow can be quantified by intravenous infusion of a marker, such as, bromsulfalein (BSP). As BSP is highly extracted by the liver, hepatic clearance of BSP is mainly dependent on liver blood flow. Decreases in blood clearance of BSP have been attributed to exercise-induced splanchnic vasoconstriction, leading to decreased portal vein blood flow.[46]

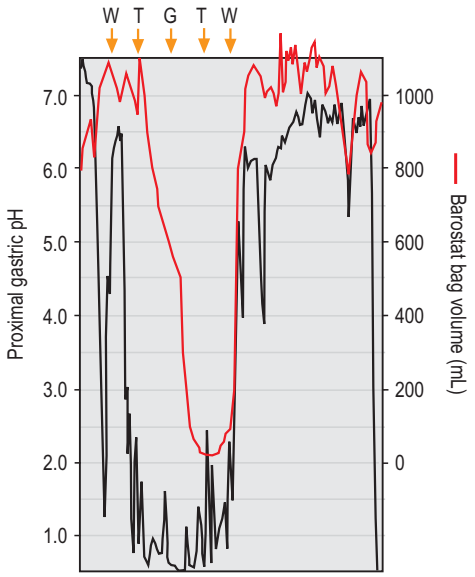


Fig. 46.2
Composite of continuous pH and intragastric barostat bag volume monitoring in two different horses respectively during exercise. In red: changes in intragastric pressure were indirectly measured by changes in volume of a bag placed within the proximal stomach, with its internal pressure constantly controlled at 6 mmHg by an electronic barostat. The decrease in volume indicates increased pressure > 6 mmHg on the bag. In black: intragastric pH was measured by a self-referencing pH electrode positioned 2 cm below the entrance of the stomach. Both patterns are characteristic responses to exercise. W, walk; T, trot; G, gallop.

Continuous pH monitoring

Continuous pH monitoring of the GIT luminal contents with a self-referencing pH electrode may be useful for tracking the effects of exercise on digestive function. The stomach and distal small colon are accessible without special preparation; other parts of the tract would need to be surgically cannulated. Continuous recording of pH changes within the proximal portion of the stomach has suggested that exposure of the squamous mucosa to hydrochloric acid is increased during exercise (Fig. 46.2).[2] There are no data in the literature that describe pH changes within the small colon in response to exercise. Such data have the potential to provide information about the effect of exercise on mucosal secretion, net electrolyte flux and fermentation activity within the large intestine.

Measurement of GI regulatory peptides and steroids

Modification of gastrointestinal regulatory peptides and steroids in response to exercise may either result in, or reflect changes in, gastrointestinal function. Some of these substances have been measured in horses under different exercise regimens, varying in type, intensity, and duration.

Exercise stimulates adrenal secretion and activity of the sympathetic autonomic nervous system. This stimulation is

reflected in increased plasma levels of ACTH, catecholamines, cortisol, and β-endorphins,[7,47–49] which are used as indices of physical stress. As the horse's fitness improves, these hormonal responses to exercise diminish.[50] Variations in plasma cortisol are more sensitive to duration of exercise, whereas ACTH and catecholamine levels are more closely correlated with exercise intensity.[7,51] The effect of variations of stress hormone levels upon equine gastrointestinal function is still unknown. In other species, cortisol can have a deleterious effect on mucosal immune function and epithelial permeability,[52] whereas catecholamines have the potential to delay gastric emptying, prolong transit time,[53,54] and decrease perfusion of the gastric mucosa.[55]

Gastrin is a major regulatory peptide of acid secretion, the plasma concentration of which was increased after prolonged exercise in the horse in one study,[56] but not in another.[57] In a third study, gastrin concentration did not increase after short, sprint exercise, but was higher postprandially in trained horses compared to non-trained horses.[58] Plasma concentrations of inhibitors of gastric acid secretion, such as somatostatin in man[59] and vasoactive intestinal polypeptide (VIP) in man[60] and horse,[56] may increase with exercise. Additionally, somatostatin may favor colonic electrolyte transport and inhibit nutrient absorption.[61]

Potential exercise-induced changes in fluid absorption and secretion within the gut may reflect changes in expression of some regulatory hormones, and vice versa. Exercise increases plasma levels of secretagogs, such as VIP and glucagon, in the horse,[56] and secretin, gastric inhibitory polypeptide, and prostaglandins in man.[59,62,63] On the other hand, atrial natriuretic peptide and aldosterone, which favor sodium absorption, also increase during prolonged exercise in horses.[48, 64]

Agents such as motilin,[65] neuropeptide Y[66] and prostaglandins[63] can affect motility and are released during endurance-type exercise in man. The effect of exercise on GI motility can, therefore, be indirectly studied by measuring endogenous expression of hormones that control intestinal motility.

Finally, alterations of hormone levels may result from a decrease in GIT blood flow, leading to decreased hepatic and renal clearance.[42] VIP[56] and arginine vasopressin[8] in horses, and endothelin-1[67] and angiotensin II[68] in other species, are released during exercise and act as vasoconstrictors. The resulting decrease in blood flow may affect function and regulation of the GIT.

Methods that could potentially be useful in horses, based upon experience in other species

Gastric motility and emptying

In contrast to the phenol red technique mentioned above, barium *contrast radiography*[69] and *scintigraphy*[70] have the advantage of non-invasiveness, and have been previously applied to equine studies. An additional advantage of the latter technique is the differentiation between solid- and liquid-phase emptying.

Breath tests employing stable isotopically labeled tracers are potentially very useful, since they are non-invasive, non-radioactive, and easy to perform (Fig. 46.3). As it empties the stomach, the ^{13}C-enriched marker is readily absorbed in the proximal intestine and metabolized to CO_2. Thus, breath $^{13}CO_2$ enrichment reflects the rate of GE of the labeled meal. The effect of exercise on GE of carbohydrate meals marked with ^{13}C acetate has been studied in humans.[71,72] The ^{13}C-octanoate breath test has been validated in the horse[73] and its use in exertional studies is promising.

Imaging of the stomach by ultrasound has shown that strenuous exercise disrupts gastric motility in man, although the examination was done right after, rather than during, the active exertion.[74] Another available technique in humans is electrogastrography (EGG), which consists of measuring

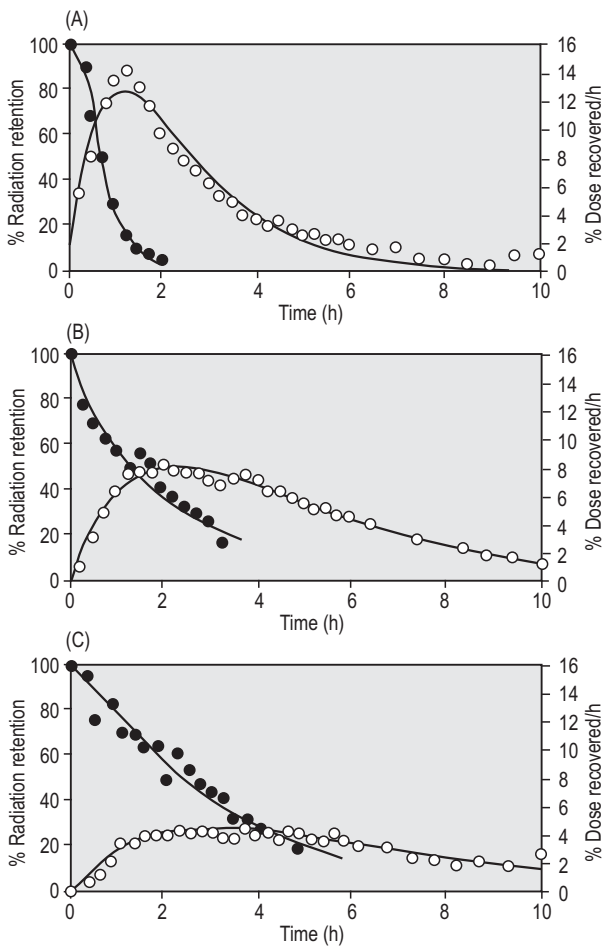


Fig. 46.3
Results of simultaneous ^{13}C-octanoic acid breath test and gastric radioscintigraphy in three typical cases. (A) Rapid gastric emptying rate ($T_{1/2}$ = 0.73 h). (B) Normal gastric emptying curve ($T_{1/2}$ = 1.34 h). (C) Slow gastric emptying pattern ($T_{1/2}$ = 2.62 h). Scintigraphic data (•) on the left y-axis and breath test data (○) on the right y-axis are plotted against time. The continuous lines represent a modeled fit. (Reproduced with kind permission from Sutton et al.[73])

gastric myoelectrical activity by electrodes positioned on the surface of the epigastrium.[75] Although both techniques as applied to the stomach are unsuitable in the horse for anatomic reasons, they could be potentially used to measure cecal motility percutaneously – also known as electrocecography[76] – during the recovery period after exercise.

Gastric secretion

Collection of gastric contents from cannulated dogs has allowed constant measurement of acid and pepsin during exercise.[36] This method could be useful in determining changes in acid secretion and other gastric components in cannulated horses. It would require that the animal be fasted, however.

Gastric ischemia

Air tonometry measures changes in luminal intragastric P_{CO_2} and seems to be a more reliable indicator of gastric ischemia than measuring splanchnic blood flow. Detection of ischemia is based on the difference between arterial P_{CO_2} and intragastric P_{CO_2}, which better reflects mucosal balance between needed and supplied levels of O_2.[77] It would be interesting to apply this technique to the horse.

Intestinal transit and motility

Mouth-to-cecum transit time can be measured by the *H_2 breath test* during exercise.[78,79] For this test, lactulose, a non-absorbable disaccharide, is added to the meal. Breath H_2 starts rising when lactulose reaches the cecum and is degraded by bacterial fermentation. Though fermenting bacteria are also present in the equine stomach and small intestine, the cecum and the large colon are the primary sites of microbial fermentation.[80] However, not all horses exhale excess hydrogen after ingestion of lactulose, so this technique may not be reliable.[81] Lactose, another disaccharide, has been used as a marker for H_2 breath test,[81] since adult horses appeared to be lactose intolerant.[82] Yet the presence of brush border lactase in the small intestine of adult horses has been recently reported,[83] and also excludes the usefulness of this sugar to measure oro–cecal transit time. The *lactose-^{13}C ureide breath test* (LUBT) is another method under investigation in horses. The labeled lactose ureide reaches the large intestine intact, where it is hydrolyzed by bacteria, producing ^{13}C-labeled CO_2. In contrast to the H_2 breath test, LUBT seems to be a repeatable and more reliable method.[84]

Motor activity of the intestinal tract can be studied by several invasive techniques. For example, *electrodes* implanted on the serosa of the gut can detect surface potentials or voltages generated by the gastrointestinal muscle. These electrodes measure two different patterns of electrical potentials: slow waves, which reflect basal electric rhythm, and action potentials, which correlate with contractions. By implantation of bipolar electrodes in dogs, slow wave patterns and the migrating motor complex (MMC) of the proximal jejunum have been studied in relation to exercise of different intensities.[85] This technique has certainly been successfully applied to horses,[86] but not, as yet, to evaluate the effects of exercise.

Strain gauge transducers have also been secured onto the serosa of the GI segment to be studied; they measure mechanical instead of myoelectrical activity. They detect unidirectional, isometric muscle contractions and monitor the stress/tension applied by these muscle contractions on them. Colonic MMCs have been evaluated during long-distance exercise in dogs using this method.[87] As with the serosally applied electrodes, this technique has been used successfully in horses,[88,89] but never in association with exercise.

Manometers and transducers are used to measure changes in intraluminal pressure, which are interpreted as contractions that generate them. This technique has been used to study changes in the small intestinal MMC in dogs during exercise.[36] Unlike the methods mentioned above, this technique does not need surgical implantation so long as the GIT section of interest is accessible by either mouth or anus.

Mucosal permeability and absorption

Intestinal permeability can be assessed non-invasively in vivo by *orally administered markers.* These markers are cleared unaltered by renal excretion, wherein their concentrations in urine can be quantified over a specified postfeeding time period to determine the amount absorbed. Appearance, or not, of these markers in the urine will depend on the integrity of the intestinal mucosa,[90] since they are not absorbed through the intact mucosa.

Polyethylene glycol (PEG) polymers of different molecular weights have been widely used for assessment of permeability. This marker is also used to determine net water absorption, which is calculated directly by changes in PEG concentration within the gut contents.[91] PEGs of high molecular weights have also been used as markers of gastrointestinal transit time in the horse.[92] PEG is not, however, an ideal marker for these kinds of studies, since its purported size can be somewhat variable, and too large a dose can induce an osmotic hypersecretion.[93]

Sugars are also commonly used as probes to evaluate intestinal integrity. Disaccharides, such as lactulose, and monosaccharides, such as L-rhamnose, D-xylose, 3-*O*-methyl-D-glucose and mannitol are used to assess both transcellular and paracellular transport capacity across the intestinal mucosa. Their natural transport across the epithelium may be impaired by cellular damage, whereas necrosis may facilitate their passive movement into the bloodstream due to compromise of the mucosal barrier. Sugars have been used in humans to study the effect of running and cycling on intestinal transport.[94,95] Agents such as these are preferable over PEG because of their uniformity of respective size, making them better discriminators at specific sites of GIT permeability. However, results of these tests should be regarded with caution when they are applied to the horse, since sugar absorption may be highly variable among individuals.[81] This variability most probably originates from regional variations in the GIT microbial population among horses, particularly in the stomach.[80]

Finally, isotopic tracers like ^{51}Cr-labeled ethylenediaminetetra-acetic acid (^{51}Cr-EDTA) and ^{99m}Tc-diethylenetriamino-

penta-acetate (^{99m}Tc-DTPA) can be added to drinks and used to measure unidirectional flux, from the intestinal lumen to the vascular compartment. Although the activity of these tracers in blood is readily measured, their radioactive character is a clear disadvantage[90] largely limiting application to a laboratory setting.

Exercise and gastrointestinal function: what is known in other species that is pertinent to horses

Gastric motility and emptying

Different GI symptoms occur in as many as 30–50% of human participants in endurance events.[96] Lower GI symptoms, which include diarrhea, rectal incontinence, urge to defecate, rectal bleeding, and abdominal cramps, are more common than upper GI symptoms, such as gastroesophageal reflux, nausea, vomiting, and stomach pain. A direct effect of exercise on GI motility has been hypothesized to explain many of these disorders. Because of this high prevalence and the severity of some of the symptoms, many experiments have focused on the study of GI motor function and transit. In the horse, exercise does not seem to directly result in signs of GI disturbance, but this observation should not exclude the possibility of GI alterations in response to the high demand imposed on the horse's body. Dehydration, musculoskeletal or metabolic disorders may mask mild GI tract dysfunction during long, intense exercise.

During moderate exercise (less than 75% $\dot{V}O_{2max}$), gastric emptying in man occurs at a rate similar or slightly greater than that during rest.[97] However, more intense exercise appears to inhibit gastric emptying.[17,97] In equine events where oral supplementation with electrolyte and carbohydrate solutions may be important to compensate a deficit of water, electrolytes, and carbohydrates, the rate of gastric emptying may limit the availability of administered fluids.[98] Solutions with higher carbohydrate concentration seem to delay gastric emptying in humans,[34] though increasingly larger volumes leave the stomach at faster rates.[33,99] Pyloric closure and reduced antral contractions, observed by ultrasound after exercise, may be in part responsible for the delay in GE in humans.[74] In horses, solid meals ingested before exercise may be retained within the stomach for prolonged periods, favoring their bacterial fermentation, with production of volatile fatty acids and lactic acid, which may be deleterious to the squamous gastric mucosa.[100] By contrast, GE of fluid does not seem to be affected by exercise. Sosa et al[35] reported that GE of a single dose of isotonic fluid administered after intense exercise (70% $\dot{V}O_{2\,max}$) in the horse did not differ from rest, which suggests that GE is not a limitation for rehydration. However, as discussed by the authors of this study, the results were highly variable, suggesting high measurement error due to the technique.[35]

Intestinal motility and transit

In humans, inactivity has often been considered a cause of constipation; conversely, physical activity seems to promote colonic transit. Soffer et al found that bicycle exercise could convert the motor-fed pattern of the small intestine into a migrating motor complex (MMC), and that this effect was intensity related, although there was no effect on oro–cecal transit time.[79] By contrast, Moses et al observed that moderate and intense treadmill exercise delayed small intestinal transit in humans.[101,102] In a study performed in fed dogs, moderate treadmill exercise decreased jejunal myoelectric activity only when exercise was prolonged beyond 30 minutes, and this inhibitory effect continued during recovery.[85] Furthermore, prolonged exercise induced MMCs characteristic of the interdigestive motor pattern in the jejunum of fed dogs,[85] whereas it can interrupt MMCs in the stomach and duodenum of fasted dogs.[36] Therefore, exercise can alter motor activity, which may explain some of the GI symptoms associated with exercise in humans.

Increased stool frequency and diarrhea induced by strenuous exercise in humans has been attributed to accelerated colonic transit time, or alternatively, to changes in absorption/secretion by the intestinal epithelium.[96] Acute graded bicycle exercise decreases colonic phasic motor activity in an intensity-dependent way. This may facilitate transit by offering less resistance to colonic flow. After the end of exercise, propagated activity is increased, and this also may enhance colonic propulsion.[103] In fasted dogs, exercise decreases the frequency of colonic MMCs, and stimulates non-migrating colonic contractile activity within 3 hours after ingestion of a meal. Exercise also stimulates defecation, giant migrating contractions and mass movements in the colon, in both fasted and postprandial states.[87]

Current knowledge regarding exercise-induced changes in GI motility in the horse is meager. Pearson and Merritt studied the effect of a 14-km walk in donkeys, and neither GI transit nor the digestibility of hay was affected.[30] On the other hand, Pagan et al showed that 8 km of trotting and galloping by a group of Thoroughbreds resulted in a small, but significant decrease in dry matter digestibility, whereas transit rates of both a forage diet and a forage/grain diet were increased at 24 hours after the exercise.[32] Finally, Orton et al studied the effect of 12-km daily trotting in yearling horses. Exercise increased apparent digestibility of dry matter, and increased the transit rate of particulates, but decreased the transit rate of the fluid phase (Fig. 46.4).[31]

As mentioned, release of catecholamines and β-endorphins into the bloodstream, and stimulation of the sympathetic nervous system occur in the horse and in other species in response to exercise. This effect correlates with intensity of exercise and diminishes with continued training.[47–50] Each of the components of this stress response affects gastrointestinal

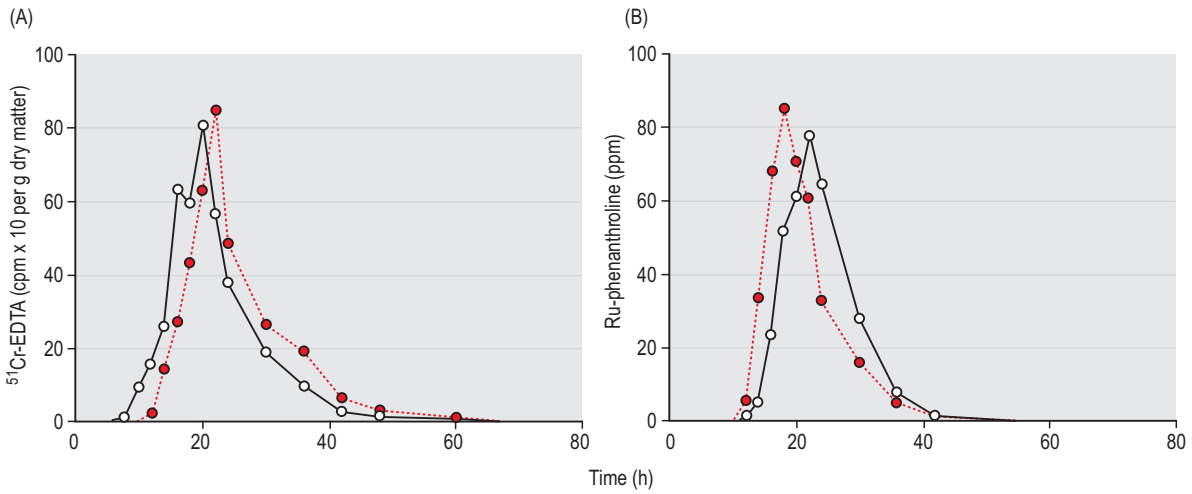


Fig. 46.4
Effect of exercise on rate of passage of fluid (A) and particulate (B) digesta.
(A) Concentration of ^{51}Cr-EDTA in the feces of exercised (broken red line) and non-exercised (solid black line) yearling horses. Four animals per group. (B) Concentration of ruthenium (Ru)-phenanthroline in the feces of exercised (broken red line) and non-exercised (solid black line) yearling horses. Four animals per group. Exercise: 12 km trotting at 12 km/h. Transit of the fluid phase marker (A) was delayed in exercised horses, whereas transit of the particulate phase marker (B) was accelerated. These results are supported by Pagan et al,[32] who observed that fecal excretion of the particulate marker ytterbium was accelerated in Thoroughbreds trotted and galloped for 8 km/day. (Reproduced with kind permission from Orton et al.[31])

motor function. Inhibition of gastric emptying and stimulation of colonic motor function are the characteristic pattern in response to different stressors. Central CRH seems to be a main component in the induction of this stress-related motor response. In some studies, CRH modulation of autonomic nervous system activity was found to be independent of activation of pituitary–adrenal hormone release.[104] Alexander et al measured plasma concentrations of CRH and ACTH in the horse during and after acute intense exercise; ACTH was elevated, whereas CRH concentrations were not different from resting values.[8] However, as suggested above, central rather than peripherally circulating CRH may be responsible for the GI motor changes[104] and could be involved in the exercise-induced changes in GI transit documented in horses.[31,32]

Gastrointestinal blood supply

Reduced splanchnic blood flow during high-intensity exercise may also play a role in slowing the rate of gastric emptying. Manohar et al reported a significant reduction in splanchnic blood flow during moderate exercise in the horse (Fig. 46.5).[43] Likewise, acute exercise decreased the clearance of BSP from the blood in an intensity-dependent manner in horses as a result of decreased splanchnic blood flow (Fig. 46.6).[46] Splanchnic vasoconstriction in the horse may be induced by epinephrine (adrenaline) and norepinephrine (noradrenaline),[7] or by release of hormones such as arginine vasopressin,[8] and VIP.[56] Endothelin, another potent vasoconstrictor released by endothelial cells, increases with exercise in humans[105] and horses.[106] Its effect should be further investi-

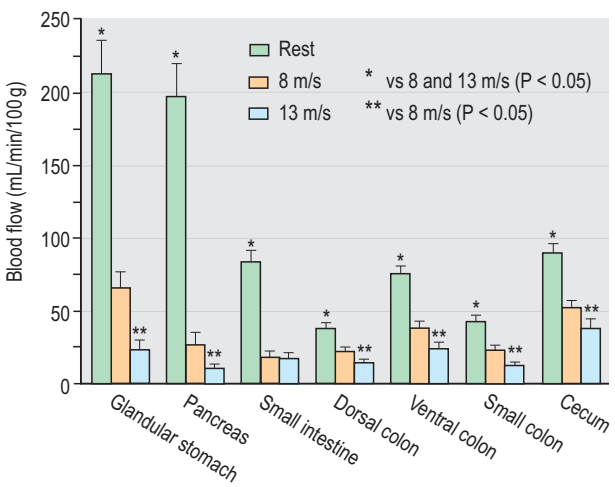


Fig. 46.5
Blood flow to pancreas and various gastrointestinal tract tissues in standing (rest) and exercised horses (n = 9 horses). (Reproduced with kind permission from Manohar et al.[43])

gated in horses, especially in view of a recent study that demonstrated a significant association between plasma endothelin-like immunoreactivity and pathogenesis of certain GIT disorders.[107]

Reduced blood flow during exercise also disrupts intestinal absorption. Carrier-mediated glucose uptake decreased with intense cycling in humans.[108] This decrease in absorptive capacity may be a consequence of impaired blood flow and insufficient energetic supply for glucose active transport, which relies on ATPase activity, and could: (i) prevent adequate plasma volume restitution, or; (ii) increase osmotic pressure within the

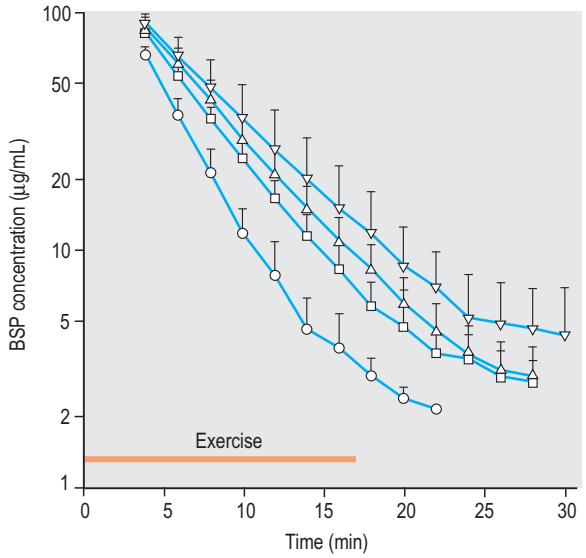


Fig. 46.6
Mean (±SD) plasma concentrations of bromsulfalein (BSP) for eight horses exercising on a treadmill at four intensities. Bromsulfalein (5 mg/kg of bodyweight) was administered, i.v., during a 45- to 60-second period. ○, Resting; □, 40% $\dot{V}O_{2max}$; Δ, 60% $\dot{V}O_{2max}$; ∇, 80% $\dot{V}O_{2max}$. (Reproduced with kind permission from Dyke et al.[46])

gut, which could result in diarrhea or loose stools.[42,109] On the other hand, 1 hour of exercise on a treadmill at 71% $\dot{V}O_{2max}$ did not affect glucose, D-xylose, water, sodium, chloride and bicarbonate intestinal uptake in humans.[110] In the horse, impaired glucose absorption could lead to its accumulation within the intestinal lumen, creating an osmotic load and/or an increase in the substrate available for bacterial digestion within the large intestine. However, it is unlikely that this would have any significant detrimental effects on the animal.

Mechanical factors

Mechanical bouncing of the body during exercise or compression of the viscera by abdominal muscles may also affect GI motility, since GI symptoms in humans occur more frequently during running than cycling events. Some cases of postrunning volvulus have been reported in humans.[109] Although light exercise has often been used as a way to facilitate passage of gas and promote transit in the large intestine of sick horses, strenuous exercise may promote excessive visceral movement. This, especially if combined with GIT dysmotility, could potentially promote intestinal displacement. The amount of colonic filling could have an influence on this bouncing effect.

Increased concentrations of prostaglandins and VIP, released by rubbing of the intestinal mucosa and distension,[109] may shift intestinal absorption into secretion. Upregulated expression of these agents in the horse, especially within the distal large intestine, could theoretically result in diarrhea.

Mucosal barrier integrity

Fecal occult blood has been documented repeatedly in endurance athletes, but its etiology is still unknown. However, the stomach is the most frequent site of running-associated hemorrhage in humans, possibly due to ischemic damage or trauma from the diaphragm.[96] Bleeding may reflect pronounced tissue damage. Inadequate perfusion to the intestinal epithelium can compromise the protective barrier function. Compromised barrier function might also facilitate bacterial and endotoxin translocation and initiate a local immune response. Subsequent production and release of inflammatory mediators would exacerbate this whole process. Reduced mesenteric blood flow may also generate O_2 free radicals,[111] which can also contribute to tissue damage. For example, running by some human subjects at 80% $\dot{V}O_{2max}$ increased small intestinal permeability of lactulose compared with rest and running at 40 and 60% $\dot{V}O_{2max}$. Since lactulose crosses the epithelium only paracellularly, its increased transport is a strong indication of breakdown of the small intestinal barrier.[112] To date, no studies have been done to investigate the effect of exercise on the integrity of the mucosal barrier in horses.

Clinical implications of exercise-associated changes in gastrointestinal function

As has already been alluded to, the anatomically and physiologically complex ceco-colon of horses could, in particular, predispose them to GIT disturbances during athletic training and competition. Undoubtedly a major confounding factor in this consideration is the feeding program, especially abrupt changes in diet composition or feeding routine. In fact, with respect to incidence of colic, the majority of the recent epidemiologic studies more strongly indicate change in feeding program than type or duration of athletic activity as a high risk factor.[113–117] Concerning the effect of exercise, Cohen et al[114] reported that primary use of the horse was not significantly associated with colic, although they then remarked that horses with colic were significantly more likely than control horses to have had a change in activity level during the 2-week period prior to examination. Likewise, Tinker et al[116] found that horses used for eventing or training had a significantly higher incidence rate of colic when compared to mature horses that were sedentary. This is not to say that the origin of the problem in all these cases was large intestinal (there was no information on site in the report) but, because of that organ's complexity, it must be considered as a highly likely origin nonetheless.

Anatomic considerations

From an anatomic standpoint, the fact that a large section of mid-colon floats freely within the abdominal cavity makes it

prone to various forms of displacement that can result in serious colic. Whether any of these conditions may result from, for example, a combination of physical characteristics of the contents therein (e.g. collected sand; the gas : ingesta ratio) and type of exercise the horse is asked to perform remains to be established.

Physiologic considerations

From a physiologic standpoint, at least three areas deserve attention in future research on the effects of exercise on GIT function in horses. The first concerns factors that determine daily net water movement across the gut mucosa, between lumen and plasma. It is a common practice to withhold food hours before an event to decrease gut fill, and consequently, bodyweight. However, eating before or during a competition may have beneficial effects, as observed in human endurance athletes.[118] Ingestion of food may attenuate the reduction in blood flow induced by moderate to severe exercise.[119] Accordingly, blood flow to the digestive tract during exercise seems to be higher in fed than fasted ponies.[119] Fed horses may start with elevated blood flow of the GI tract, so that the impact of exercise on blood distribution is not so marked. Ingestion of food is accompanied by saliva production, and gastric and pancreatic secretion.

Forage stimulates more water ingestion and digestive secretions than concentrate meals.[120] Factors which determine daily net water flux across ceco-colonic mucosa are complex and are characterized by regional compartmentalization.[121] Such factors include timing and composition of ingested food which impact directly on fermentative activity, water and electrolyte status of the horse, and efficacy of gastrointestinal motility. For instance, Clarke et al have shown that during early postprandial stages of a large meal of balanced ration pellets, the VFA production from its fermentation within the colons may outstrip the subsequent VFA absorption, resulting in a large flux of water into the colonic lumen from the plasma space.[122] This can deplete plasma volume to a point where renin–angiotensin and aldosterone are released to promote plasma water conservation, the degree of which may be great enough to result in significant rebound dehydration of distal colonic contents (Fig. 46.7).[123] Combine a strenuous training session on top of this, and you have the makings of a serious impaction. By contrast, when that same meal was split into small volumes and given over 12 hours, mass movement of plasma water into the colons did not occur.[122]

Second, the effect of exercise on increasing GI mucosal permeability in humans has been discussed earlier in the chapter. So far, no untoward effects from this have been documented in people, and this would certainly appear to be the same for horses, should it occur. However, it is safe to assume that there is, at any given time, a much greater load of endotoxin within the equine ceco-colonic lumen than in that of humans.[124] Detrimental effects of endotoxemia in horse are well recognized and include leukopenia, hypotension, intestinal dysmotility and hypersecretion, and laminitis.[124,125] Clearly, if athletic activities consistently caused signs indicative of endotoxemia in a large number of horses, the beast would not be used for the many things humans ask of it. However, it would still be important to know if exercise,

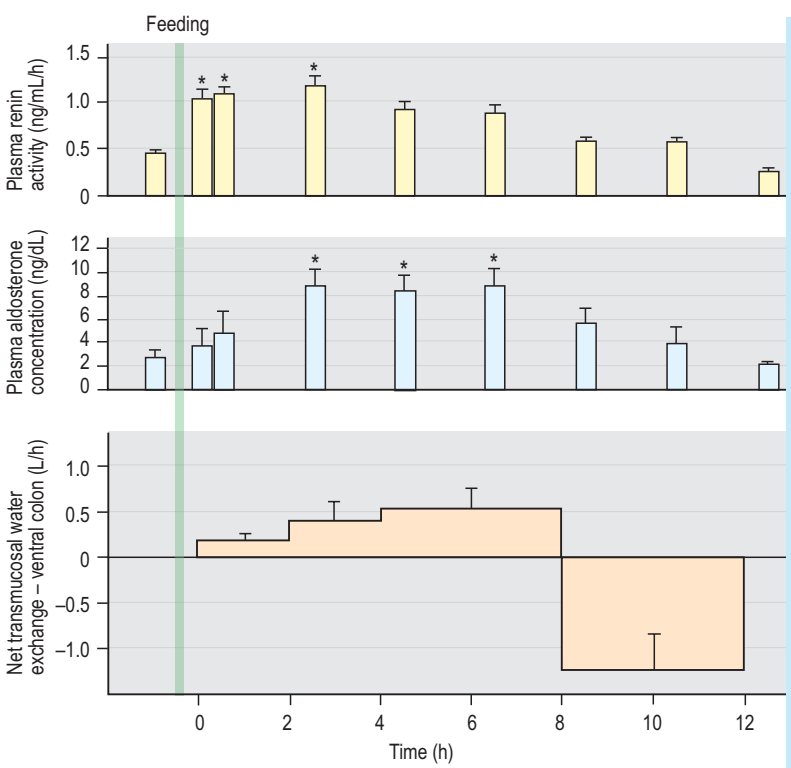


Fig. 46.7
Postprandial activation of the renin–angiotensin–aldosterone system superimposed on net fluid transport in pony ventral colon. Rapid accumulation of bacterially produced volatile fatty acids within the colon after ingestion of a single large meal results in net flux of water from the plasma compartment into the colonic lumen. In response to this plasma volume depletion, renin–angiotensin and aldosterone are released to promote water absorption from the luminal compartment back into the vascular system. Addition of strenuous exercise during this period could exacerbate dehydration of colonic contents, and therefore, increase the risk of colonic impaction. [*Significantly ($P < 0.05$) greater than preceding value.] (Reproduced with kind permission from White.[123])

especially if strenuous, does cause a degree of endotoxemia that could be clinically important.[126] This suggestion is further supported by the observation that physical stress enhances colonic epithelial permeability in rats via peripheral release of CRH.[127] Accordingly, Baker et al[128] reported in 1988 that a group of racing-fit horses had significantly higher serum anti-lipopolysaccharide antibody concentrations than a similar group of horses that were not trained, suggesting that increased intestinal permeability could have occurred as a result of their repeated exertion. More studies following up on this important observation need to be done.

Third, the transient defecation of non-formed, sometimes quite watery feces from some horses when they are subjected to a training session or race environment is a well-recognized phenomenon. It is usually of little consequence to the horse, but can be very bothersome to owners and trainers, especially when it occurs during a public display. Commonly, it is attributed to 'nerves,' which could be one reasonable explanation. Nonetheless, this is an exercise-related event and it would be interesting to know its functional basis because it might be controllable. Probably the first place to look would be the small colon, where final desiccation of colonic contents takes place resulting in the formation of the fecal balls. This process involves a coordinated interaction between mechanisms that control motility and net transmucosal water flux; this is undoubtedly closely monitored by the enteric nervous system, much of which we still need to learn about with respect to equine small colon function. What we do know is that at least some of the water absorption is determined by a Na^+/K^+-ATPase pump, the functional status of which is under the control of aldosterone.[25] It seems unlikely, however, that the transient, exercise-related loose feces problem would be due to a downregulation of this system. More likely possibilities would be either a small colon dysmotility that allows more rapid passage of contents through the organ, the upregulation of a secretagog such as CRH, VIP, or some combination thereof.[56,104,126,127]

References

1. Houpt KA. Biological rhythms and behavior. In: Houpt KA ed. Domestic animal behavior for veterinarians and animal scientists. 3rd edn. Ames: Iowa State University Press; 1998: 95–98.
2. Lorenzo-Figueras M, Merritt AM. Effects of exercise on gastric volume and pH in the proximal portion of the stomach of horses. Am J Vet Res 2002; 63:1481–1487.
3. Clark CS, Kraus BB, Sinclair J, et al. Gastroesophageal reflux induced by exercise in healthy volunteers. JAMA 1989; 261:3599–3601.
4. Porter AM. Case report: marathon running and the caecal slap syndrome. Br J Sports Med 1982; 16:178.
5. Soffer EE, Merchant RK, Duethman G, et al. Effect of graded exercise on esophageal motility and gastroesophageal reflux in trained athletes. Dig Dis Sci 1993; 38:220–224.
6. Soffer EE, Wilson J, Duethman G, et al. Effect of graded exercise on esophageal motility and gastroesophageal reflux in nontrained subjects. Dig Dis Sci 1994; 39:193–198.
7. Nagata S, Takeda F, Kurosawa M, et al. Plasma adrenocorticotropin, cortisol and catecholamines response to various exercises. Equine Vet J 1999; Suppl 30:570–574.
8. Alexander SL, Irvine CH, Ellis MJ, et al. The effect of acute exercise on the secretion of corticotropin-releasing factor, arginine vasopressin, and adrenocorticotropin as measured in pituitary venous blood from the horse. Endocrinology 1991; 128:65–72.
9. Begaut M. Occurrence, absorption and metabolism of short chain fatty acids in the digestive tract of mammals. Comp Biochem Physiol 1987; 86B:439–472.
10. Campbell-Thompson ML, Merritt AM. Basal and histamine-stimulated gastric secretion in young horses. Am J Physiol 1990; 259:R1259–R1266.
11. Birschneider H, Blikslager AT, Roberts MC. Role of duodenal reflux in nonglandular gastric ulcer disease of the mature horse. Eq Vet J 1999; Suppl 29:24–29.
12. Widenhouse TV, Lester GD, Merritt AM. Effect of hydrochloric acid, pepsin, or taurocholate on bioelectrical properties of gastric squamous mucosa of horses. Am J Vet Res 2002; 63:744–749.
13. Andrews FM, Sifferman RL, Bernard W, et al. Efficacy of omeprazole paste in the treatment and prevention of gastric ulcers in horses. Eq Vet J 1999; Suppl 29:81–86.
14. Alexander F, Hickson JCD. The salivary and pancreatic secretion of the horse. In: Phillipson AT, ed. Physiology of digestion and metabolism in the ruminant. Newcastle upon Tyne: Oriel Press; 1970; 375–389.
15. Merritt AM. Normal equine gastroduodenal secretion and motility. Eq Vet J 1999; Suppl 29:7–13.
16. Merritt AM, Cimprich RE, Beech J. Granulomatous enteritis in nine horses. JAVMA 1976; 169:603–609.
17. Leiper JB, Broad NP, Maughan RJ. Effect of intermittent high-intensity exercise on gastric emptying in man. Med Sci Sports Exerc 2001; 33:1270–1278.
18. Lorenzo-Figueras M, Jones G, Merritt AM. Effects of various diets on gastric tone in the proximal portion of the stomach of horses. Am J Vet Res 2002; 63:1275–1278.
19. Mayer EA. The physiology of gastric storage and emptying. In: Johnson LR, ed. Physiology of the gastrointestinal tract, 3rd edn. New York: Raven; 1994: 929–976.
20. Soderholm JD, Perdue MH. Stress and gastrointestinal tract. II. Stress and intestinal barrier function. Am J Physiol 2001; 280:G7–G13.
21. Sanderson IR. Nutritional factors and immune functions of gut epithelium. Proc Nutr Soc 2001; 60:443–447.
22. Shao L, Serrano D, Mayer L. The role of epithelial cells in immune regulation in the gut. Immunology 2001; 13:163–175.
23. Campbell NB, Blikslager AT. The role of cyclooxygenase inhibitors in repair of ischaemic-injured jejunal mucosa in the horse. Equine Vet J 2000; Suppl 32:59–64.
24. Campbell NB, Jones SL, Blikslager AT. The effects of cyclo-oxygenase inhibitors on bile-injured and normal equine colon. Equine Vet J 2002; 34:493–498.
25. Clarke LL, Roberts MC, Grubb BR, et al. Short-term effect of aldosterone on Na–Cl transport across equine colon. Am J Physiol 1992; 262:R939–R946.
26. Freeman DE. In vitro concentrative accumulation of D-xylose by jejunum from horses and rabbits. Am J Vet Res 1993; 54:965–969.
27. Freeman DE, Inoue OJ, Eurell TE. Effects of flunixin meglumine on short circuit current in equine colonic mucosa in vitro. Am J Vet Res 1997; 58:915–919.
28. Inoue OJ, Freeman DE, Wallig M. Effects of hypochlorous acid and ascorbic acid on conductance, permeability, and

structure of equine colonic mucosa in vitro. Am J Vet Res 1998; 59:82–87.
29. Engleking LR, Anwer MS. Liver and biliary tract. In: Anderson NV, ed. Veterinary gastroenterology, 2nd edn. Philadelphia: Lea and Febiger, 1992:211–274.
30. Pearson RA, Merritt JB. Intake, digestion and gastrointestinal transit time in resting donkeys and ponies and exercised donkeys given ad libitum hay and straw diets. Equine Vet J 1991; 23:339–343.
31. Orton RK, Hume ID, Leng RA. Effects of exercise and level of dietary protein on digestive function in horses. Equine Vet J 1985; 17:386–390.
32. Pagan JD, Harris P, Brewster-Barnes T, et al. Exercise affects digestibility and rate of passage of all-forage and mixed diets in thoroughbred horses. J Nutr 1998; 128 (suppl):2704S–2707S.
33. Mitchell JB, Voss KW. The influence of volume on gastric emptying and fluid balance during prolonged exercise. Med Sci Sports Exerc 1991; 23:314–319.
34. Owen MD, Kregel KC, Wall PT, et al. Effects of ingesting carbohydrate beverages during exercise in the heat. Med Sci Sports Exerc 1986; 18:568–575.
35. Sosa León LA, Hogdson DR, Rose RJ. Gastric emptying of oral rehydration solutions at rest and after exercise in horses. Res Vet Sci 1997; 63:183–187.
36. Kondo T, Naruse S, Hayakawa T, et al. Effect of exercise on gastroduodenal functions in untrained dogs. Int J Sports Med 1994; 15:186–191.
37. Drogoul C, de Fombelle A, Julliand V. Feeding and microbial disorders in horses: 2: Effect of three hay : grain ratios on digesta passage rate and digestibility in ponies. JEVS 2001; 21:487–491.
38. Azpiroz F, Malagelada JR. Physiological variations in canine gastric tone measured by an electronic barostat. Am J Physiol 1985; 248:G229–G237.
39. Desai KM, Sessa WC, Vane JR. Involvement of nitric oxide in the reflex relaxation of the stomach to accommodate food or fluid. Nature 1991; 351:477–479.
40. Vu MK, Straathof JW, v d Schaar PJ, et al. Motor and sensory function of the proximal stomach in reflux disease and after laparoscopic Nissen fundoplication. Am J Gastroenterol 1999; 94:1481–1489.
41. Whitehead W, Delvaux M. Standardization of barostat procedures for testing smooth muscle tone and sensory thresholds in the gastrointestinal tract. Dig Dis Sci 1997; 42:223–241.
42. Brouns F, Saris WH, Rehrer NJ. Abdominal complaints and gastrointestinal function during long-lasting exercise. Int J Sports Med 1987; 8:175–189.
43. Manohar M, Goetz TE, Saupe B, et al. Thyroid, renal, and splanchnic circulation in horses at rest and during short-term exercise. Am J Vet Res 1995; 56: 1356–1361.
44. Reddy VK, Kammula RG, Randolph A, et al. Regional blood flow to the stomach and small intestine in ponies. Am J Vet Res 1977; 38:2047–2048.
45. Neutze JM, Wyler F, Rudolph AM. Use of radioactive microspheres to assess distribution of cardiac output in rabbits. Am J Physiol 1968; 215:486–495.
46. Dyke TM, Sams RA, Hinchcliff KW. Intensity-dependent effects of acute submaximal exercise on the pharmacokinetics of bromsulphalein in horses. Am J Vet Res 1998; 59:1481–1487.
47. Golland LC, Evans DL, Stone GM, et al. Maximal exercise transiently disrupts hormonal secretory patterns in standardbred geldings. Equine Vet J Suppl 1999; 30:581–585.
48. Kokkonen UM, Poso AR, Hyyppa S, et al. Exercise-induced changes in atrial peptides in relation to neuroendocrine responses and fluid balance in the horse. J Vet Med A Physiol Pathol Clin Med 2002; 49:144–150.
49. Mehl ML, Sarkar DK, Schott HC 2nd, et al. Equine plasma beta-endorphin concentrations are affected by exercise intensity and time of day. Equine Vet J Suppl 1999; 30:567–569.
50. McCarthy RN, Jeffcott LB, Funder JW, et al. Plasma beta-endorphin and adrenocorticotrophin in young horses in training. Aust Vet J 1991; 68:359–361.
51. Desmecht D, Linden A, Amory H, et al. Relationship of plasma lactate production to cortisol release following completion of different types of sporting events in horses. Vet Res Commun 1996; 20:371–379.
52. Soderholm JD, Perdue MH. Stress and gastrointestinal tract. II. Stress and intestinal barrier function. Am J Physiol Gastrointest Liver Physiol 2001; 280:G7–G13.
53. Jenkinson DH, Morton IK. The role of alpha- and beta-adrenergic receptors in some actions of catecholamines on intestinal smooth muscle. J Physiol 1967; 188: 387–402.
54. Rees MR, Clark RA, Holdsworth CD, et al. The effect of beta-adrenoceptor agonists and antagonists on gastric emptying in man. Br J Clin Pharmacol 1980; 10:551–554.
55. Holzer P, Livingston EH, Paul HG. Neural, metabolic, physical, and endothelial factors in the regulation of the gastric circulation. In: Johnson LR, ed. Physiology of the gastrointestinal tract, 3rd edn. New York: Raven; 1994:1311–1329.
56. Hall GM, Adrian TE, Bloom SR, et al. Changes in circulating gut hormones in the horse during long distance exercise. Equine Vet J 1982; 14:209–212.
57. Sandin A, Girma K, Sjoholm B, et al. Effects of differently composed feeds and physical stress on plasma gastrin concentration in horses. Acta Vet Scand 1998; 39:265–272.
58. Furr M, Taylor L, Kronfeld D. The effects of exercise training on serum gastrin responses in the horse. Cornell Vet 1994; 84:41–45.
59. Hilsted J, Galbo H, Sonne B, et al. Gastroenteropancreatic hormonal changes during exercise. Am J Physiol 1980; 239:G136–G140.
60. MacLaren DP, Raine NM, O'Connor AM, et al. Human gastrin and vasoactive intestinal polypeptide responses to endurance running in relation to training status and fluid ingested. Clin Sci (Lond) 1995; 89:137–143.
61. Walsh JH. Gastrointestinal hormones. In: Johnson LR, ed. Physiology of the gastrointestinal tract, 3rd edn. New York: Raven; 1994:1–128.
62. Hurley RS, Bossetti BM, O'Dorisio TM, et al. The effect of exercise training on bodyweight and peptide hormone patterns in normal weight college-age men. J Sports Med Phys Fitness 1991; 31:52–56.
63. Demers LM, Harrison TS, Halbert DR, et al. Effect of prolonged exercise on plasma prostaglandin levels. Prostaglandins Med 1981; 6:413–418.
64. Schott HC 2nd, McGlade KS, Molander HA, et al. Bodyweight, fluid, electrolyte, and hormonal changes in horses competing in 50- and 100-mile endurance rides. Am J Vet Res 1997; 58:303–309.
65. Sullivan SN, Champion MC, Cristophides ND, et al. Gastrointestinal regulatory responses in long-distance runners. Phys Sportsmed 1984; 12:78–82.
66. Saelsen L, Andersen HB, Bratholm P, et al. Radioimmunoassay of plasma neuropeptide Y using HPLC for separation of related peptides and fragments. Scand J Clin Lab Invest 1994; 54:207–214.

67. Maeda S, Miyauchi T, Waku T, et al. Plasma endothelin-1 level in athletes after exercise in a hot environment: exercise-induced dehydration contributes to increases in plasma endothelin-1. Life Sci 1996; 58: 1259–1268.
68. Stebbins CL, Symons JD. Role of angiotensin II in hemodynamic responses to dynamic exercise in miniswine. J Appl Physiol 1995; 78:185–190.
69. Ross MW, Donawick WJ, Sellers AF, et al. Normal motility of the cecum and right ventral colon in ponies. Am J Vet Res 1986; 47:1756–1762.
70. Lohmann KL, Roussel AJ, Cohen ND, et al. Comparison of nuclear scintigraphy and acetaminophen absorption as a means of studying gastric emptying in horses. Am J Vet Res 2000; 61:310–315.
71. Mudambo KS, Leese GP, Rennie MJ. Gastric emptying in soldiers during and after field exercise in the heat measured with the [^{13}C]acetate breath test method. Eur J Appl Physiol Occup Physiol 1997; 75:109–114.
72. van Nieuwenhoven MA, Wagenmakers AJ, Senden JM, et al. Performance of the [^{13}C]acetate gastric emptying breath test during physical exercise. Eur J Clin Invest 1999; 29:922–928.
73. Sutton DG, Bahr A, Preston T, et al. Validation of the ^{13}C-octanoic acid breath test for measurement of equine gastric emptying rate of solids using radioscintigraphy. Equine Vet J 2003; 35:27–33.
74. Brown BP, Ketelaar MA, Schulze-Delrieu K, et al. Strenuous exercise decreases motility and cross-sectional area of human gastric antrum. A study using ultrasound. Dig Dis Sci 1994; 39:940–945.
75. Koch KL, Stern RM. Functional disorders of the stomach. Semin Gastrointest Dis 1996; 7:185–195.
76. Sasaki N, Mizuno Y, Yoshihara T. The application of electrocecography for evaluation of cecum motility in horses. J Vet Med Sci 1998; 60:1221–1226.
77. Otte JA, Oostveen E, Geelkerken RH, et al. Exercise induces gastric ischemia in healthy volunteers: a tonometry study. J Appl Physiol 2001; 91:866–871.
78. Kayaleh RA, Meshkinpour H, Avinashi A, et al. Effect of exercise on mouth-to-cecum transit in trained athletes: a case against the role of runners' abdominal bouncing. J Sports Med Phys Fitness 1996; 36:271–274.
79. Soffer EE, Summers RW, Gisolfi C. Effect of exercise on intestinal motility and transit in trained athletes. Am J Physiol 1991; 260:G698–G702.
80. Argenzio RA, Southworth M, Stevens CE. Sites of organic acid production and absorption in the equine gastrointestinal tract. Am J Physiol 1974; 226:1043–1050.
81. Murphy D, Reid SW, Love S. Breath hydrogen measurement in ponies: a preliminary study. Res Vet Sci 1998; 65:47–51.
82. Roberts MC. Carbohydrate digestion and absorption studies in the horse. Res Vet Sci 1975; 18:64–69.
83. Dyer J, Fernandez-Castano Merediz E, Salmon KS, et al. Molecular characterisation of carbohydrate digestion and absorption in equine small intestine. Equine Vet J 2002; 34:349–358.
84. Sutton DGM, Preston T, Love S. Comparison of lactose-[^{13}C]ureide and hydrogen breath exhalation tests for the measurement of equine gastrointestinal transit time. In: BEVA Congress. Newmarker, Suffolk, UK: British Equine Veterinary Association (BEVA); 2000:212, (abstract).
85. Kenney MJ, Flatt A, Summers RW, et al. Changes in jejunal myoelectrical activity during exercise in fed untrained dogs. Am J Physiol 1988; 254:G741–G747.
86. Merritt AM, Campbell-Thompson ML, Lowrey S. Effect of xylazine treatment on equine proximal gastrointestinal tract myoelectrical activity. Am J Vet Res 1989; 50:945–949.
87. Dapoigny M, Sarna SK. Effects of physical exercise on colonic motor activity. Am J Physiol 1991; 260:G646–G652.
88. Eades SC, Moore JN. Blockade of endotoxin-induced cecal hypoperfusion and ileus with an alpha 2 antagonist in horses. Am J Vet Res 1993; 54:586–590.
89. King JN, Gerring EL. The action of low dose endotoxin on equine bowel motility. Equine Vet J 1991; 23:11–17.
90. Bjarnason I, MacPherson A, Hollander D. Intestinal permeability: an overview. Gastroenterology 1995; 108:1566–1581.
91. Gisolfi CV, Summers RW, Schedl HP, et al. Human intestinal water absorption: direct vs. indirect measurements. Am J Physiol 1990; 258:G216–G222.
92. Roberts MC, Argenzio A. Effects of amitraz, several opiate derivatives and anticholinergic agents on intestinal transit in ponies. Equine Vet J 1986; 18:256–260.
93. Hammer HF, Santa Ana CA, Schiller LR, et al. Studies of osmotic diarrhea induced in normal subjects by ingestion of polyethylene glycol and lactulose. J Clin Invest 1989; 84:1056–1062.
94. Lambert GP, Broussard LJ, Mason BL, et al. Gastrointestinal permeability during exercise: effects of aspirin and energy-containing beverages. J Appl Physiol 2001; 90:2075–2080.
95. Van Nieuwenhoven MA, Brummer RM, Brouns F. Gastrointestinal function during exercise: comparison of water, sports drink, and sports drink with caffeine. J Appl Physiol 2000; 89:1079–1085.
96. Moses FM. The effect of exercise on the gastrointestinal tract. Sports Med 1990; 9:159–172.
97. Neufer PD, Young AJ, Sawka MN. Gastric emptying during walking and running: effects of varied exercise intensity. Eur J Appl Physiol Occup Physiol 1989; 58:440–445.
98. Schott HC 2nd, Hinchcliff KW. Treatments affecting fluid and electrolyte status during exercise. Vet Clin North Am Equine Pract 1998; 14:175–204.
99. Noakes TD, Rehrer NJ, Maughan RJ. The importance of volume in regulating gastric emptying. Med Sci Sports Exerc 1991; 23:307–313.
100. Nadeau J, Andrews FM. Pathogenesis of acid injury in the nonglandular equine stomach. In: Barton M, Love S, Proudman C, et al, eds. 7th International Equine Colic Symposium; Newmarket, Suffolk, UK: British Equine Veterinary Association (BEVA); 2002:78.
101. Moses FM, Ryan C, DeBolt J, et al. Oral–cecal transit time during a 2 hr run with ingestion of water of glucose polymer. Am J Gastroenterol 1988; 83:1055.
102. Moses FM, Singh A, Villanueva V, et al. Lactose absorption and transit during prolonged high intensity running. Am J Gastroenterol 1989; 84:1192.
103. Rao SS, Beaty J, Chamberlain M, et al. Effects of acute graded exercise on human colonic motility. Am J Physiol 1999; 276:G1221–G1226.
104. Tache Y, Martinez V, Million M, et al. Stress and the gastrointestinal tract III. Stress-related alterations of gut motor function: role of brain corticotropin-releasing factor receptors. Am J Physiol Gastrointest Liver Physiol 2001; 280:G173–G177.
105. Ahlborg G, Weitzberg E, Lundberg J. Metabolic and vascular effects of circulating endothelin-1 during moderately heavy prolonged exercise. J Appl Physiol 1995; 78: 2294–2300.
106. McKeever KH, Antas LA, Kearns CF. Endothelin response during and after exercise in horses. Vet J 2002; 164:38–46.

107. Ramaswamy CM, Eades SC, Venugopal CS, et al. Plasma concentrations of endothelin-like immunoreactivity in healthy horses and horses with naturally acquired gastrointestinal tract disorders. Am J Vet Res 2002; 63:454–458.
108. van Nieuwenhoven MA, Brouns F, Brummer RJ. The effect of physical exercise on parameters of gastrointestinal function. Neurogastroenterol Motil 1999; 11:431–439.
109. Gil SM, Yazaki E, Evans DF. Aetiology of running-related gastrointestinal dysfunction. How far is the finishing line? Sports Med 1998; 26:365–378.
110. Fordtran JS, Saltin B. Gastric emptying and intestinal absorption during prolonged severe exercise. J Appl Physiol 1967; 23:331–335.
111. Baron P, Traber LD, Traber DL, et al. Gut failure and translocation following burn and sepsis. J Surg Res 1994; 57:197–204.
112. Pals KL, Chang RT, Ryan AJ, et al. Effect of running intensity on intestinal permeability. J Appl Physiol 1997; 82:571–576.
113. Cohen ND, Peloso JG. Risk factors for history of previous colic and for chronic, intermittent colic in a population of horses. JAVMA 1996; 208:697–703.
114. Cohen ND, Gibbs PG, Woods AM. Dietary and other management factors associated with colic in horses. JAVMA 1999; 215:53–60.
115. Hudson JM, Cohen ND, Gibbs PG et al. Feeding practices associated with colic in horses. JAVMA 2001; 219:1419–1425.
116. Tinker MK, White NA, Lessard P, et al. Prospective study of equine colic risk factors. Equine Vet J 1997; 29:454–458.
117. Traub-Dargatz JL, Kopral CA, Hillberg A, et al. Estimate of the national incidence of and operation-level risk factors for colic among horses in the United States, spring 1998 to spring 1999. JAVMA 2001; 219:67–71.
118. Brouns F, Beckers E. Is the gut an athletic organ? Digestion, absorption and exercise. Sports Med 1993; 15:242–257.
119. Duren S. The gut during exercise. In: Bishop K, ed. KER Equine Nutrition Conference. Versailles, KY: Kentucky Equine Research Inc; 1997: 39–43.
120. Kronfeld DS. Body fluids and exercise: influences of nutrition and feeding management. J Equine Vet Sci 2001; 21:417–428.
121. Argenzio RA, Lowe JE, Pickard DW, et al. Digesta passage and water exchange in the equine large intestine. Am J Physiol 1974; 226:1035–1042.
122. Clarke LL, Roberts MC, Argenzio RA. Feeding and digestive problems in horses. Physiologic responses to a concentrated meal. Vet Clin North Am Equine Pract 1990; 6:433–450.
123. Argenzio RA. Physiology of digestive, secretory, and absorptive processes. In: White NA, ed. The equine acute abdomen. Philadelphia: Lea & Febiger; 1990: 25–35.
124. Moore JN. A perspective on endotoxemia. AAEP Proc 2001; 47:61–74.
125. MacKay R. Endotoxemia. In: Robinson NE, ed. Current therapy in equine medicine. Philadelphia: WB Saunders, 1992:225–323.
126. Soderholm JD, Perdue MH. Stress and gastrointestinal tract. II. Stress and intestinal barrier function. Am J Physiol 2001; 280:G7–G13.
127. Saunders PR, Santos J, Hanssen NPM, et al. Physical and psychological stress in rats enhances colonic epithelial permeability via peripheral CRH. Dig Dis Sci 2002; 47:208–215.
128. Baker B, Gaffin SL, Wells M, et al. Endotoxaemia in racehorses following exertion. J S Afr Vet Assoc 1988; 59:63–66.

CHAPTER 47

Oral and dental disease

Jack Easley

Introduction

Today's performance horse is involved in a wide variety of disciplines. In most disciplines, horses carry bridle and bit for guidance and control. If a horse is to respond correctly to subtle pressures placed on the bit by rider or driver, it must have sound dentition and a healthy oral cavity.

Sound dentition is of such importance that every performance horse pre-purchase examination should begin at the head and include an evaluation of the mouth and temporomandibular joints. Oral and dental problems can lead to bad habits and vices, such as resisting the bridle, being sensitive around the poll, and head shaking. Serious problems can compromise and even end a horse's performance career.

Many serious problems can be prevented with annual oral examinations which lead to early detection and correction of dental problems. Treatment varies from simple procedures with immediate positive results to prolonged and expensive procedures that might not be successful. Horses used for breeding should be selected for sound dentition. The inherited or congenital nature of some oral and dental conditions should exclude some horses from being retired to a breeding status.

Over 100 years ago, Merillat in his thesis on horse dentition accurately summarized the importance of teeth in the management of the performance horse.

> In drivers, runners and saddle horses, sharp teeth are of greatest sources of annoyance. The expert reinsmen will properly recognize their presence by the horses's behavior in harness. Lugging, side reining, ptyalism and tenderness about the seat of the bit are manifestations of pain from the bridle. The aim in dressing the teeth of a horse should be to simply blunt the enamel points along the course of the arcades and to round up the first superior and inferior molars as smooth as ivory.[1]

Bits and bridles

For more than 5000 years, the bit and reins have been used to transmit cues from the rider or driver to the horse. Bits are grouped under two basic types – snaffle and curb.[2,3]

Snaffle bits have only one cheek ring that connects to the bridle, and reins, and the mouthpiece can be either jointed or solid. Curb bits are leverage bits that provide a mechanical advantage to the rider. They have two sets of bit rings with the upper ring attaching to the bridle and the lower rings to the reins. A curb chain or strap goes under the horse's chin. The ratio between the length of shank from upper ring to the mouth piece and down to the lower ring and reins determines the mechanical leverage that is employed. Depending on the bit type used, a pull on the reins can put pressure on the tongue, hard palate, bars, lips, chin groove, bridge of the nose, or poll. Hackamores, cavesanes, bosals and nosebands place pressure on the cheeks (Fig. 47.1).

Dental anatomy

The equine species has unique tools to detect, prehend, masticate and initiate the digestion of grass during frequent grazing. These unique tools include molarized hypsodont cheek teeth, facial bone construction, tactile and prehensile lips, muscles of mastication, tongue, hard palate, olfactory organs, taste buds, salivary glands and ducts, blood, lymphatics and nerves that support them.

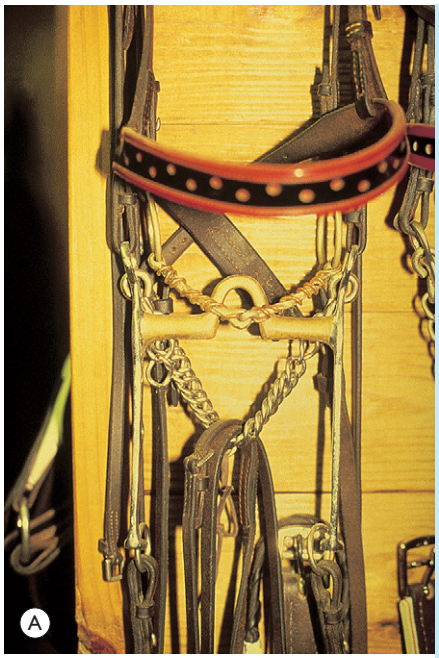


Fig. 47.1
(A) A double bridle. The mouthpiece of the snaffle bit or Bridoon is broken or hinged in the middle and wrapped with a strand of copper wire. The mouthpiece of the curb bit or Weymouth has a medium port to give the tongue some relief. The reins are hanging in the curb chain. (B) Show horse working in a double bridle. The upper set of reins is attached to the snaffle or Bridoon bit and is used to turn the horse. The lower set of reins attaches to the leverage bit or Weymouth and is used to set the horse's head position.

The horse is anesognathic, meaning the bottom jaw is more narrow than the upper. The molar tables are sloped at a 10–15 degree angle from dorsal lingual to buccal ventral. As the horse chews, the jaw moves in a rotating motion from side to side with limited rostral-caudal excursion. The extent of lateral excursion of the mandible during normal mastication is affected by the feed being consumed. A horse on pasture or being fed hay has a full or wide area of mandibular excursion while horses eating pellets or concentrates have a limited amount. Horses on pellets or limited long-stemmed roughage are apt to have incomplete wear of the molar surface, which predisposes the arcades to sharp enamel edges, vaulted ceiling of occlusion, and/or shear mouth.[4]

The mature mouth of a horse contains three upper and three lower incisors and six upper and six lower cheek teeth on each side of the mouth. The rostral three cheek teeth are premolars and the caudal three are molars. Premolars have deciduous and permanent sets while molars come in at an older age and only one set is present. The premolars and molars of the upper jaw are broad and square and contain two infundibula. The lower cheek teeth retain a more narrow, rectangular shape. Equine males normally have two upper and two lower canine or bridle teeth, while mares generally do not.

The Modified Triadon three-digit system of dental nomenclature has been used to designate equine teeth. The first digit designates the quadrant and arch location and whether the teeth are deciduous or permanent. For adult teeth, the quadrants are numbered from 1 to 4 in a clockwise direction, beginning at the right maxillary quadrant. For the deciduous teeth, these quadrants are numbered 5 through 8. The teeth in each quadrant are numbered from the central incisor (01) to the last molar (11). For example, the upper right permanent second premolar would be designated as 106.

A hypsodont tooth has a long anatomic crown and a relatively short root. Much of the crown is held in reserve in the alveolar bone with the root. The root apices complete their development in early middle age (normally 6–9 years). Once fully formed, the tooth no longer grows in length, but continues to erupt as occlusal wear takes place, usually at the rate of 2–3 mm per year. The reserve crown length is 80–90 mm in an unworn first molar tooth.[5–7]

Oral examination

All horses should have their oral cavity examined every 6–12 months, with proper dental maintenance performed as needed. The examination findings should be recorded as part of an effort to formulate an appropriate treatment protocol and to monitor progress after treatment (Fig. 47.2).

Clinical signs that a horse is suffering from dental problems include abnormal head carriage, taking a long time to eat, dysphagia, dribbling feed, quidding forage, eating hay before grain, and being reluctant to drink cold water because of dental pain.[8]

Proper mechanical digestion of feed allows better carbohydrate absorption in the small intestine and improved fiber fermentation in the cecum and large colon. If the horse is masticating properly examination of the horse's manure should not reveal whole grain or stem particles longer than 5 mm. Chronic colic or choke can result from improper mastication of feed due to dental problems.

A horse's overall condition should be evaluated in light of its use and dietary intake as part of a dental examination. Temperament should also be noted. Breed, body type and head conformation should be considered in evaluating the masticatory system. Horses with small heads have more of an angle in the curve of the mandibular ramus (curvature of Spee) and are predisposed to dental crowding and ramps on the lower dental arcade.[9]

Age is a factor, with different conditions arising at various stages of development and maturity. Use, especially if the

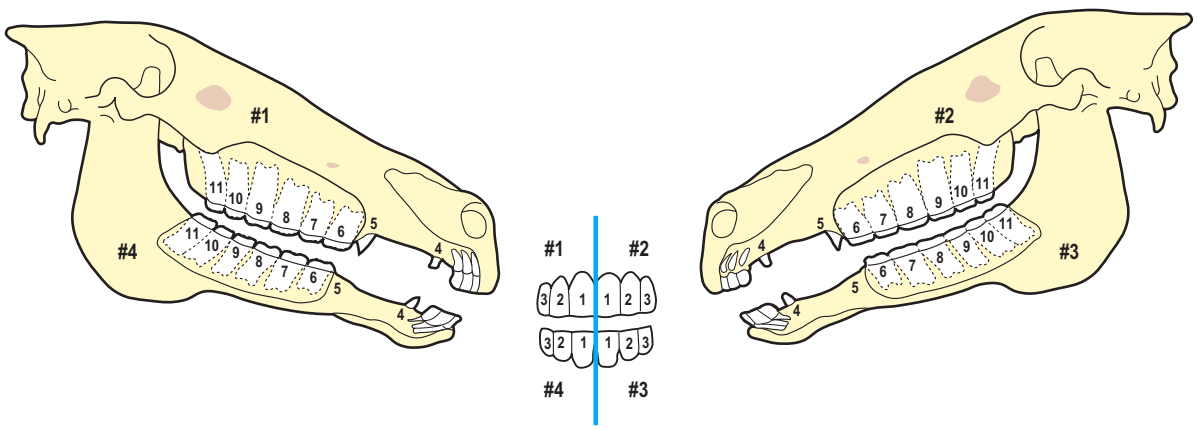
DENTAL EXAMINATION RECORD

Date	Owner	Farm name/phone			Work phone
Address	City	State	Zip		Home phone
Horse reg. name	Stable name	Color	Breed	Sex	Yr. foaled

Hair coat: ❑ Ex ❑ Vg ❑ G ❑ P Condition score: Feces: ❑ Fine ❑ Med. ❑ Coarse

D.age _____ Lateral jaw excursion: N AB Palpation: + –

History: _____ Soft tissue _____



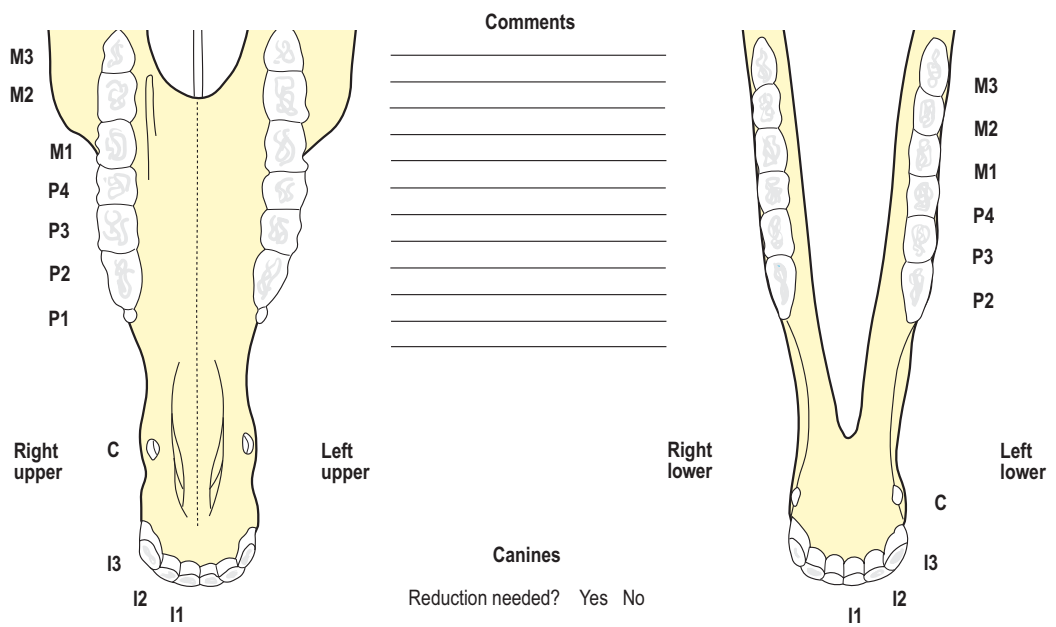


Fig. 47.2
Dental record form utilizing the Modified Triadan System of Dental Nomenclature.

horse is worked in bridle and bit, should be given consideration. Additionally, stable surroundings should be carefully observed for evidence of vices, such as cribbing or poor eating habits.

The head should be observed from both sides and the front for symmetry, protuberances, or swellings. Epiphora should be noted as well as any nasal discharge. Neurologic evaluation should be considered if any cranial nerve deficit is detected. External palpation of the head should be performed.

Fig. 47.3
Complete oral examination requires the use of a full mouth dental speculum and good light source. The oral cavity should be inspected both visually and with a digit to detect both dental and soft tissue abnormalities.

The frontal and maxillary sinuses should be percussed with the mouth open. The width between the mandibular rami should be noted as this is possibly correlated with room for the bit. The sides of the head lateral to the upper dental arcades are palpated, beginning at the orbit and moving forward to the first cheek tooth at the level of the nasal notch. Any protuberance, depression, asymmetry or evidence of pain should be noted. The commissures of the lips should be observed and palpated for evidence of trauma from sharp teeth or improperly fitting bits.

The oral examination should begin with rinsing the mouth, taking note of volume, consistency and odor of material flushed. A loose-fitting halter is necessary to properly evaluate the oral cavity. After observing the incisors for approximate age, they should be evaluated for symmetry and evenness of wear. The diastema or interdental space should be observed for canine teeth or remnants as well as bar enlargements, blind wolf teeth, unerupted canines, or thickening of the palate. The tongue should be observed for lesions from bits, sharp teeth, or tongue ties. The upper rostral arcades should be thoroughly palpated for detection of wolf teeth, hooks, and/or sharp buccal cusps.

Range of motion of the mandible is evaluated by holding the head stationary with one hand while sliding the mandible from side to side with the other. Resistance or abnormal incisor separation during this maneuver should be noted.

To complete the oral examination, a full mouth speculum should be applied and the mouth examined digitally and visually with a flashlight or headlamp (Fig. 47.3). An endo-

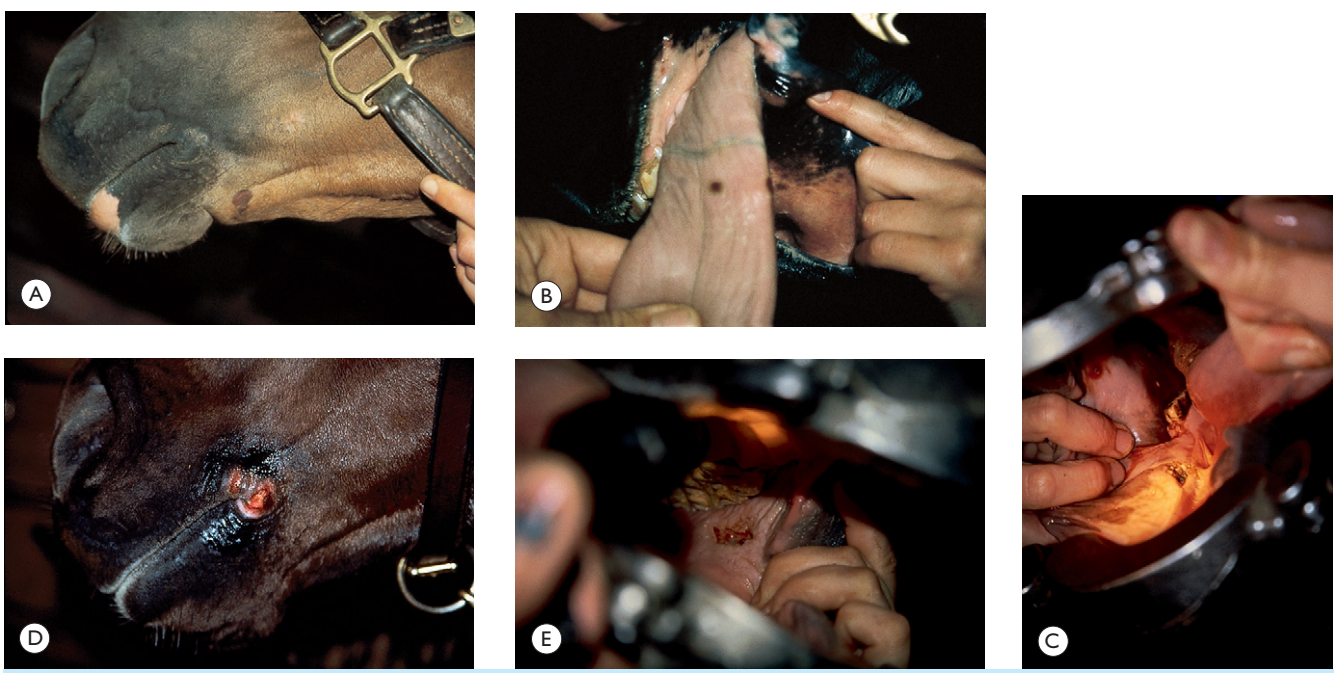


Fig. 47.4
(A) A swollen chin groove from severe curb chain trauma. (B) Tongue bruising from severe pressure on a curb bit. (C) Severe mucosal and osseous trauma to the interdental space and bar. This young Tennessee Walking Horse had been worked in a curb bit with a broken or hinged mouthpiece. (D) Extensive trauma to the commissure of the lips due to misuse of a damaged snaffle bit. (E) Cheek trauma from a snaffle bit being pulled against sharp enamel points on the buccal edges of the upper dental arcade.

scope or buccal retractor and mirror may aid in a more detailed examination.

If areas of impacted or trapped feed are present, they should be removed with the examiner's digit or a dental pick and the mouth rinsed completely. Horses with sharp buccal points on the upper dental arcades resist the full mouth speculum and floating the upper arcades early in the examination may be beneficial.

Diagnostic radiology is a valuable aid. Good-quality films can be obtained with portable X-ray machines and rare earth intensifying screens without a grid. Indications for head radiology are any suspicions of dental infection, facial swelling, deformity, neoplasm, trauma or fracture, maleruption of teeth, or oral pain of unknown origin. Radiographs should be taken before and after dental extraction.

Oral injuries

Injuries to the lips, tongue and buccal mucosal can be caused by sharp enamel points or rough use of the bit. Tongue damage can be performance limiting (Fig. 47.4). A tongue can protrude from the mouth secondary to hypoglossal nerve paresis, hyoid bone injuries, a drooping lower lip, or missing canine or incisor teeth. Tongue lacerations can be repaired if the blood supply to the rostral portion of the injury is adequate. The rostral aspect of the tongue can be amputated up to the frenulum without compromising function.[10]

Injuries to the bars are most often bit induced. Acute bar injuries cause swelling and pain. Bar lacerations or fracture are common. More chronic cases develop scar formation or exostosis in the interdental space. Some injuries lead to bone sequestrum formation with a draining tract.[11–13]

Bar injuries may be diagnosed by careful palpation and radiography. Conservative treatment of bar injuries may consist of bit changes. Cases that do not respond to conservative therapy might require surgical correction.[14]

Dental floating

The main purpose of molar floating or leveling is to remove sharp enamel points from the buccal aspect of the upper and lingual aspect of the lower cheek teeth. Floating might also entail removing minor hooks or ramps from the rostral or caudal aspect of the arcades or leveling minor elevations on the occlusal surface of the arcades.

Float blades made of carbide chips or solid tungsten carbide make the work of floating more efficient. The outward curve of the upper arcade makes the central buccal area involving PM3 through M2 the easiest to reach with the float. To reach the rostral aspect of upper PM2 (106 and 206) and the caudal aspect of lower M3 (111 and 211) requires an offset or angled head on the rasps. In most cases, floating the lower arcade to remove the lingual enamel points can be done with a flat, long-handled rasp.

The mouth speculum or a dental wedge can make floating easier if the horse closes its mouth on the float. In horses with slightly ramped back teeth due to a greater curvature of Spee, a mouth speculum and a slightly curved or swivel head float might be needed to reach the table of the last two or three molars.[15]

For correction of rostral and caudal hooks, solid carbide blades and power burrs might be necessary. In performance horses, a seat for the bit is made by rounding the first upper and lower cheek teeth and lowering of the buccal cusps from

Fig. 47.5
(A) Fingers placed on the outside of the horse's face, outlining wolf tooth position. This horse reluctantly wore a flash noseband. (B) Buccally displaced sharp wolf tooth. This tooth was extracted and the horse had immediate relief from noseband discomfort.

Fig. 47.6
A sharp upper wolf tooth just rostral to the upper second premolar.

Fig. 47.7
Two extracted upper wolf teeth and the set of extraction instruments used to remove the teeth.

upper PM2 to PM3 (106, 206 to 107, 207). The dental contouring requires an offset head float or an S-shaped rasp. Floating and other corrective measures may require the physical restraint of dental halter and/or sedation.

Wolf teeth (rudimentary first premolars)

Wolf teeth (105 and 205) can cause difficulties if sharp or displaced (Fig. 47.5). They can cause buccal mucosa pain when pressure is applied to the bit. If erupted, their presence causes a problem in creating a bit seat on the rostral edge of PM2 (106 and 206) (Fig. 47.6). Clinical experience indicates the incidence of upper wolf teeth is at least 80% in horses 1–3 years of age. They usually erupt between 6 and 18 months of age and, typically, are positioned just rostral to the first cheek tooth. Lower wolf teeth (305 and 405) are occasionally positioned rostral to the first cheek tooth in the mandible. Unlike incisors and cheek teeth, wolf teeth (and canine teeth) are brachyodont or short crowned, with no reserve crown. As a result, they do not continue to erupt throughout the horse's life. Unerupted or blind wolf teeth can be as troublesome as those visible on dental examination.

Commonly, wolf teeth are removed from horses between $1^1/_2$ and 3 years of age before a bit is introduced. Tools used for wolf tooth extraction include a cylinder- or Burgess-type wolf tooth elevator set, a dental root elevator, and a pair of small dental extraction forceps (Fig. 47.7).

The first objective in extraction is to cut the gingival attachment to the crown of the tooth. This is best achieved by placing a cylinder-type punch extractor over the crown. A dental root elevator is then introduced deep into the alveolus to loosen the tooth from its periodontal and alveolar attachment. Once freed, the tooth can be elevated from the dental socket either by the root elevator or with the use of extraction forceps. The process should not be attempted by using the first cheek tooth as a fulcrum, as this increases the risk of fracturing the wolf tooth root. Care should be taken to avoid damaging the soft tissues of the mouth during extraction. Misguided use of instruments can easily lacerate the palatine artery which runs the length of the hard palate immediately axial to each upper arcade.

The procedure for extraction of blind or unerupted wolf teeth is similar to that for erupted teeth. Evaluation of the size and position of the unerupted teeth may be aided with radiography. Proper restraint during the procedure includes chemical sedation and assistance from a trained handler.

Canine teeth

Canine teeth (104, 204, 304, and 404) are present in most male horses over $4^1/_2$ years of age. They normally cause few problems. The upper canine is located in the juncture of the incisive and maxillary bones with the lower canine positioned just rostral. Some mares have small rudimentary canines that generally do not cause problems unless they become loose or accumulate tartar. Long or sharp canines in a stallion or gelding can interfere with bitting.

In older horses, the crown enamel can become worn and pitted, allowing tartar accumulation and gingivitis. By polishing or grinding down the canines, these problems can be avoided. Care should be taken not to shorten the canines to such an extent that the pulp is exposed or the tongue is allowed to protrude from the mouth (Fig. 47.8). Erupting canine teeth in the 4- to 6-year-old horse can cause subgingival pain and bit irritation which often is manifested by head-shaking or other bad habits. The mucosa should be removed

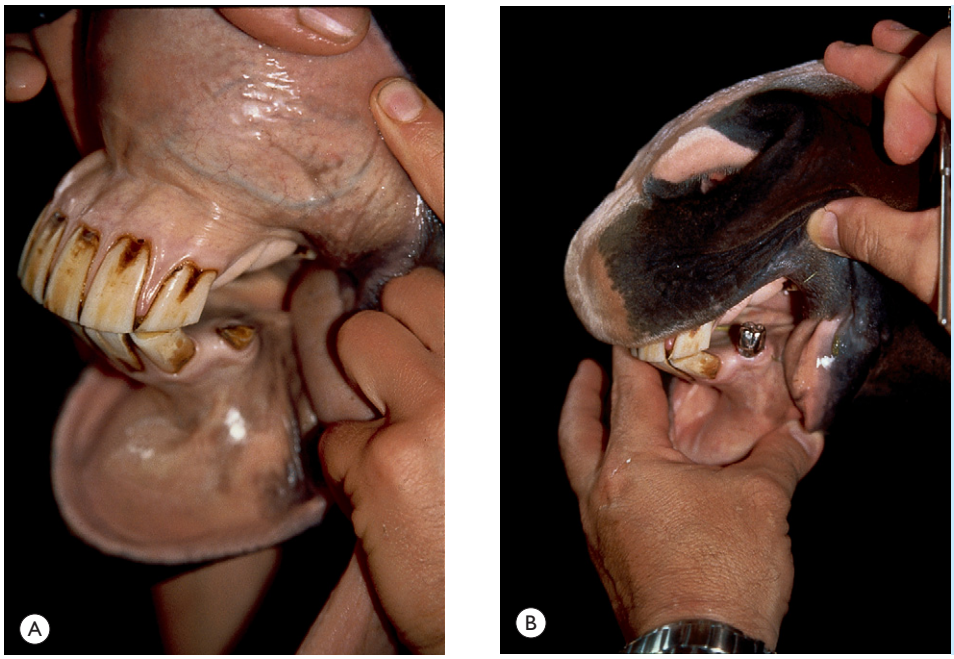


Fig. 47.8
(A) A severely worn lower canine tooth crown on a 16-year-old gelding. This show horse dropped his tongue out when wearing a curb bit. (B) A titanium cap placed over the worn canine tooth crown to help support the horse's tongue. This technique allowed the horse to show successfully.

over canines if gingival eruption cysts are present (Fig. 47.9). This problem was reported by Percivall over 100 years ago:

> I was requested to give my opinion concerning a horse, then in his fifth year, who had fed so sparingly for the last fortnight, and so rapidly declined in condition in consequence, that his owner, a veterinary surgeon, was under no light apprehensions about his life. He had himself examined his mouth without having discovered any defect or disease, though another veterinary surgeon was of the opinion that the difficulty or inability manifested in mastication, and the consequent cudding, arose from the preternatural bluntness of the surfaces of the molar teeth, which were, in consequence, filed but without beneficial result. It was after this that I saw the horse, and I confess that I was, at my first examination, quite as much at a loss to offer any satisfactory interpretation as others had been. While meditating, however, after my inspection, on the apparently extraordinary nature of the case, it struck me that I had not seen the tusks. I went back into the stable and discovered two little tumors, red and hard, in the situation of the inferior tusks, which, when pressed, gave the animal insufferable pain. I instantly took out my pocket knife and made crucial incisions through them both, down to the coming teeth, from which moment the horse recovered his appetite and, by degrees, his wonted condition.[16]

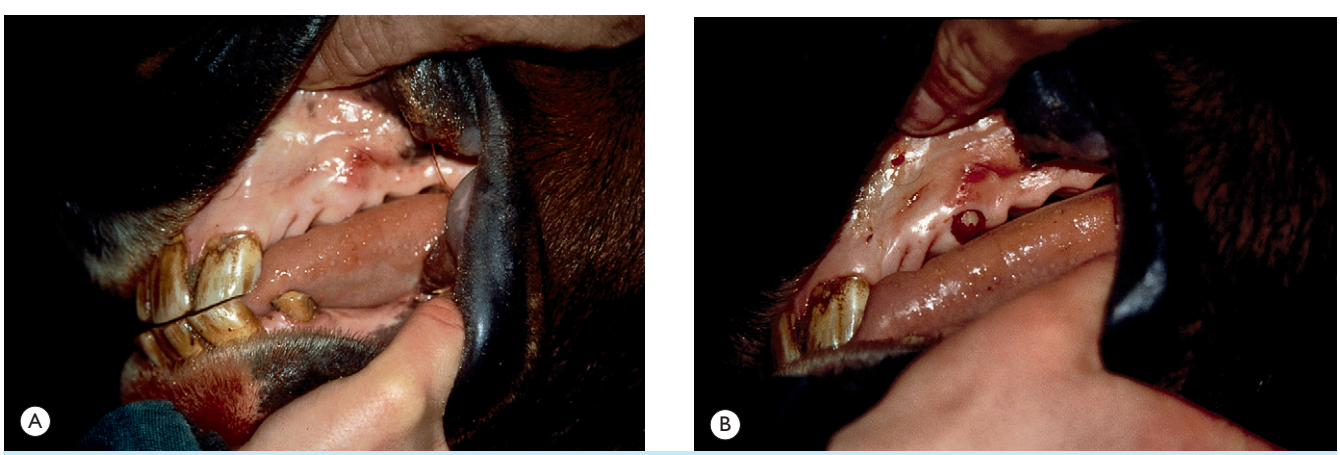


Fig. 47.9
(A) Upper canine tooth eruption cyst on a 7-year-old Saddlebred gelding. The horse exhibited head tossing behavior when driven in a snaffle bit and overcheck. (B) The eruption cyst was opened and the mucosa removed from over the erupting canine tooth. The horse responded well to this treatment.

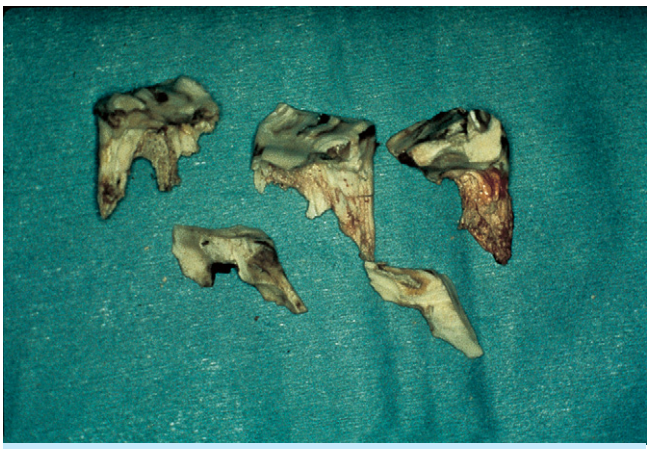


Fig. 47.10
Deciduous tooth caps and cap fragments can be a source of oral discomfort for 2–4-year-old horses. These cap fragments have large root slivers that can be broken off below the gum and cause chronic gingivitis.

Caps (deciduous teeth)

The premolars and incisors should be closely evaluated when examining the dentition of horses of 2–4 years of age as these teeth are shedding their deciduous caps. The caps normally are shed in sets of four; one cap from each arcade. Generally, the shedding time is as follows: $2^1/_2$ years for the first set (506, 606, 706, 806); 3 years for the deciduous 07s, and $3^1/_2$ to 4 years for the deciduous 08s. Irregular shedding, if not corrected, can lead to severe problems in the development of the permanent arcade. Clinical signs that indicate retained or loose caps include feed being impacted under the caps, excessive salivation, oral malodor, tilt of the head, dribbling feed, tongue lolling, and ill response to the bit.

To detect problem caps, one should palpate along the lingual surface of the premolars and cheek for pain. If a cap is present, an indentation at the gingival line will demarcate between the deciduous premolar cap and the erupting permanent tooth. Ideally, one will feel and visualize the demarcation midway between the gingiva and the occlusal surface of the cap. If this indentation is below the gum, removal of the upper cap could result in exposing the premature permanent premolar with an underdeveloped infundibulum.

To remove caps, an extraction forceps is clamped firmly on the base of the cap and gently rocked lingually. Care should be taken not to place the forceps below the level of the gingiva as the palatine vessels along the upper arcade could be disrupted upon clamping, resulting in potentially severe hemorrhage. Rolling the cap toward the lingual surface will reduce breakage of the buccal roots (slivers) of the cap (Fig. 47.10).

Abnormal dental wear patterns

The most common abnormal dental wear pattern is formation of rostral upper overgrowths (hooks) on PM2 (106 and 206). A hook can begin as a ramp or a small enamel point or beak, depending on the degree of rostral protuberance of the upper molar arcade. The most severe form of this condition is seen in parrot mouth horses with a malocclusion of the incisors and molar arcades. The more common presentation is a horse with normal incisor occlusion and a small malalignment of the cheek tooth arcades.

Horses that eat forage from an elevated hay rack or those that chew with their heads elevated have a predisposition to rostral upper PM2 hook formation. These hooks form because when the head is held in an elevated position, the lower jaw is slightly retracted caudal on the upper jaw, bring-

Fig. 47.11
(A) Rostral upper premolar hooks usually become longer and broader at the base over time. (B) Enlarging cheek teeth hooks can place caudal pressure on the lower jaw causing an incisor overjet.

ing the rostral order of the upper arcade out of occlusion with the lower, preventing normal wear. A sharp rostral hook or beak can cause cheek pain if the horse wears a snaffle bit.

As the rostral hook becomes longer and broader at its base, it begins to put caudal pressure on the lower jaw when the horse closes its mouth. This caudal retraction of the lower jaw brings the distal molars further out of occlusion, contributing to ramp and hook formation in the back of the mouth as well. The caudal pressure on the mandible or lower jaw also places abnormal stress on the temporomandibular joints. In addition, the caudal jaw position leads to malocclusion of all cheek teeth and can contribute to abnormal wear. These exhibit as abnormal transverse ridges and enamel points, cupping out of some upper cheek teeth, and wave formation on the occlusal surfaces. Abnormal wear patterns can be subtle in the early stages, but become progressively worse during the life of the horse (Fig. 47.11).

Clinical signs of a horse with a hook problem include not flexing at the poll, head throwing when asked to work in collection, shortening of the stride, soreness in the neck and back muscles, opening of the mouth when asked to collect, bouncing of the head during collection, and inefficient eating.

Many horses with hooks function well in activities where head carriage is not important, such as hunting and trail riding. In activities where head carriage is important for balance and collection, such as dressage, hook problems can be career ending if not properly diagnosed and treated. The most successful therapy is routine reduction of abnormal wear patterns as they develop.

A physical examination should be used to confirm a diagnosis of soreness due to dental hooks. Soreness at the insertion of the masseter muscles just below the temporomandibular joint is often evident. Horses with a severe problem can develop temporomandibular degenerative joint disease, exhibited as crepitation on joint palpation, reluctance to open the mouth or move the jaw to the side.[17]

Open-mouth radiographs can document the presence of dental hooks, but radiology has not been rewarding in evaluation of the temporomandibular joint. Other imaging modalities, such as nuclear scintigraphy, magnetic resonance imaging, and computed tomography, have been used to evaluate the temporomandibular joints, along with thermography.[18] Arthrocentesis and synovial fluid analysis can help with the diagnosis of temporomandibular degenerative joint disease and also aid in giving a prognosis and formulating a therapy plan.[19,20]

Oral examination with the aid of a full-mouth speculum and good light source will allow the evaluation of the dental arcades. Careful palpation is necessary to avoid confusing the normal upward curvature of the mandibular third molar in short-headed horses with an actual hook. Examination should include checking for other abnormal cheek teeth wear patterns.

Therapy should consist of hook removal and balancing the dental arcades. After hook reduction and dental equilibration, it is important to evaluate lateral excursion and cheek teeth contact. Often, horses that have had hooks and caudal jaw retraction for a prolonged period, also have some malalignment and subsequent abnormal wear of the incisor arcades. The incisors often need crown reductions and alignment to bring the cheek teeth into proper occlusal contact.[21]

Hand floating is a common method for reducing hooks. A long-handled, straight-head float set to cut on the pull is required for reducing caudal hooks. Rostral hooks are best reduced using an offset float or an angled float.

Two other tools are the sliding percussion chisel and molar cutters, but both should be used with caution. Chisels do not cut, but fracture the tooth crown. Excessive or incorrectly positioned force may shatter the tooth or repel it. Molar cutters should be reserved for older horses, as those under 9 years of age have less secondary dentition and structurally weaker teeth. Fracture of the tooth or extraction is a potential complication of this method, as is removal of too much hook and exposure of the pulp cavity.

Three types of power tools which increase precision and reduce effort are available. They are reciprocating, rotary burr and disk-type, and can be electric or air powered. The horse must be well restrained and sedated when power tools are used.

Incisor overgrowth might become evident after hook correction as caudal pressure on the mandible is released and the incisors once again come in full occlusal contact. Overgrown incisors, when returned to full occlusal contact, may take the cheek teeth completely out of occlusion. When lateral jaw excursion is attempted, no contact between the cheek teeth arcades is evident. Incisor length should be reduced as necessary to return cheek teeth to occlusion during lateral excursion and normal mastication.

The immediate relief of caudal pressure on the mandible changes the jaw position and acutely shifts the mechanical forces placed on the temporomandibular joint, muscles of mastication, and dental arcades. This can lead to mild inflammation and short-term soreness after treatment.

Inflammation can be treated symptomatically with nonsteroidal anti-inflammatory drugs. Some horses with residual temporomandibular joint pain after dental correction show quick relief of clinical signs with intra-articular therapy. Oral supplements, such as hyaluronic acid, methylsulfonylmethane (MSM), glucosamine, and chondroitin, have been shown to be of some value. Additionally, physical therapy and/or acupuncture can be of benefit.

References

1. Merillat LA. Animal dentistry and diseases of the mouth. In: Veterinary surgery. vol 1. Chicago: Alexander Eger; 1905.
2. Bennett DG. Bits and bitting: form and function. AAEP Proc 2001; 47:130–137.
3. Scoggins RD. Bits, bitting and dentistry. AAEP Proc 2001; 47:138–141.
4. Dixon PM, Tremaine WH, Pickles K, et al. Equine dental disease, part 3, a long-term study of 400 cases: disorders of wear, traumatic damage, idiopathic fractures, tumours and miscellaneous disorders of the cheek teeth. Equine Vet J 2000; 32:9–19.

5. Kilic S, Dixon PM, Kempson SA. A light microscopic and ultrastructural examination of calcified dental tissues of horses, 4 part series. Equine Vet J 1997; 29:190–220.
6. Muylle S. Aging. In: Baker GJ, Easley J, eds. Equine dentistry. London: WB Saunders; 2000:35–46.
7. Lowder MQ, Mueller E. Dental embryology, anatomy, development and aging. Vet Clin North Am 1998; 227–247.
8. Easley KJ. Dental and oral examination. In: Baker GJ, Easley J, eds. Equine dentistry. London: WB Saunders; 2000:107–126.
9. Baker GJ. Dental physical examination. Vet Clin North Am 1998; 14:247–259.
10. Greet T. Oral and dental trauma. In: Baker GJ, Easley J, eds. Enquine dentistry. London: WB Saunders; 2000:60–69.
11. Hague BA, Honnas CM. Traumatic dental disease and soft tissue injuries of the oral cavity. Vet Clin North Am 1998; 14:333–347.
12. Jansson N, Hesselholt M, Falmer-Hansen J. Extirpation of a mandibular canine tooth in a horse as a treatment for severe bit-induced trauma to the bar. Equine Vet Educ 1998; 10:143–145.
13. Tremaine WH. Management of equine mandibular injuries. Equine Vet Educ 1998; 10:146–154.
14. Johnson TJ. Surgical removal of mandibular periostitis (bone spurs) caused by bit damage. AAEP Proc 2002; 48:458–462.
15. Scrutchfield WL. Equine dental instrumentation. In: Baker GJ, Easley J, eds. Equine dentistry. London: WB Saunders; 2000:173–184.
16. Percivall W. Hippopathology 1852. In: Mechener CB, ed. Special report on diseases of the horse. Washington: US Department of Agriculture; 1911:42–43.
17. Baker, GJ. Equine temporomandibular joints (TMJ): morphology, function and clinical disease. AAEP Proc 2002; 48:458–462.
18. Rosenstein DS, Bullock MF, Ocello PJ, et al. Arthrocentesis of the temporomandibular joint in adult horses. Am J Vet Res 2001; 62:729–733.
19. May KA, Moll HD, Howard RD, et al. Arthroscopic anatomy of the equine temporomandibular joint. Vet Surg 2001; 30:554–571.
20. Weller R, Maierl J, Bowen IM, et al. The arthroscopic approach and intra-articular anatomy of the equine temporomandibular joint. Equine Vet J 2002; 34:421–424.
21. Rucker BA. Utilizing cheek teeth angle of occlusion to determine length of incisor shortening. AAEP Proc 2002; 48:448–452.

CHAPTER 48

Gastrointestinal diseases of performance horses

Guy D. Lester

Equine gastric ulcer syndrome

- Spontaneous erosion or ulceration of the gastric mucosa represents the most important gastrointestinal disease of the athletic horse, both in terms of prevalence and economic impact. The latter is influenced not only by reduced earnings due to diminished performance, but also by the high costs associated with therapeutic and prophylactic medication.
- The pathophysiologic basis of gastric squamous ulceration in horses is multifactorial.
- The history and clinical signs of gastric ulceration in adult horses are often vague and not specific.
- The most effective treatment strategies are those that reduce gastric acidity. These include administration of antacids, H_2 receptor antagonists, or proton pump blockers.

Gastric anatomy

The horse is a hindgut fermenter with an extensive and complex cecum and large colon, but has a simple stomach similar in shape to that of domestic carnivores and omnivores. The nonglandular, squamous mucosal lining of the distal esophagus spreads through the cardia and covers the proximal half of the stomach. The margo plicatus defines the lower border of the squamous mucosa with the glandular mucosa. The glandular mucosa covers the remainder of the stomach through the antrum and down to the pylorus. Histologically the glandular mucosa is divided into three areas: the cardiac, fundic and pyloric regions. The cardiac gland region is a narrow strip of mucosa that lies immediately beneath the margo plicatus. The natural bend to the stomach permits further anatomic classification into greater and lesser curvatures.

Recognition of the disease

Equine gastric ulcer syndrome (EGUS) is not a single disease entity, but rather a term that embraces a group of distinct disorders that can affect horses of all ages.[1] These disorders include not only primary gastric disorders, but also related diseases of the distal esophagus and proximal duodenum. Many of these diseases share aspects of pathology, but likely differ widely in terms of primary pathophysiology.

1. *Neonatal gastric ulceration*. As the name indicates this syndrome is usually limited to diseased or otherwise highly stressed newborn foals. Ulceration and occasional perforation frequently, but not exclusively, occur in the cardiac gland region of the stomach. This syndrome is often clinically silent due to the coexistence of severe primary diseases such as systemic sepsis or peripartum asphyxia syndromes. The first signs may not be apparent until fatal perforation has occurred. Attenuated mucosal protection through reduced blood flow is a likely key component of the pathophysiology of neonatal gastric ulceration.
2. *Gastroduodenal ulcer disease (GDUD)*. This form of EGUS occurs primarily in suckling foals and in its most severe form involves the proximal duodenum, pylorus, stomach, and distal esophagus.[2,3] It is highly likely that the initial lesion in affected foals is a diffuse duodenitis. This initially results in a functional delay to gastric emptying with secondary gastric and esophageal irritation, probably due to prolonged exposure of susceptible mucosa to acidic luminal contents. During the healing process strictures may form in the duodenum and/or pylorus which result in a mechanical obstruction to emptying, again leading to gastric distension and secondary gastric and esophageal erosion. Of all of the forms of EGUS this syndrome is the one most likely to have a precipitating infectious

component. This is further supported by the observation that cases frequently occur in clusters and are often preceded by episodes of diarrhea. Acid suppression is a key component in the management of GDUD when delayed gastric emptying (either functional or mechanical) is present, but does not have a role in prophylaxis.

3. *Glandular ulceration*. Experimental induction of glandular ulceration is easily achieved using repeated high doses of non-steroidal anti-inflammatory drugs, such as phenylbutazone.[4] Lesions in the glandular mucosa also occur spontaneously in both athletic and non-athletic horses and often coexist with squamous mucosal lesions. They are usually seen in response to some form of stress, such as training or concurrent diseases. Glandular lesions are often associated with the most overt clinical signs of EGUS, such as postprandial abdominal pain and inappetence.
4. *Squamous mucosal ulceration*. Most discussion of ulcer disease in performance horses refers to erosion or ulceration of the squamous mucosa, the most common form of EGUS in this type of horse. The regions adjacent to the margo plicatus are most frequently diseased and are usually more prominent on the lesser curvature between the cardia and the margo plicatus.[5]

This discussion focuses on the glandular and squamous ulceration syndromes of performance horses. Readers are directed to other more general equine medicine texts for further information on neonatal cardiac gland disease and GDUD.

Clinical signs

In sharp contrast to young foals with GDUD, the history and clinical signs of gastric ulceration in adult horses are often vague and not specific. Only since the release of the 3-m endoscope has an association between signs and disease evolved. This has however been complicated by the frequent disparity between clinical signs and disease severity. It is not uncommon to observe horses with severe endoscopic lesions with no reported abnormal clinical signs. Conversely, there are horses with typical signs that have minimal changes on gastroscopy.

Probably the most common and consistent findings associated with gastric squamous ulceration are related to consumption of feed. Affected animals will typically take a longer than expected time to consume a concentrate feed and owners or trainers often report problems in achieving or maintaining body condition. More overt signs may include colic, particularly after eating. Anecdotally, horses with moderate signs of pain due to gastric ulceration commonly have glandular lesions, often around the pylorus, with or without squamous disease. This reinforces the importance of a complete endoscopic examination in animals presenting with colic in the absence of other abnormal findings.

Other reported signs consistent with ulcer disease include a rough hair coat, aggressive or nervous attitude, intermittent diarrhea, and poor performance. It is the latter sign that is most difficult to directly ascribe to gastric disease, but trainers will often report improved performance when horses are placed on antiulcer therapy.

Diagnosis

Endoscopy of the stomach is the most accurate method for establishing a diagnosis of gastric ulcer disease. This is best achieved using a 2.5- to 3-m flexible endoscope in the standing, sedated horse. The duration of fasting prior to endoscopy varies with the type of examination required. Examination of the antrum, pylorus and duodenum usually necessitates an overnight fast of 12–16 hours and withdrawal of water 1–2 hours prior to the procedure. The fasting period can be shortened to 6–8 hours if the examination is limited to the squamous mucosa. Adding air to the stomach will make the procedure easier to perform, but care should be taken not to overdistend the stomach particularly in foals and young horses. A suction system aids not only in evacuation of air at the completion of the procedure, but also to remove any excess fluid in the antrum.

A 2.5-m endoscope may not permit complete examination of the margo plicatus in large horses. This may be problematic as squamous ulceration tends to be more severe at the lesser curvature due to the greater exposure of this region to acidic fluid. The gastric squamous mucosa is scored using a simplified system that ranges from 0 to 3.[1] Examples are included in Fig. 48.1. Lesions are graded as follows: Grade 0, intact mucosal epithelium with or without reddening or hyperkeratosis; Grade 1, single or multiple small ulcers; Grade 2, single or multiple large ulcers; and Grade 3, extensive ulceration with coalescing of ulcerated areas. A modified system was recently published to categorize lesions of the squamous mucosa, glandular body of the stomach, antrum, pylorus, and duodenum.[6] The authors used the following 0–4 scoring system: Grade 0, intact epithelium with no apparent mucosal changes; Grade 1, mucosal reddening or squamous hyperkeratosis; Grade 2, small single or multifocal lesions; Grade 3, large single or multifocal lesions or extensive superficial lesions; and Grade 4, extensive lesions with apparent deep ulceration.

In other species, elevations in the serum concentration of pepsinogen have been observed in association with ulcerative diseases of the stomach and duodenum. Pepsinogen is converted to pepsin by autocatalytic activation under acidic conditions. Although equine pepsinogen has been isolated and appropriate assays developed, no such association has been published to date in adult horses.[7,8] Serum levels in foals with confirmed or suspected gastric or duodenal ulcers were significantly greater than serum pepsinogen levels in apparently healthy age-matched foals.[9]

Indirect methods of diagnosis include recognition based on clinical signs, although the vague nature of these signs can be problematic, and through response to treatment. Given the expense of treatment and the difficulty in evaluating improvement associated with therapy it is often more economical to perform gastroscopy.

Treatment

As discussed below, the pathophysiologic basis of gastric ulceration is likely multifactorial. Despite the apparent complexity of the disease the role of gastric acidity appears to be

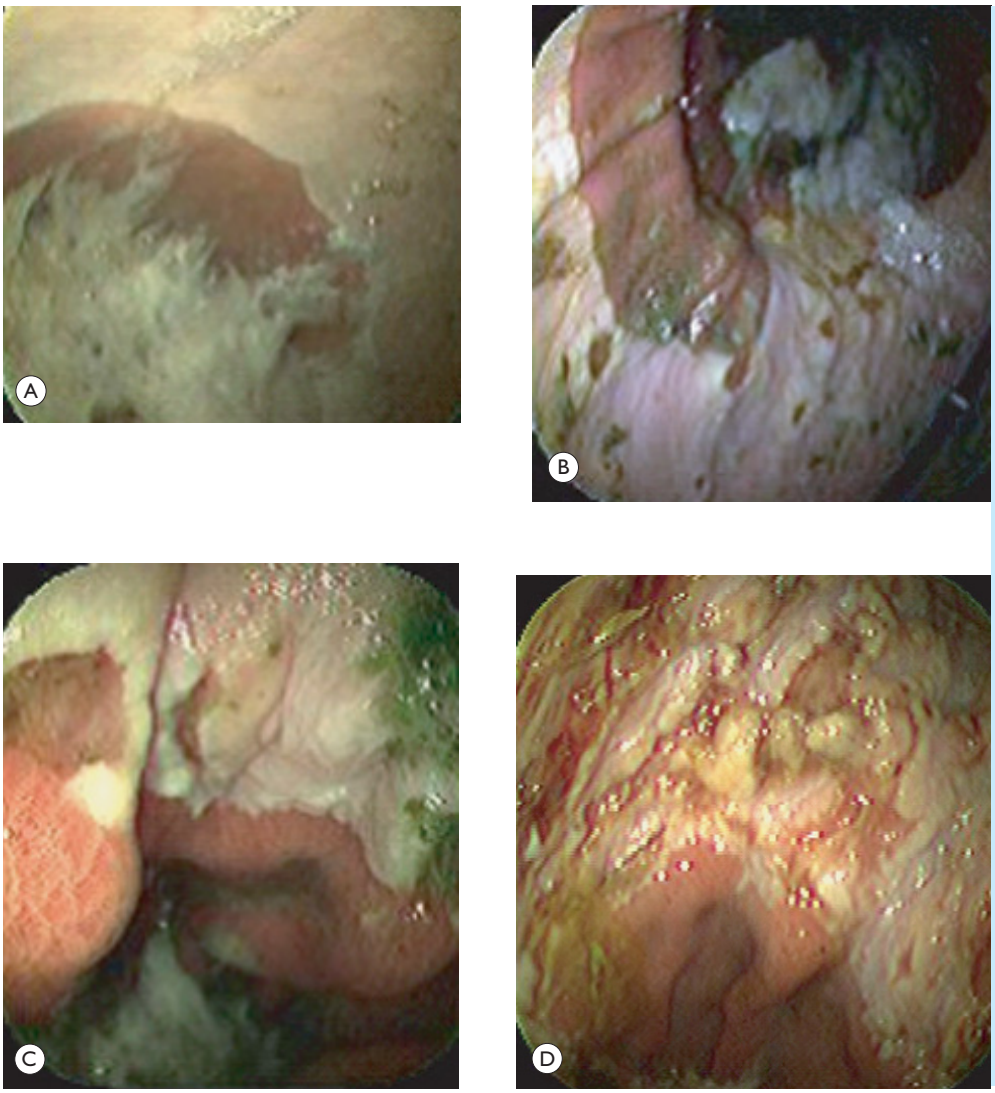


Fig. 48.1
Gastric ulcer scoring system.(A) Grade 0: Intact mucosal epithelium with or without reddening or hyperkeratosis. (B) Grade 1: Single or multiple small ulcers. (C) Grade 2: Single or multiple large ulcers. (D) Grade 3: Extensive ulceration with coalescing of ulcerated areas.

pivotal. Consequently, the most effective treatment strategies are those that reduce gastric acidity. These include administration of antacids, H_2 receptor antagonists, or proton pump blockers.

Antacids are most commonly used to provide temporary symptomatic relief from ulcer disease. They are used in relatively large volumes (240–360 mL) to improve appetite, feed consumption, and athletic performance in affected horses. Unfortunately, the effect of antacids is short-lived necessitating frequent treatment (q 2–6 hours) if ulcer healing is required. The oral administration of 30 g of aluminum hydroxide and 15 g of magnesium hydroxide resulted in a mean hourly gastric pH ≥ 4.0 for at least 120 minutes in one study.[10] A cautionary note: antacids reduce the bioavailability of many concurrently administered oral medications.

Histamine type-2 receptor antagonists have been widely used in equine practice to successfully treat and prevent gastric ulceration.[11,12] These drugs block histamine binding to receptors on the parietal cell. The duration of action is dependent on plasma levels, but is generally between 2 and 8 hours. Bioavailability of H_2 receptor antagonists is relatively poor and variable between animals; approximately 27% for ranitidine in adult horses[13] and between 7 and 22% for cimetidine.[14] The recommended oral dose for ranitidine is 6.6 mg/kg q 8 hours in the adult horse. Response data derived from healthy neonatal foals indicates that a dosing interval of 12 hours may be adequate in that age group.[15] The reported recommended dose of oral cimetidine in the literature is highly variable. Most veterinarians are using a total daily dose of 60–100 mg/kg divided and administered three to four times daily. Famotidine has been evaluated in adult horses, but further studies are required in order to characterize an optimal dose rate for acid control.[16] A dose of 2 mg/kg bodyweight was effective at significantly elevating the intragastric pH.

Proton pump blockers are effective at increasing intragastric pH and healing gastric ulcers in adult horses.[17–22] These drugs irreversibly bind parietal cell H^+-K^+-ATPase, the 'proton pump' responsible for H^+ secretion. Omeprazole is the most commonly prescribed proton pump blocking agent in

horses. The drug is well absorbed and at recommended doses will suppress acid production for approximately 24 hours. The recommended therapeutic dose rate of commercial omeprazole paste (GastroGard (USA) and GastroShield (Australia), Merial, Ltd) is 4 mg/kg bodyweight once daily. A dose of 1 mg/kg bodyweight daily has been recommended for the human preparation of omeprazole, a 20-mg capsule of enteric-coated granules.[23] Omeprazole paste has been shown to not only heal squamous mucosal ulcers, but also to maintain healing in Thoroughbred race horses maintained in active training.[19]

The effect of H_2 receptor antagonists and proton pump blockers on gastrin levels requires further investigation in horses. The secretion of gastrin is inhibited by gastric acid, therefore treatments that reduce acid secretory responses increase gastrin release and increase enterochromaffin-like (ECL) cell numbers. The prolonged usage of acid-suppressing drugs has been linked to the development of ECL cell tumors, although direct causal data are lacking.[24] Of more practical concern is the possibility of rebound hypersecretion of acid after withdrawal of acid-suppressing therapy.

Additional strategies involved in antiulcer therapy include coating of the ulcer with an acid-resistant compound and simulating or supplementing protective prostaglandins. The use of sucralfate – a polysulfated sugar (sucrose octasulfate) combined with aluminum hydroxide – in horses is controversial.[25,26] Anecdotal evidence suggests that sucralfate can be an important adjunct in the management of glandular ulcers. Sucralfate has a number of potentially beneficial properties, including binding to exposed gastric mucosa, stimulating mucus production and local prostaglandin synthesis, and improving mucosal blood flow. An effective dose rate has not been determined; commonly quoted dose rates range between 10 and 20 mg/kg bodyweight given orally every 6–8 hours. Additional problems associated with sucralfate administration include interference with the absorption of other drugs (e.g. certain antibiotics and H_2 receptor antagonists) and the requirement for an acid medium for maximum efficacy. As a result of the latter problem, most clinicians dose the drug 60 minutes prior to the administration of acid-suppressing agents.

Prostaglandin replacement therapy is often considered in animals undergoing prolonged therapy with non-steroidal anti-inflammatory agents and in those experiencing high levels of physiologic stress. Direct replacement with a PGE_2 analog, such as misoprostol, is costly and has been associated with undesirable gastrointestinal side effects (diarrhea and colic). Reported dose rates range between 1.5 and 2.5 μg/kg bodyweight every 8 hours. An indirect method of supplementing PGE_2 centers on feeding linoleic acid in the form of corn oil. Supplementation at a rate of 20 mL/100 kg bodyweight significantly increased PGE levels in the gastric fluid of cannulated ponies (AM Merritt, personal communication).

Etiology and pathophysiology

The pathophysiologic basis of squamous ulceration is likely multifactorial. A simplistic approach is to conclude that erosions or ulcers occur when there is an imbalance between ulcerogenic factors, such as the presence of hydrochloric acid, pepsin, or bile salts, and mucosal defense mechanisms. The glandular mucosa requires an extensive defense system because it is constantly exposed to acidic luminal contents. Prostaglandins, particularly PGE_2, play a key role in glandular mucosal defense through a number of mechanisms, including promotion of effective mucosal blood flow, increased mucus and bicarbonate secretion, supporting epithelial cell restitution, and by reducing acid output. The importance of homeostatic prostaglandins is clearly demonstrated through the experimental induction of glandular ulcers using NSAIDs.

The stomach is covered by a continuous layer of viscoelastic mucus.[27,28] This layer acts as the primary physical barrier to luminal contents. The gastric mucus covering the glandular stomach is actually made up of overlapping layers of mucin secreted by highly specialized cells of the glandular mucosa. Luminal acid, bradykinin and PGE_2 all increase the thickness of the mucus layer.[27] Within the mucus barrier is a pH gradient that varies from around 1.0 at the luminal surface to 7.0 pH units at the mucosal junction. Active mucosal secretion and entrapment of bicarbonate (HCO_3^-) within the mucus barrier is the primary factor responsible for the gradient. Bicarbonate secretion is enhanced during acid secretion through a process referred to as the 'alkaline tide'.[28] Briefly, within the parietal cell 1 mole of HCO_3^- is produced for each mole of H^+. The HCO_3^- is transported across the basolateral surface of the parietal cell in exchange for Cl^-. The HCO_3^- is subsequently transported via the local vascular supply to the epithelial cells where it is excreted. Acidic luminal contents provide the primary stimulus for bicarbonate secretion.[27] Sympathetic stimulation, mediated primarily through α_2-adrenoreceptors, is inhibitory to gastric and duodenal bicarbonate secretion.[28] This may be an important mechanism whereby stress can lead to reduced mucosal defense and ulceration.

Acid secretion

The horse stomach is similar to that of most other mammals in that it is capable of secreting large volumes of 0.16 N hydrochloric acid.[29] The acid is produced by gastric parietal cells located in the oxyntic glands of the glandular mucosa. The mucus layer that prevents the luminal contents from coming into direct contact with the epithelial surface does not impede the transport of acid or pepsin from the crypts into the gastric lumen.[28] The secreted hydrogen ions travel through small channels within the mucus gel created by hydrostatic pressure with the glands.

Acid secretion is regulated both centrally and peripherally, but it is the latter that has been the primary focus for pharmacologic control. The key local stimuli of acid secretion are acetylcholine, histamine, and gastrin. Acetylcholine release from postganglionic fibers at the level of the fundic mucosa directly binds to muscarinic receptors of the M_3 subtype.[30] Equally or more importantly acetylcholine also stimulates local ECL cells to release histamine, which subsequently bind

with histamine type 2 (H_2) receptors on the parietal cell, causing acid release.[29] Acetylcholine can also indirectly stimulate ECL cells through augmentation of gastrin release from G-cells. It does this by directly acting on G-cells and also by inhibiting the release of somatostatin from D-cells.[29]

ECL cells are small cells that lie subepithelially, and are therefore not directly exposed to luminal contents. The cells contain numerous cytoplasmic vesicles and function to synthesize, store and release histamine. Histamine release from ECL cells is stimulated by gastrin, acetylcholine, and β-adrenergic agonists. Release is inhibited by somatostatin and by histamine itself, through an autocrine feedback mechanism. Gastrin is a long-recognized acid secretagog and acts directly on the ECL cells by binding to the cholecystokinin B subtype (CCK_B) receptor to cause histamine release. Gastrin also has a hypertrophic and hyperplastic effect on ECL cells, as well as a key role in regulating the relative proportions of different gastric epithelial cell types, including stimulation of parietal cell differentiation.[31] In contrast to ECL cells, the gastrin-producing G-cells do have direct contact with gastric contents. A number of factors are known to regulate gastrin release, acting at either the luminal or basolateral surfaces of the G-cell. These include acetylcholine, gastrin-releasing peptide, somatostatin, and the chemical effects of luminal contents. The known luminal stimuli of gastrin release include amino acids (particularly aromatic amino acids), dietary amines, and calcium.[31] Gastrin is also released in response to sham feeding, oropharyngeal stimulation, and gastric distension. The pH of gastric contents has an important effect on gastrin, such that release is inhibited when the luminal pH is less than 3. This probably occurs indirectly through the paracrine release of somatostatin and provides an important feedback mechanism for parietal cells. Gastrin is considered to be a true peptide hormone in that it travels to target tissues via the blood. The hormone can therefore be measured in peripheral blood. The application of kits used to measure human gastrin in horses has been questioned as antisera raised against human gastrin binds poorly to equine gastrin.[32,33] Consistent with data derived from other species, serum gastrin levels in horses were increased after meal feeding.[34,35] The magnitude of the postprandial increase was also greater in treadmill-conditioned animals. These factors could provide a basis for the increased prevalence of squamous ulcers in Thoroughbreds in race training. Gastric distension in response to abdominal disease in horses also resulted in a significant increase in serum gastrin levels.[36]

Somatostatin is released from enteric fibers as well as fundic and antral D-cells. Somatostatin has a variety of functions in the stomach, one of which is inhibition of gastrin release from G-cells. Administration of the somatostatin analog, octreotide, at doses between 0.1 and 5 μg/kg bodyweight to healthy ponies resulted in a significant increase in intragastric pH that was sustained for between 2.4 and 5.4 hours.[37]

On the cellular level acid secretion from the parietal cell involves an elevation of intracellular calcium and cAMP, followed by activation of protein kinase cascades, which in turn trigger the translocation and insertion of the proton pump enzyme, H^+-K^+-ATPase, into the apical membrane of the cell.[38] After insertion the apical membrane opens up potassium and chloride ion conductance pathways. The H^+-K^+-ATPase enzyme catalyzes the electroneutral exchange of intracellular protons for extracellular potassium ions, thereby generating the proton gradient associated with HCl secretion.[38]

The parietal cell has a number of probable receptors, including those for histamine (H_2 receptor), acetylcholine (M_3 receptor), gastrin (CCK-B receptor), somatostatin, prostaglandins, and epidermal growth factor.[29,38] The latter three are thought to be inhibitory to the parietal cell.

Enterogastric reflux

Evidence exists to support a role of enterogastric reflux in gastric homeostasis. Visual inspection of the pylorus during routine gastroscopy in fasted horses frequently reveals entry of bile-colored fluid from the duodenum into the antrum. Bile salt concentrations obtained from the stomach of fasted horses with gastric cannulas averaged 0.23–0.44 mmol/L with some samples approaching 1.0 mmol/L.[39] Other investigators have measured intragastric concentrations of bile acids up to 2–3 mmol/L (AM Merritt, personal communication). Concentrations in fed animals are lower, usually less than 0.2 mmol/L.[39]

The importance of enterogastric reflux in the pathogenesis of squamous ulcer disease is not clear. Bile salts, such as taurodeoxycholate, have been incriminated in the pathophysiology of gastro-esophageal reflux disease (GERD) in people.[40] Several groups have demonstrated a harmful effect of bile acids on squamous mucosa in the presence of a low pH.[39–42] At a pH below their p*K*a bile acids are mostly non-ionized and insoluble, permitting mucosal uptake and damage. At a low pH (1.7 pH units) high concentrations of taurocholate (2.5 mmol) failed to cause additional damage to equine squamous mucosa above that induced by acid alone.[43] At a neutral intragastric pH bile acids are predominately ionized and remain in the gastric lumen. In vitro experiments have confirmed that bile acids at a neutral pH have no deleterious effect on the bioelectric properties of equine gastric squamous mucosa.[39,43]

Alternatively, the frequent refluxing of duodenal contents into the stomach may provide protection against mucosal ulceration or erosion by acting as a buffer. The continuous measurement of intragastric pH from healthy horses often reveals periodic and sudden elevations in pH. These pH shifts often occur at 15- to 30-minute intervals and are seen in both fed and fasted states. It is likely that these increases reflect enterogastric reflux of bicarbonate-rich fluid, rather than any abrupt cessation to local acid production.

Epidemiology

There is little doubt that the importance of gastric squamous ulceration has increased with the advent of 2.5-m and 3-m flexible videoendoscopes. These endoscopes have given us a

clear understanding of the prevalence of ulceration across a variety of horse types and activities. A number of important, albeit unexpected, observations have been made with respect to the prevalence of equine gastric squamous ulceration. For example, squamous ulceration occurs commonly (up to 50%) in young suckling foals in the absence of clinical signs and heals spontaneously without medication.[2]

Squamous mucosal ulceration has also been frequently reported in adult horses but the prevalence is dependent on a range of factors that include activity type and level, feed intake, management (diet, housing), and the presence of clinical signs compatible with ulcer disease.[5,6] Reported rates of disease frequently range between 50 and 90%, with horses in race training carrying the greatest risk of squamous mucosal ulcer disease (80–90%).[5,6,44] In this group the severity of disease usually increases as the intensity of training increases. By contrast, horses that are pastured and have limited controlled exercise are usually free of squamous ulcers.

The prevalence of gastric glandular ulceration is also greater in exercising horses, but the frequency of lesions is usually less than that reported in the squamous mucosa. In a retrospective study of 162 horses squamous ulceration was observed in 58% of animals.[6] By contrast, erosions and ulcers in the body of the glandular region were seen in only 8% of animals. Interestingly, antral and pyloric lesions were again noted in 58% of horses, but the authors could not find any association between sites with respect to either the presence or severity of lesions.

Role of feed and diet composition

The association between race training and gastric squamous ulceration has frequently led to speculation that diet may be a critical factor in the development of ulcer disease. Animals in race condition commonly receive high caloric diets, rich in concentrates and low in roughage.[5] Potentially ulcerogenic short chain volatile fatty acids (VFAs) are produced in the stomach from fermentable carbohydrates through the action of resident bacteria.[45] In the acidic conditions of the equine stomach these VFAs often exist in non-ionized forms and consequently are likely to penetrate and damage squamous epithelial cells.[46] The addition of the short chain fatty acid, acetate, to the mucosal side of isolated porcine gastric squamous epithelium in the presence of a low pH, resulted in reduced tissue electrical resistance consistent with damage to the mucosa.[41]

In a study using similar methodology on harvested equine gastric squamous mucosa the authors concluded that butyric, propionic, and valeric acid, but not acetic acid, were identified as potential ulcerogenic VFAs in that species.[47] This finding prompted the same group of investigators to examine the effect of diet on gastric squamous epithelium ulceration using healthy mixed breed horses with surgically implanted gastric cannulas.[46] The two diets contrasted in the experiment were a grass hay (bromegrass) diet and a combination of legume hay (alfalfa) and grain. In an unanticipated outcome, the number and severity of squamous ulcers were greater in horses that received the grass hay only diet. This was associated with a lower postprandial intragastric pH, and lower concentrations of acetic, propionic, valeric and isovaleric acid, and higher concentrations of butyric acid in animals that received the bromegrass hay. The authors suggested that the high calcium and/or protein content of the alfalfa and grain diet could have provided a protective buffer to the gastric contents. Alternatively, the transient postprandial increase in butyric acid with the grass hay diet may have been injurious to the squamous mucosa, particularly in light of the group's in vivo finding and documentation of a falling postprandial intragastric pH. These results further support the contention that gastric acidity may be a critical factor in the development of gastric ulceration.

Feeding frequency has an important impact on gastric squamous ulceration. Murray and Eichorn demonstrated that squamous ulceration could be induced in normal adult horses by alternating 24-hour periods of feed deprivation and ad libitum access to hay over an 8-day period.[11] Changes occurred rapidly and were usually apparent within 24–48 hours of cumulative feed deprivation. Feed deprivation results in increased gastric acidity.[48] The median intragastric pH during a 24-hour period with ad libitum access to grass hay was 3.1 pH units. Feed deprivation in the same group of healthy horses was associated with a lower median intragastric pH of 1.6. The common conclusion of these studies is that gastric acidity is the primary mechanism responsible for squamous ulcer disease.

The feed deprivation model for induction of squamous ulcer disease does not appear to result in glandular lesions.[6] This is not an unexpected finding in that the glandular mucosa is better suited to acid resistance, through a variety of mechanisms including secretion and maintenance of mucus-bicarbonate layer and mucosal blood flow.

Exercise

The prevalence data support a strong link between exercise and gastric ulceration. Using a barostat system, investigators recently measured the change in gastric volume in response to feeding and exercise.[49,50] Gastric volume was abruptly and significantly reduced during treadmill exercise in healthy horses. The authors concurrently measured intra-abdominal pressure and concluded that exercise-induced increases in intra-abdominal pressure were likely responsible for the observed reduction in gastric volume. The decrease in volume resulted in greater exposure of the squamous mucosa to the acidic contents of the ventral or dependent area of the gastric lumen.[49] The significance of these findings with respect to ulcer development is yet to be fully elucidated, particularly as the duration of exercise is often limited to minutes each day.

A further consideration is the effect of exercise on antroduodenal motility and gastric emptying. Data derived from human athletes indicated that exercise can delay gastric emptying.[51] Similar data are not available from horses, but it would not be unreasonable to assume that upper gastrointestinal tract motility was attenuated in exercising horses.

Stress

Diminished mucosal defenses associated with physiologic stress are thought to play an important role in the development of glandular lesions in humans. Similar mechanisms are likely responsible for glandular lesions in sick adult horses and newborn foals. It is highly unlikely that physiologic stress has a direct negative effect on squamous mucosa. By contrast, the role of psychologic stress in EGUS is not clear. Several studies have reported a higher prevalence of ulceration in horses that appeared to be more anxious or nervous, though differences were not great.[44,52] It has been hypothesized that horses of a nervous disposition may have reduced gastric volume in response to persistent tension of their abdominal muscles. This presumptive elevation in intra-abdominal pressure may force acidic contents into the dorsal region of the stomach (see above).

Housing

Simply relocating horses from pasture to a stall environment can induce gastric squamous ulcer disease.[11] Lesions are apparent within 7 days of the change. This occurs despite allowing free and continual access to grass hay. There could be a number of factors responsible for the increased incidence after confinement, including changes in diet and exercise, and induction of psychologic stress.

Right dorsal colitis

- An ulcerative syndrome of right dorsal colitis (RDC) that is associated with non-steroidal anti-inflammatory drug use, most commonly phenylbutazone.
- The clinical signs of RDC are variable depending on the duration and severity of the underlying colonic lesion, but include colic, weight loss, poor hair coat, diarrhea, reduced feed intake, and dependent edema.
- Both surgical and medical treatments have been utilized in the management of RDC. Surgery is usually performed on horses with narrowing of the right dorsal colon and correction involves surgical bypass or resection of affected tissue. Conservative medical management includes dietary control, medications, and avoidance of NSAIDs.

Recognition of the disease

Clinical signs

The clinical signs of RDC are variable depending on the duration and severity of the underlying colonic lesion. Commonly reported clinical signs include colic, weight loss, poor hair coat, diarrhea, reduced feed intake, and dependent edema. Signs of abdominal pain are often mild, but recurrent. The exception is horses where colonic stricture has occurred as a chronic response to persistent inflammation.[53] These horses often present with moderate and persistent pain due to impaction of proximal colonic segments and require surgical exploration or euthanasia. The diarrhea is highly variable in terms of volume and consistency, but is often of normal volume and soft, but formed consistency. The edema is due to hypoproteinemia secondary to loss across the inflamed and ulcerated colonic mucosa. The edema is most prominent in dependent regions including the ventrum, prepuce, distal limbs, and muzzle. In most horses with RDC dependent edema is absent or mild.

It is not uncommon for persistently affected animals to have flare ups of clinical signs. During these episodes horses may be febrile and colicky with diarrhea. The fever is likely due to the absorption of luminal toxins across the compromised mucosa.

Diagnosis

The diagnosis of right dorsal colitis is most commonly based on clinical signs, laboratory data, and a history of non-steroidal anti-inflammatory usage. Hypoproteinemia, specifically hypoalbuminemia, is the most characteristic laboratory finding in horses with RDC. Peripheral leukocyte changes are variable, and total white cell counts may be decreased, normal, or elevated. The count reflects the stage and severity of colitis at the time of sampling, and frequently, during acute exacerbations of the disease, there may be endotoxemia with resultant leukopenia with neutropenia, left shifting, and toxic neutrophil changes. As the disease progresses the total white cell count is commonly in the upper normal range or is mildly increased. Mild hyperfibrinogenemia is a common feature of RDC.[53] There may be a range of other biochemical and electrolyte abnormalities, but none is specific for RDC. Commonly reported derangements include hypocalcemia, hypophosphatemia, hyperbilirubinemia, and azotemia. Many abnormalities are attributable to a combination of mild dehydration and reduced feed intake.

Ultrasound may be a useful diagnostic aid although sensitivity and to a lesser extent specificity data are lacking. The colon on the right side of the abdomen may appear thickened with a distinctive hypoechoic line caused by edema formation. In some cases ultrasound is also used to assess disease progression and response to therapy. Recently, the use of ^{99m}Tc-HMPAO-labeled white blood cells in establishment of a diagnosis of RDC was described.[54] The authors reported linear uptake of radiolabeled white cells in the right craniioventral abdomen at 20 hours postinjection in two horses with RDC. The technique is clearly limited to referral practices with access to appropriate nuclear medicine facilities.

Treatment

A range of surgical and medical methods have been utilized in the management of RDC.[53,55–57] Surgery is usually performed on horses with narrowing of the right dorsal colon and correction involves surgical bypass or resection of affected tissue. Many cases have been successfully managed

conservatively, through a combination of dietary control, medications, and avoidance of NSAIDs.

Dietary management of RDC is aimed at minimizing the mechanical load on the colon.[55,57] This is achieved primarily by reducing the volume of long-stem roughage. Successful management often involves feeding of a complete pelleted ration, that is, a processed feed that contains both concentrates and fiber (roughage). If such a feed is not available or is not readily eaten then roughage is best provided in the form of frequent but brief access to pasture. Supplemented concentrates should be offered as frequent, small feeds. Psyllium mucilloid (30–100 g daily) has been fed to horses with RDC to aid in mucosal healing. The theoretic basis of psyllium supplementation is as a prebiotic, to promote the numbers of healthy bacteria that may facilitate mucosal healing, and to alter the concentration of luminal short chain acids to favor a ratio of acids that accelerate mucosal healing.[55,58] Feeding of psyllium is usually recommended for a minimum of 12 weeks after the diagnosis has been established.

The addition of linoleic acid, usually in the form of corn oil, to the diet of affected animals has been commonly advocated as a preventative strategy against gastric glandular ulceration in animals maintained on high doses of NSAIDs. Linoleic acid is a precursor of eicosanoids, such as PGE_2, and therefore may promote mucosal defensive mechanisms and aid in healing. An additional benefit of oil is the provision of calories, absorbed predominately in the small intestine.

Drug therapy in the management of RDC is controversial. Metronidazole has been used in many cases based on data derived from other species where certain intestinal obligate anaerobic bacteria, such as *Bacteroides vulgatus*, perpetuated the development of colitis.[59] Metronidazole also has anti-inflammatory effects and protects against the uncoupling of mitochondrial oxidative phosphorylation caused by NSAIDs.[60]

Sucralfate has been used in the management of RDC despite very little supportive data. Justification for use in colonic disease is based on limited cost, oral administration, an apparent absence of side effects, and limited efficacy data derived from humans.

There are a number of other drugs that have theoretical use in the management of RDC in horses, based on efficacy in the management of inflammatory bowel disease (IBD) in humans.[61] Pentoxifylline and thalidomide have anti-tumor necrosis factor alpha (TNF-α) effects that are of benefit, given the pivotal role of TNF-α in IBD. It is not known whether this cytokine plays a role in perpetuating the inflammation in RDC.

The avoidance of NSAIDs is often highly problematic in horses with RDC. This is particularly true for those with intermittent abdominal pain associated with the disease. If necessary, attending veterinarians should aim to minimize dosing and maximize interval times between doses. Preference is usually given to flunixin over phenylbutazone, but all drugs of this type should ideally be avoided. The other common circumstance of continued use involves persistent skeletal problems. Phenylbutazone is particularly attractive to horse owners because it is cheap, easy to administer, and effective. The development of RDC appears to be an idiosyncratic response to phenylbutazone in many horses, and as such, even infrequently administered small doses of the drug may be detrimental.

It has also been recommended to reduce physical and physiological 'stress' in animals to facilitate healing.[57] It is particularly important to ensure that rehabilitating animals are not exposed to episodes of dehydration. This means avoidance of forced exercise and unnecessary transportation.

A positive response to treatment can be gauged by an improvement in clinical signs, normalization of circulating protein concentrations, and a reduction in bowel wall thickness on ultrasound. Improvement is gradual, usually over 4–8 weeks, and it may take months to normalize many of these parameters. Animals are at risk of relapse, particularly in response to dietary changes and/or administration of NSAIDs.

Pathophysiology

The pathophysiologic basis of RDC remains to be fully elucidated. The adverse effects of NSAIDs on the gastrointestinal tract are however well described across a wide range of species.[62] Most of these are ascribed to the suppression of protective endogenous prostanoids, particularly PGE_2, and result in mucosal erosion or ulceration. Excessive doses of NSAIDs reliably produce gastric glandular ulceration in normal horses, but member drugs do so with differing potencies.[63,64] The variability between drugs with respect to adverse side effects is likely due to their relative inhibition of cyclooxygenase I or cyclooxygenase II isoenzymes.[65] Ulcerative lesions involving the right dorsal colon have also been induced experimentally in normal horses by giving 6 g of phenylbutazone daily for 5 days in the face of reduced access to water.[56] The susceptibility of the right dorsal colon over other regions of the colon has been the focus of much discussion. An inflammatory disease of the colon has also been described in humans associated with the administration of NSAIDs.[66]

Both phenylbutazone and indometacin influence in vitro ion transport in tissues collected from the right dorsal colon.[67] The primary effect is likely mediated by prostaglandins as changes were reversed when PGE_2 was added to the bathing media. There was a strong association between prostaglandin supplementation and chloride and bicarbonate secretion. The authors reported that the major histologic lesion induced by phenylbutazone was consistent with the induction of apoptosis.[67]

Salmonella species have been isolated from the feces of animals with RDC, raising the possibility of a direct causal relationship. Given that the recovery of *Salmonella* is uncommon in horses with suspected RDC, and that the organism is often shed by small numbers of healthy animals, this association remains doubtful.[57]

Epidemiology

The ulcerative syndrome of right dorsal colitis (RDC) is associated with non-steroidal anti-inflammatory drug use, most com-

monly phenylbutazone. Most cases are reported to occur after prolonged or excessive courses of the drug, but some have occurred in horses that have received appropriate doses of phenylbutazone for as little as 3–5 days.[55,56] Although uncommon, RDC has been reported after the administration of other anti-inflammatory drugs, such as flunixin meglumine.

Cecal emptying defect

- Cecal emptying defect (CED) is a primary motility disease involving the cecum or ileocecocolic region.
- The pathophysiology of CED is not known, but the syndrome may best mimic postoperative ileus in humans, which is considered a large intestinal disorder.
- Clinical signs are often subtle unless cecal perforation has occurred.
- Management of CED includes fluid therapy in combination with lubricants or laxatives, such as mineral oil or magnesium sulfate, and careful use of anti-inflammatory drugs.

Recognition of the disease

Clinical signs

Clinical signs are often subtle unless cecal perforation has occurred. In horses with CED after anesthesia evident signs are usually apparent 3–5 days after the procedure; early signs include depression and a reduction in both feed intake and fecal output. Ineffective emptying results in overfilling of the cecum with moist contents, which is manifest by signs of mild to moderate colic. Cecal distension with digesta can be palpated rectally in horses with advanced cecal dysfunction. If recognized late or untreated the cecum may rupture resulting in fatal peritonitis.

Treatment

Fluid therapy is an important component in the management of CED, usually in combination with lubricants or laxatives, such as mineral oil or magnesium sulfate, and with careful use of anti-inflammatory drugs. Horses with primary cecal impaction or impaction secondary to an emptying defect frequently require surgery in order to prevent fatal rupture. The surgical management of these cases is controversial and may include typhlotomy alone, typhlotomy with a bypass procedure such as ileocolic or jejunocolic anastomosis, or a bypass without typhlotomy.[68] Most horses that undergo simple typhlotomy have an uneventful recovery,[69] although a small number will reimpact and require a second laparotomy. The use of prokinetics in the prevention and treatment of CED is also controversial. Intravenously administered erythromycin lactobionate (1.0 mg/kg i.v.) hastens cecal emptying in normal animals and induces colonic MMC-like activity across the colon.[70] Administration is often associated with defecation and abdominal discomfort. The drug may be helpful at preventing cecal impaction in horses after anesthesia, though its effectiveness on cecal motility in the immediate postoperative period may be reduced.[71] High doses, constant infusion or prolonged use of erythromycin induces receptor downregulation and inhibition of activity. Erythromycin can induce diarrhea in adults therefore dosing over many days should be avoided. Other drugs that may be useful include bethanechol, lidocaine (lignocaine), or yohimbine, although efficacy data are lacking.[72]

Pathophysiology

The pathophysiology of CED is not known, but the syndrome may best mimic postoperative ileus in humans, which is considered a large intestinal disorder. An important difference in horses is that laparotomy is a rare predisposing factor, and most cases occur in horses undergoing routine extra-abdominal surgical procedures. General anesthesia itself is a potent inhibitor of gastrointestinal motility in horses, but these effects are short-lived and reversible within hours of anesthetic withdrawal.[73] The return of normal motility in horses after experimental ileus was most delayed in the cecum, suggesting that this may be a common site of ileus in horses.[71] A link between routine postoperative medications, such as phenylbutazone and aminoglycoside antibiotics, has been suspected but not established. An inhibitory effect of NSAIDs on large colon contractility has been demonstrated using in vitro techniques.[74] Primary sympathetic overstimulation could be involved as many of the affected animals are young, male horses, or animals with painful diseases. The development of small intestinal postoperative ileus but not cecal emptying dysfunction, is influenced by the duration of surgery.[75,76]

Epidemiology

Cecal emptying defect (CED) is a primary motility disease involving the cecum or ileocecocolic region.[76–78] The syndrome occurs sporadically, but anecdotally appears to be more prevalent in young athletic horses. Most cases are reported after general anesthesia and extra-abdominal surgery, particularly orthopedic and upper airway procedures. Others occur spontaneously, often in animals with painful primary conditions such as uveitis or septic tenosynovitis.

Stress-associated diarrhea

Diarrhea occurs commonly in certain animals when placed under stressful conditions. These include transportation, placement into a foreign environment, exposure to unknown animals, or associated with moderate to heavy exercise. The intermittent nature of the diarrhea, coupled with an absence of abnormal clinical findings, likely reflect a physiologic rather than pathologic basis. In any animal exposure to hostile condi-

tions initiates a stress response that comprises alterations in behavior, autonomic function, and the secretion of multiple hormones.[79] The latter includes increased secretion of epinephrine (adrenaline) and norepinephrine (noradrenaline), the release of corticotropin-releasing factor (CRF) and vasopressin, and the secretion of adrenocorticotrophin (ACTH).

Corticotropin-releasing factor is the neurohormonal factor of greatest interest with respect to stress-induced alterations in colonic motility. The central release of CRF acts in the brain to inhibit gastric emptying; while CRF-induced modulation of parasympathetic outflow stimulates colonic motility and fecal excretion in response to psychologic stress.[80] Hypersecretion of CRF may contribute to stress-related exacerbation of irritable bowel syndrome in man.[80] Similar neurohormonal responses to stress have not been reported in horses, although exercise in conditioned horses was not associated with significant increases in CRF levels collected from pituitary venous blood.[81]

Treatment is rarely indicated in horses with stress-associated diarrhea as the volume of diarrhea rarely results in clinical dehydration. Novel treatments for irritable bowel syndrome in humans include tachykinin receptor antagonists, 5-HT_3 receptor antagonists, and 5-HT_4 agonists, but none of these agents has been evaluated clinically in horses.

References

1. Recommendations for the diagnosis and treatment of equine gastric ulcer syndrome (EGUS). Equine Vet Educ 1999; October:122–134.
2. Acland HM, Gunson DE, Gillette DM. Ulcerative duodenitis in foals. Vet Pathol 1983; 20:653–661.
3. Rebhun WC, Dill SG, Power HT. Gastric ulcers in foals. J Am Vet Med Assoc 1982; 180:404–407.
4. Traub JL, Gallina AM, Grant BD, et al. Phenylbutazone toxicosis in the foal. Am J Vet Res 1983; 44:1410–1418.
5. Hammond CJ, Mason DK, Watkins KL. Gastric ulceration in mature thoroughbred horses. Equine Vet J 1986; 18:284–287.
6. Murray MJ, Nout YS, Ward DL. Endoscopic findings of the gastric antrum and pylorus in horses: 162 cases (1996–2000). J Vet Intern Med 2001; 15:401–406.
7. Khittoo G, Vermette L, Nappert G, et al. Isolation of a major form of pepsinogen from gastric mucosa of horses. Am J Vet Res 1991; 52:713–717.
8. Sayegh AI, Anderson NV, Harding JW, et al. Purification of two equine pepsinogens by use of high-performance liquid chromatography. Am J Vet Res 1999; 60:114–118.
9. Wilson JH, Pearson MM. Serum pepsinogen levels in foals with gastric or duodenal ulcers. In: Proceedings of the 31st Annual Convention of the AAEP. 1985:149–156.
10. Clark CK, Merritt AM, Burrow JA, et al. Effect of aluminum hydroxide/magnesium hydroxide antacid and bismuth subsalicylate on gastric pH in horses. J Am Vet Med Assoc 1996; 208:1687–1691.
11. Murray MJ, Eichorn ES. Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. Am J Vet Res 1996; 57:1599–1603.
12. Campbell-Thompson ML, Merritt AM. Effect of ranitidine on gastric acid secretion in young male horses. Am J Vet Res 1987; 48:1511–1515.
13. Holland PS, Ruoff WW, Brumbaugh GW, et al. Plasma pharmacokinetics of ranitidine HCl in adult horses. J Vet Pharmacol Ther 1997; 20:145–152.
14. Sams RA, Gerken DF, Dyke TM, et al. Pharmacokinetics of intravenous and intragastric cimetidine in horses. I. Effects of intravenous cimetidine on pharmacokinetics of intravenous phenylbutazone. J Vet Pharmacol Ther 1997; 20:355–361.
15. Sanchez LC, Lester GD, Merritt AM. Effect of ranitidine on intragastric pH in clinically normal neonatal foals. J Am Vet Med Assoc 1998; 212:1407–1412.
16. Murray MJ, Grodinsky C. The effects of famotidine, ranitidine and magnesium hydroxide/aluminium hydroxide on gastric fluid pH in adult horses. Equine Vet J Suppl 1992; 52–55.
17. Andrews FM, Sifferman RL, Bernard W, et al. Efficacy of omeprazole paste in the treatment and prevention of gastric ulcers in horses. Equine Vet J Suppl 1999; 81–86.
18. MacAllister CG, Sifferman RL, McClure SR, et al. Effects of omeprazole paste on healing of spontaneous gastric ulcers in horses and foals: a field trial. Equine Vet J Suppl 1999; 77–80.
19. Vatistas NJ, Nieto JE, Snyder JR, et al. Clinical trial to determine the effect of omeprazole given once or twice daily on gastric ulceration. Equine Vet J Suppl 1999; 87–90.
20. Andrews FM, Doherty TJ, Blackford JT, et al. Effects of orally administered enteric-coated omeprazole on gastric acid secretion in horses. Am J Vet Res 1999; 60:929–931.
21. Daurio CP, Holste JE, Andrews FM, et al. Effect of omeprazole paste on gastric acid secretion in horses. Equine Vet J Suppl 1999; 59–62.
22. Vatistas NJ, Snyder JR, Nieto J, et al. Acceptability of a paste formulation and efficacy of high dose omeprazole in healing gastric ulcers in horses maintained in race training. Equine Vet J Suppl 1999; 71–76.
23. Andrews FM, Doherty TJ, Blackford JT, et al. Effects of orally administered enteric-coated omeprazole on gastric acid secretion in horses. Am J Vet Res 1999; 60:929–931.
24. Creutzfeldt W, Lamberts R. Is hypergastrinaemia dangerous to man? Scand J Gastroenterol Suppl 1991; 180:179–191.
25. Borne AT, MacAllister CG. Effect of sucralfate on healing of subclinical gastric ulcers in foals. J Am Vet Med Assoc 1993; 202:1465–1468.
26. Geor RJ, Petrie L, Papich MG, et al. The protective effects of sucralfate and ranitidine in foals experimentally intoxicated with phenylbutazone. Can J Vet Res 1989; 53:231–238.
27. Guha S, Kaunitz JD. Gastroduodenal mucosal defense: an integrated protective response. Curr Opin Gastroenterol 2002; 18:650–657.
28. Flemstrom G, Isenberg JI. Gastroduodenal mucosal alkaline secretion and mucosal protection. News Physiol Sci 2001; 16:23–28.
29. Hersey SJ, Sachs G. Gastric acid secretion. Physiol Rev 1995; 75:155–189.
30. Wilkes JM, Kajimura M, Scott DR, et al. Muscarinic responses of gastric parietal cells. J Membr Biol 1991; 122:97–110.
31. Dockray GJ, Varro A, Dimaline R, et al. The gastrins: their production and biological activities. Annu Rev Physiol 2001; 63:119–139.
32. Johnsen AH, Sandin A, Rourke IJ, et al. Unique progastrin processing in equine G-cells suggests marginal tyrosyl sulfotransferase activity. Eur J Biochem 1998; 255:432–438.
33. Young DW, Smyth GB. Validation of a radioimmunoassay for measurement of gastrin in equine serum. Am J Vet Res 1988; 49:1179–1183.

34. Brown CM, Sonea I, Nachreiner RF, et al. Serum immunoreactive gastrin activity in horses: basal and postprandial values. Vet Res Commun 1987; 11:497–501.
35. Furr M, Taylor L, Kronfeld D. The effects of exercise training on serum gastrin responses in the horse. Cornell Vet 1994; 84:41–45.
36. Schusser GF, Obermayer-Pietsch B. Plasma gastrin levels in horses with colic. Tierarztl Prax 1992; 20:395–398.
37. Sojka JE, Weiss JS, Samuels ML, et al. Effect of the somatostatin analogue octreotide on gastric fluid pH in ponies. Am J Vet Res 1992; 53:1818–1821.
38. Yao X, Forte JG. Cell biology of acid secretion by the parietal cell. Annu Rev Physiol 2003; 65:103–131.
39. Berschneider HM, Blikslager AT, Roberts MC. Role of duodenal reflux in nonglandular gastric ulcer disease of the mature horse. Equine Vet J Suppl 1999; 24–29.
40. Lillemoe KD, Gadacz TR, Harmon JW. Bile absorption occurs during disruption of the esophageal mucosal barrier. J Surg Res 1983; 35:57–62.
41. Argenzio RA, Eisemann J. Mechanisms of acid injury in porcine gastroesophageal mucosa. Am J Vet Res 1996; 57:564–573.
42. Lang J, Blikslager A, Regina D, et al. Synergistic effect of hydrochloric acid and bile acids on the pars esophageal mucosa of the porcine stomach. Am J Vet Res 1998; 59:1170–1176.
43. Widenhouse TV, Lester GD, Merritt AM. Effect of hydrochloric acid, pepsin, or taurocholate on bioelectric properties of gastric squamous mucosa in horses. Am J Vet Res 2002; 63:744–749.
44. Vatistas NJ, Snyder JR, Carlson G, et al. Cross-sectional study of gastric ulcers of the squamous mucosa in thoroughbred racehorses. Equine Vet J Suppl 1999; 34–39.
45. Argenzio RA, Southworth M, Stevens CE. Sites of organic acid production and absorption in the equine gastrointestinal tract. Am J Physiol 1974; 226:1043–1050.
46. Nadeau JA, Andrews FM, Mathew AG, et al. Evaluation of diet as a cause of gastric ulcers in horses. Am J Vet Res 2000; 61:784–790.
47. Nadeau JA, Andrews FM, Patton CS, et al. Volatile fatty acid injury in the nonglandular region of the equine stomach: implications in the pathogenesis of gastric ulcer disease. J Vet Int Med 2001; 854.
48. Murray MJ, Schusser GF. Measurement of 24-h gastric pH using an indwelling pH electrode in horses unfed, fed and treated with ranitidine. Equine Vet J 1993; 25:417–421.
49. Lorenzo-Figueras M, Merritt AM. Effects of exercise on gastric volume and pH in the proximal portion of the stomach of horses. Am J Vet Res 2002; 63:1481–1487.
50. Lorenzo-Figueras M, Jones G, Merritt AM. Effects of various diets on gastric tone in the proximal portion of the stomach of horses. Am J Vet Res 2002; 63:1275–1278.
51. Leiper JB, Broad NP, Maughan RJ. Effect of intermittent high-intensity exercise on gastric emptying in man. Med Sci Sports Exerc 2001; 33:1270–1278.
52. Murray MJ, Schusser GF, Pipers FS, et al. Factors associated with gastric lesions in thoroughbred racehorses. Equine Vet J 1996; 28:368–374.
53. Hough ME, Steel CM, Bolton JR, et al. Ulceration and stricture of the right dorsal colon after phenylbutazone administration in four horses. Aust Vet J 1999; 77:785–788.
54. East LM, Trumble TN, Steyn PF, et al. The application of technetium-99m hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO) labeled white blood cells for the diagnosis of right dorsal ulcerative colitis in two horses. Vet Radiol Ultrasound 2000; 41:360–364.
55. Cohen ND, Carter GK, Mealey RH, et al. Medical management of right dorsal colitis in 5 horses: a retrospective study (1987–1993). J Vet Int Med 1995; 9:272–276.
56. Karcher LF, Dill SG, Anderson WI, et al. Right dorsal colitis. J Vet Int Med 1990; 4:247–253.
57. Cohen ND. Equine right dorsal colitis. In: Mair T, Divers T, Ducharme NG, eds. Manual of equine gastroenterology. London: WB Saunders; 2002:438–442.
58. Kanauchi O, Mitsuyama K, Araki Y, et al. TNF therapy for Crohn's disease. Curr Pharm Dis 2003; 9:289–294.
59. Rath HC. Role of commensal bacteria in chronic experimental colitis: lessons from the HLA-B27 transgenic rat. Pathobiology 2002; 70:131–138.
60. Leite AZ, Sipahi AM, Damiao AO, et al. Protective effect of metronidazole on uncoupling mitochondrial oxidative phosphorylation induced by NSAID: a new mechanism. Gut 2001; 48:163–167.
61. Blam ME, Stein RB, Lichtenstein GR. Integrating anti-tumor necrosis factor therapy in inflammatory bowel disease: current and future perspectives. Am J Gastroenterol 2001; 96:1977–1997.
62. Rostom A, Dube C, Wells G, et al. Prevention of NSAID-induced gastroduodenal ulcers. Cochrane Database Syst Rev 2002; CD002296.
63. MacAllister CG, Morgan SJ, Borne AT, et al. Comparison of adverse effects of phenylbutazone, flunixin meglumine, and ketoprofen in horses. J Am Vet Med Assoc 1993; 202:71–77.
64. MacAllister CG. Effects of toxic doses of phenylbutazone in ponies. Am J Vet Res 1983; 44:2277–2779.
65. Brideau C, Van Staden C, Chan CC. In vitro effects of cyclooxygenase inhibitors in whole blood of horses, dogs, and cats. Am J Vet Res 2001; 62:1755–1760.
66. Katsinelos P, Christodoulou K, Pilpilidis I, et al. Colopathy associated with the systemic use of nonsteroidal antiinflammatory medications. An underestimated entity. Hepatogastroenterology 2002; 49:345–348.
67. Richter RA, Freeman DE, Wallig M, et al. In vitro anion transport alterations and apoptosis induced by phenylbutazone in the right dorsal colon of ponies. Am J Vet Res 2002; 63:934–941.
68. Gerard MP, Bowman KF, Blikslager AT, et al. Jejunocolostomy or ileocolostomy for treatment of cecal impaction in horses: nine cases (1985–1995). J Am Vet Med Assoc 1996; 209:1287–1290.
69. Roberts CT, Slone DE. Caecal impactions managed surgically by typhlotomy in 10 cases (1988–1998). Equine Vet J Suppl 2000; 74–76.
70. Lester GD, Merritt AM, Neuwirth L, et al. Effect of erythromycin lactobionate on myoelectric activity of ileum, cecum, and right ventral colon, and cecal emptying of radiolabeled markers in clinically normal ponies. Am J Vet Res 1998; 59:328–334.
71. Hooper RN, Roussel AJ, Cohen ND. Erythromycin stimulates myoelectric activity in the ileum and pelvic flexure of horses in the post-operative period. In: Proceedings of the Sixth Equine Colic Research Symposium, Athens, Georgia. 1998:42.
72. Lester GD, Merritt AM, Neuwirth L, et al. Effect of alpha 2-adrenergic, cholinergic, and nonsteroidal anti-inflammatory drugs on myoelectric activity of ileum, cecum, and right ventral colon and on cecal emptying of radiolabeled markers in clinically normal ponies. Am J Vet Res 1998; 59:320–7.J 1987; 64:85–6.
73. Lester GD, Bolton JR, Cullen LK, et al. Effects of general anesthesia on myoelectric activity of the intestine in horses. Am J Vet Res 1992; 53:1553–1557.

74. Van Hoogmoed LM, Snyder JR, Harmon F. In vitro investigation of the effect of prostaglandins and nonsteroidal anti-inflammatory drugs on contractile activity of the equine smooth muscle of the dorsal colon, ventral colon, and pelvic flexure. Am J Vet Res 2000; 61:1259–1266.
75. Roussel AJ Jr, Cohen ND, Hooper RN, et al. Risk factors associated with development of postoperative ileus in horses. J Am Vet Med Assoc 2001; 219:72–78.
76. Hilbert BJ, Little CB, Bolton JR, et al. Caecal overload and rupture in the horse. Aust Vet J 64:85–86.
77. Campbell ML, Colahan PC, Brown MP, et al. Cecal impaction in the horse. J Am Vet Med Assoc 1984; 184:950–952.
78. Ross MW, Martin BB, Donawick WJ. Cecal perforation in the horse. J Am Vet Med Assoc 1985; 187:249–253.
79. Carrasco GA, Van de Kar LD. Neuroendocrine pharmacology of stress. Eur J Pharmacol 2003; 463:235–272.
80. Tache Y, Martinez V, Million M, et al. Corticotropin-releasing factor and the brain-gut motor response to stress. Can J Gastroenterol 1999; 13 (Suppl A):18A–25A.
81. Alexander SL, Irvine CH, Ellis MJ, et al. The effect of acute exercise on the secretion of corticotropin-releasing factor, arginine vasopressin, and adrenocorticotropin as measured in pituitary venous blood from the horse. Endocrinology 1991; 128:65–72.

CHAPTER 49

Veterinary aspects of racing and training Thoroughbred race horses

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Providing optimal veterinary services to Thoroughbred race horses requires an understanding of both the veterinary aspects of their care, and the dynamics and economics of the racing industry. This chapter provides a demographic overview of Thoroughbred racing and in particular wastage. Commonly encountered diseases are discussed with an emphasis on the veterinary management and disease prophylaxis during both training and racing.

Demographics and wastage

Thoroughbred racing evolved in England over 200 years ago and now exists in over 50 countries.[1] A comparison of the size of Thoroughbred industries between some of the major racing countries based on foal crop, number of races and starters, prize money and betting turnover is illustrated in Table 49.1. The figures in this table under-represent the number of Thoroughbred race horses since they do not include horses involved in National Hunt and point-to-point racing. Similarly, this chapter will concentrate on the veterinary management aspects of Thoroughbred horses racing on the flat.

All facets of the Thoroughbred racing industry rely heavily on veterinary input which extends from pre-conception to the end of a horse's athletic career. Termination of a racing career may result from veterinary advice pertaining to injury or disease, or be based on economic grounds and an assessment of athletic ability. Horses are typically retired to stud if they have accomplished a superior racing career that they are unlikely to better, or have genetic potential that would offset their future potential race earnings. Alternatively, other horses are routed to other athletic endeavors if they are functionally sound.

Horses have their first opportunity to race as 2-year-olds and their competitive longevity is the result of a multitude of veterinary and specific industry-based factors. Generally the majority of the racing population is made up of horses aged 2 to 5 years of age. Sex distribution of the racing population commences with relatively equal proportions of males and females as yearlings and 2-year-olds.[2,3] In subsequent racing years there is an attrition of females to breeding so that horses older than 4 years of age are typically gelded males (Figs 49.1, 49.2).[2–4]

Age at first race start depends on athletic conformation, degree of maturity, genetics, aspirations and expectations of the owner and trainer, as well as race programming and prize money structure of the specific country. Attempts to judge musculoskeletal maturity and suitability for racing based on objective means such as physeal closure have been generally unsuccessful.[5]

The actual time of first race start is then dependent on the response to training, health, and soundness. Interestingly, in a study examining factors affecting early career wastage there was no correlation between sex and foaling date and time of first race start.[3] While concerns over racing 2-year-old horses exist, two studies found that horses who raced first as 2-year-olds had greater numbers of career starts and raced longer than did horses that commenced racing at an older age.[2,3] This may in part be due to injury or disease that prevented these older horses competing as 2-year-olds and which may have persisted further into their career.

Wastage refers to all losses occurring at any stage in the breeding, growth, training and racing of a race horse. Wastage includes all losses in breeding, deaths at any stage, lost training days, unraced horses and retirement. Considerable wastage occurs in the Thoroughbred racing industry as a whole from the time that the mare is covered to the commencement of racing by the progeny. A UK-based

Table 49.1 A comparison of some key industry figures for international Thoroughbred flat racing among major racing countries, for the year 2000

Country	Foal crop	Number of races	Number of horses started	Average prize money $(US)	Yearly national betting turnover (US$ millions)
USA	33 360	55 486	64 443	16 201	2029
Australia	18 481	21 561	31 251	7756	699
Japan	838	25 500	29 282	34 532	4926
Great Britain	5194	4394	7685	16 445	1069
France	4180	4250	7330	15 716	795
South Africa	2527	4152	7497	5809	NA
Argentina	6582	7825	10 974	4696	46
Brazil	3391	5851	7788	2430	21
Canada	2570	5386	6557	12 421	67
New Zealand	4958	2647	5077	5054	44
Italy	1905	5110	6636	9202	334

Source: International Statistical Survey of Horse Racing and 2000 statistics, compiled by the Société d'Encouragement and presented at the 34th International Conference of Racing Authorities, Paris, France, 8 October 2001. In some cases national betting turnover includes harness racing. Total betting turnover in South Africa not available. Additional data can be found at http://home.jockeyclub.com/factbook/worldwide.html.

wastage study calculated 72.8% of mares each year fail to have progeny that will go on to race between 2 and 4 years of age.[6] In this study, the 1975 foal crop was followed and of those named and eligible for training only 50.6% raced as 2-, 3-, or 4-year-olds, this result is confounded by horses reserved for National Hunt racing that did not race on the flat.[6] Similar prospective studies of 353 and 553 yearlings sold at auctions in Australia revealed that approximately 50% of these horses raced as 2-year-olds and that 75 to 80% of horses had raced by their 6-year-old seasons.[2,3]

Lameness, followed by respiratory disease, is the major cause of wastage for Thoroughbreds in race training, manifesting as lost or affected training days.[3,6–9] A UK wastage study found that 53% of horses showed lameness at some stage during a season and in 20% of cases the lameness was sufficient to prevent racing after injury.[6] A subsequent study identified lameness (67.6%) and respiratory disorders (20.5%) as the most common cause of lost training days.[7] Similarly a USA-based study looking at 95 horses over an 81-day period reported musculoskeletal injuries altering training or racing schedules in 35–55% of horses and preventing training or racing for a period of time in 26–46% of horses.[10] A recent Australian wastage study of 2- and 3-year-old horses found that of lost or modified training days, 56% were due to lameness and 16% due to respiratory disease.[11] Similar findings have recently been reported from New Zealand, identifying musculoskeletal (82%) and respiratory diseases (11%) as the major cause of involuntary time out of training.[9]

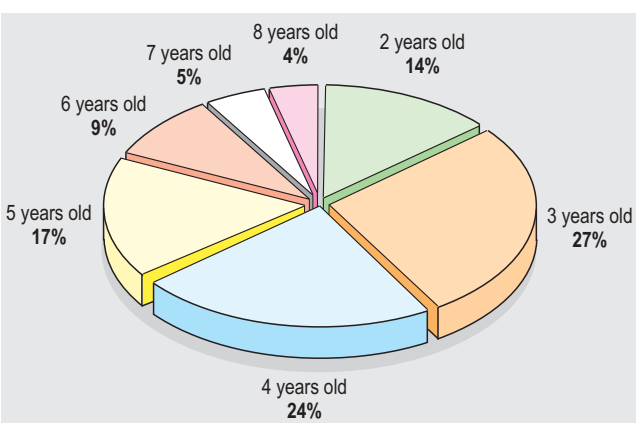

Fig. 49.1
Age distribution of Thoroughbred race horses in Australia over a 6-year period (1992/1993–1997/1998). (Source of data: VRC racing services.)

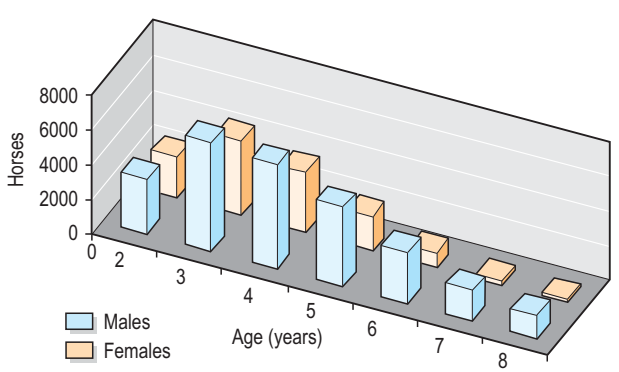

Fig. 49.2
Average age and sex distribution for horses racing in Australia over a 6-year period (1992/1993–1997/1998). (Source of data: VRC racing services.)

A further reason horses may not race or race less than the average number of times is a 'lack of athletic ability'.[2,6]

Breakdowns, fatal musculoskeletal injuries and sudden death during racing and training have been a focus of many recent studies, most aimed at identifying risk factors in an attempt to minimize these injuries.[12–23] Regional differences exist with regard to risk factors, prevalence and types of injuries between countries, states, regions and even individual tracks.[13–17] The rate of breakdown injuries during racing differs between countries with rates of 2.2/1000, 2.9/1000 and 21/1000 starters in the USA, Australia and Japan, respectively.[12,15,18] These differences are difficult to interpret since they may in part be due to potential errors inherent with epidemiologic studies and different definitions of a breakdown.[16,19] Approximate risk of fatal or catastrophic musculoskeletal injury is 0.6/1000 starters in Australia and 1.4–1.7/1000 starters in the USA, while in the UK there are 0.8 deaths/1000 starters.[15,19–22] The reasons for differences in rates between countries are multifactorial, but dirt tracks have been implicated as one factor contributing to a higher incidence of injury.[22,23]

Catastrophic life-threatening injuries appear more likely to occur when racing whereas non-fatal injuries are more common in training, which may be a function of speed.[16,18] Breakdown injuries more commonly involve a forelimb than hindlimbs; common sites of injury include fetlock and suspensory ligament, carpus, humerus, pelvis, tibia and superficial flexor tendon.[13,18,19,21] There is evidence that pre-existing lesions predispose to catastrophic injuries, highlighting the value of early identification of such lesions in preventing injury.[17,18,24–26]

A multitude of risk factors contributing to breakdown injuries has been identified including track characteristics,[15,23,27] weather and season,[23] race distance, starting postion and race quality.[19,28] Individual horse characteristics identified include racing frequency, training intensity, age at first start, duration of career, number of life time starts and the hoof or shoeing characteristics.[14,15,23,29,30] Causes of sudden death other than fatal musculoskeletal injuries that have been described include ruptured aorta, myocarditis, valvular insufficiency, sclerosis of the coronary arteries, severe pulmonary hemorrhage and disseminated massive hemorrhage.[31]

Provision of services

A working relationship between the veterinarian and trainer is paramount to providing optimal services to a stable. Excellent communication is essential, as is an appreciation of the trainer's perspective and recognition of the non-veterinary factors such as owner expectations and aims, economics and the trainer's previous personal experience. The veterinarian should also have knowledge of normal training techniques and schedules, which often differ between trainers. Veterinary services should be preventive as well as problem oriented and applied at both the individual horse and whole stable level. The level and extent of services provided on an ambulatory basis will be dictated by the ability to access a hospital center or referral clinic.

The veterinarian–farrier relationship is important because of the prevalence and significance of hoof-related problems. Ideally management and prevention of hoof-related lameness should be a joint approach as opposed to demarcating and allocating 'foot' and 'non-foot' cases. Adequate diagnostics and an understanding of the principles involved in the application of physical and alternative therapies allows the veterinarian to appropriately prescribe and substantiate or refute their use.

Establishment of a complete and reliable recording system of disease, lameness and treatment is essential. Accurate recording of administered medications is important where withdrawal times prior to racing must be considered. The system must be easily accessible, efficient and permanent. Ensuring accurate identification of horses prior to treatment or procedures is paramount in a stable environment, particularly where there are large numbers of horses and staff involved. Similarly, clear instructions and great care should be taken when dispensing and administering medications that may be regulated by racing authorities.

The importance of a thorough clinical examination cannot be overstated. It is often easy to neglect the basics in the busy stable environment. A thorough relevant history and systematic clinical examination are the foundation of any accurate and efficient diagnosis, treatment and prognosis. Horses are often presented for a particular complaint but on closer inspection reveal multiple related and unrelated problems. It is also important to judge what can and cannot be done efficiently, adequately and practically at the racetrack/stable and what is better performed in the clinic setting.

Acquisition of race horses involves selection of yearlings, 2-year-olds and tried (older) horses. Economics and method of purchase by public auction or private treaty, will determine the extent of veterinary prepurchase examination. Limiting comments to lesions and conformational faults only, and their likely effects on future athletic soundness, appears the most appropriate advice from a veterinary perspective.

General disease and injury management concepts

Prophylactic measures

Ligament, tendon and joint injuries may occur during breaking and pre-training and reports of swelling or lameness during this period warrant investigation. Subclinical conditions such as osteochondrosis may manifest during preliminary training and early identification may allow treatment with minimal impact on a horse's racing career.

Prophylactic measures to prevent and minimize problems are implemented as part of good stable management. Such measures include routine selection of horses for lameness and clinical examinations, vaccination and parasite

prophylaxis programs. Feeding and training regimens are typically established by the trainers. Sound reasoning coupled with subtle diplomacy is required to obtain trainer compliance with regard to feed and work schedule related changes.

The veterinarian has an important role in advising trainers on the value of instructing stable hands and setting up reliable recording systems that ensure staff observe and report on their horses as they go about caring for and riding them. Feedback from stable staff is important at all levels including observations such as fecal amount and consistency, feed consumption, water intake, signs of colic, coughing or evidence of stable vices, all of which can be detected by educated grooms maintaining stalls. Regular assessment of bodyweights can be used as a monitor of fitness, disease or 'training off'. Recording rectal temperatures of horses with reduced feed intake, subdued demeanor or any other clinical signs of disease should be ingrained as an automatic process.

Daily tacking up can identify a variety of subtle changes including changes in gait as horses are walked out of stall, acquired swellings, skin conditions, nasal discharge and change in response to saddling or bitting. Riders, trainers and clockers can monitor for lameness and more subtle gait changes such as 'hanging on a rein', 'feeling rough' or repeatedly changing strides. Likewise other observations such as respiratory noise, altered breathing pattern or performance and poor recovery after exercise may all facilitate early identification of problems.

Routinue 'trot-up' examinations are an efficient management tool for early detection of musculoskeletal disease and may consist of regular daily, weekly, pre-race or post-race evaluations. Ideally an environment is created where if there is any question as to what effect continued exercise will have on a horse, the trainer will be prompted to have the horse examined. Continuity and regular assessment of individual horses facilitates more specific treatment decisions and detection of subtle changes in gait or lameness. Such monitoring creates a rewarding environment for assessment of therapy, since race performance alone is not always an accurate determinant of therapeutic success.

General management of disease

Early detection and accurate diagnosis of disease coupled with appropriate therapy, rest periods and rehabilitation are all essential to maximize racing longevity. The goal of treatment should be a rapid return to soundness and functionality, without compromising long-term soundness and earning potential. The economic cost of unnecessary or incorrect therapy may be significant. Training alterations require additional considerations, including the impact on the animal's other body systems, particularly the musculoskeletal and cardiorespiratory systems. Furthermore, veterinarians should habitually establish appropriate 'informed consent' of trainers and owners because every treatment has a complication rate that may range from a mild injection site reaction to life-threatening colitis, sepsis or anaphalaxis. In this light, the veterinarian must also consider the risk of musculoskeletal injury with continued racing and training and importantly the associated risk to riders.

Medication of horses in training should include considerations of potential side effects as well as optimizing administration times in conjunction with training programs. There is often a compromise required between appropriate medication, required optimal rest and lost fitness. The final decision should be that of the trainer/owner, while the role of the veterinarian is to provide information regarding a disease and then provide a range of options for management allowing the trainer to weigh up the cost benefits of therapy and modification of their training. Regulatory concerns and drug withdrawal times warrant careful consideration, particularly the use of oral preparations or 'in feed' drugs where stall contamination represents a particular concern.

Specific disease and injury management

The purpose of this section is to provide some general approaches to managing commonly encountered injuries and diseases of Thoroughbreds in race training. While different strategies are employed to address different pathology some conceptual similarities exist with regard to the management of injured or diseased race horses, particularly with respect to the effect of alterations in training.

Musculoskeletal diseases

Dorsal third metacarpal disease, carpal and fetlock joint disease and tendon or ligamentous injuries are the most common musculoskeletal problems leading to wastage.[6,11,22] Routine, diligent observation of subtle changes in symmetry and meticulous palpation combined with use of hoof testers and flexion tests aids early identification of the most likely site of lameness. Where possible, targeted diagnostic anesthesia and imaging is used, which is both economical and time saving. Quality imaging modalities including radiography, ultrasonography and scintigraphy, are essential for accurate diagnosis, treatment and prognostication.

The presence of a secondary lameness is common and may go undetected without appropriate diagnostic anesthesia. Bilateral disease is commonly identified, particularly with carpal and fetlock injuries, tibial stress fractures and sites of osteochondrosis.[32–37] Lameness examinations can be aided in the fractious patient with a small dose of sedation.[38] Jogging in a circle or figure-8 can also be useful for assessment of mild lameness and may help differentiate among sites of lesions causing lameness.

Exercise modification

Musculoskeletal diseases often require modifications to the training program, dictated by the disease or injury and the horse's level of fitness. Changing the typical training formula is achieved by alteration of distance and/or speed. Terminology differs geographically in describing the approximate speeds at which horses train and race, and understanding local terminology allows assessment of the current workload and appropriate suggestions with regard to modifications. Speed and distance may be expressed in furlongs (220 yards or approximately 201 meters) (Table 49.2).

Trainers may have a variety of track surfaces available for training horses and advice with respect to training surface should be formulated based on knowledge of the local track characteristics, current track conditions and their contributions to injury risk. Traditionally turf has been associated with a lower risk of musculoskeletal injury than dirt although confounding factors, primarily geographic, may contribute to this apparent lower risk.[15,23,39] Some specific injuries appear to have an association with particular track surfaces. There is an apparent increase in the incidence of proximal suspensory desmitis in horses working on woodchip compared with turf tracks, and an increased incidence of subsolar inflammation and bruising is noted in horses performing high-intensity exercise on sand tracks (PE Sykes, 2002, personal communication). The incidence of dorsal third metacarpal disease is higher in horses training on dirt than on wood fiber tracks.[40]

Track condition or rating has been reported to influence the risk of injury.[15,41,42] However, several large epidemiologic studies have found no association between track condition and injury rate.[19,23] The mechanical characteristics of a track are determined in part by its structure with moisture content being the major variable influenced by weather and track maintenence.[27,41,43,44] Injury risk is higher on turf tracks when the surface moisture content is low, resulting in a harder track and faster race times.[15,18] Dirt tracks on the other hand have been associated with injuries under a variety of conditions typically when moisture content is either too low or high or surface is of inadequate depth or composition.[16,27,42] Unleveled track surfaces and areas where track is compacted such as 'crossings' for horse and vehicular access and areas around starting chutes have been associated with increased risk of injury.[27,45] An inadequate banking or camber on turns may also contribute to injuries and alterations to track camber and surfaces have shown benefits in reducing injury rates in Thoroughbred and Standardbred racing.[46–48] Therefore consideration to track characteristics should be given, especially with advice regarding horses working at high speed or rehabilitating from injury.

Hill or incline work, either under saddle or on an inclined treadmill, allows work rate to increase while limiting speed.[49,50] Inclines modify the activity and loads on various muscles,[51] probably increasing the overall load on the hindlimbs that may be beneficial if attempting to strengthen the hind quarters, or being contraindicated in horses with hindlimb injuries. Walking in waist deep water in a pool or on a submerged treadmill provides greater work to the advancing limb and may benefit attempts to improve extensor and particularly quadricep strength.

Direction around turns (clockwise versus anticlockwise) influences limb loading patterns, with the lead limb subject to a greater load than the contralateral limb, and this additional loading may predispose the lead limb to injury.[19,52] Typically in a counter-clockwise racing direction the horse preferentially leads with the left forelimb on the turn, and for clockwise racing the right forelimb, with most horses changing to the opposite lead at some stage during the straight.[53] Many injuries appear to have 'lead' or inside limb predilections depending on the direction of racing such as dorsal third metacarpal disease,[54,55] superficial digital flexor tendinitis,[42]

Table 49.2 Common terminology and speeds associated with Thoroughbred flat work

Common terms	Approximation to race speeds	Speed	Time per furlong
Trotting work (UK, Australia), jogging (USA)		Approximately 4 m/s	
Slow work 'canter' '1/2 pace' (UK, Australia) 'gallop' (USA)	~50% race speed	Approx 8–12 m/s	18 second furlong (11 m/s)
3/4 Pace work 'even time' (Australia, UK) 'breezing', 'licking' (USA) Primarily aerobic	~75% race speed	Approx 13 m/s (2 minute miles)	15 second furlong
Come or sprint home, gallop (Australia) Home, finish or sprint Some anerobic contribution	90–100% of race speed	16–18 m/s	11–13 second furlong
Top race speeds		18 m/s	11 second furlong or better

and antebrachiocarpal joint injuries, particularly the distal radius and proximal intermediate carpal bone.[53] 'Outside' limb injuries are commonly associated with the medial middle carpal joint.[53] Common musculoskeletal injuries associated with limb predilections may be minimized or prevented by training in both directions on turns. If introduced early in a training program it allows development of balance in both directions and minimizes repetitive loading of specified predilection sites.

Walking exercise can be provided by hand walking, mechanical walkers, or treadmills. Often overlooked, walking is useful in horses that are temporarily out of work and beneficial in horses susceptible to 'tying up' or with chronic joint complaints. Walking after high-intensity exercise improves recovery.[56] 'Ponying' is useful for horses that do not settle at slow speeds or horses with back complaints, particularly wither or girth rubs. Some musculoskeletal back problems may be exacerbated if the horse has a tendency to track sideways.[57]

Swimming is a primarily aerobic exercise medium useful in reducing the effects of weight-bearing work and has been suggested to decrease the rate of musculoskeletal disease (Fig. 49.3).[58] While allowing non-weight-bearing joint motion, swimming does not stimulate appropriate bone responses or maintain joint ligament tone.[59] Potential complications of pools include infection of pre-existing wounds, interference injuries (higher risk in circular pools), exercise-induced pulmonary hemorrhage, colic and rarely drowning. Swimming increases muscle activity in some selected muscle groups and therefore may be contraindicated in the presence of primary muscle injuries.[60]

The effect of complete cessation of exercise on a horse's level of cardiovascular fitness often depends on the horse's stage of training. Horses early in their training phase appear to lose significant amounts of aerobic fitness within 2 weeks, whereas horses more advanced in training are slower to detrain, losing fitness over 4–6 weeks.[61–63]

Bandages and bandaging

Support bandaging can be useful to minimize swelling and edema associated with acute pathology or intermittent limb edema. The role of athletic support bandages in preventing injury and their effect on performance is unknown; studies in healthy human athletes indicate they can be performance impairing.[64] Cohesive single layer bandages (Coban, Vetwrap, Equisport) have been shown in vitro to reduce hyperflexion of the fetlock, and increase absorbed energy.[65,66] Equisport (3M Corporation, St Paul, MN) and Elastikon (Johnson and Johnson Inc, New Brunswick, NJ) bandages provided superior energy absorbing capacity when compared with Ace (Beckton, Dickson and Company, Rutherford, NJ), Vetwrap (3M Corporation, St Paul, MN) or Coban (3M Corporation, St Paul, MN).[67] Improperly applied bandages may contribute to pathology and any bandaging may be contraindicated due to effects on heat dissipation.[68,69] Work boots or padded bandages can be used to limit and reduce the severity of interference injuries.

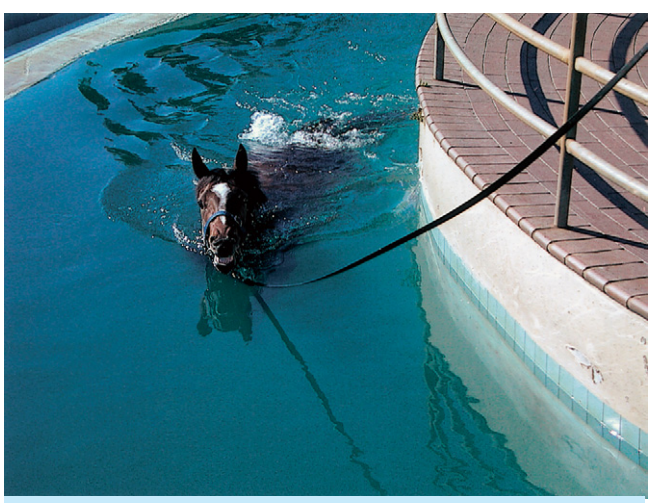

Fig. 49.3
A Thoroughbred race horse swimming in a circular pool.

Cold therapy

Cold therapy provides anti-inflammatory, analgesic effects and reduces cellular metabolic demands and should be considered in any acute or chronic injury.[70] Rapid icing of acute injuries is followed by intermittent icing for approximately 48–72 hours until inflammation is resolved; chronic injuries benefit from icing after every bout of high-intensity exercise.[50] Ice water slurries in large rubber boots are easy to apply, have the ability to include the carpus, and cool the limb more efficiently compared with commercial cold packs, reaching stable tissue temperatures in 10 minutes (Fig. 49.4).[71] Excessive icing can cause dermatitis and ice burns. Limiting 'icing' times to 30 minutes and applying multiple applications with durations of at least 20 minutes out of the ice seems to minimize this complication.

Joint diseases and injuries

Medical management of joint injuries and disease

Early and aggressive anti-inflammatory therapy is indicated with all joint injuries provided the diagnostic process is not compromised. Once the level of joint compromise is determined appropriate specific treatment can be pursued. Joint inflammation can be controlled with systemic non-steroidal anti-inflammatories (NSAIDs) at recommended doses for 24–48 hours, combined with cold therapy and bandaging. Cessation of high-intensity exercise and the substitution of walking is indicated while the joint is acutely inflamed. Trotting and swimming can be used to maintain activity until the horse is able to return to its previous level of work intensity. Rapid resolution of synovitis and capsulitis is beneficial in avoiding capsular edema and capsular fibrosis that may lead to reduced range of joint motion.[72,73] Passive joint flexion may aid in maintaining range of joint motion.

Intra-articular medications (as discussed in Chapter 23) are likely to be most efficacious if used in a planned manner with consideration given to the horse's training and racing schedules. Maximal anti-inflammatory effect is likely to be gained by early treatment followed by cessation of high-intensity exercise. Joints that are chronically affected should

Fig. 49.4
A Thoroughbred race horse receiving cold therapy immersed in an ice slurry (inset) in large rubber turbulator boots. (Photo courtesy of Dr J. Walker.)

Fig. 49.5
Intra-articular medication being administered via a dorsal approach to the left forelimb fetlock joint.

be treated after exercise on a day of planned high-intensity fast work, allowing at least 3–5 days or longer of modified low-impact activity prior to racing. Medicating chronically inflamed joints prior to prolonged layoffs may be beneficial in assisting the resolution of synovitis and capsulitis. Aseptic technique during intra-articular injections is essential and excessive ice therapy or the use of liniments or blisters should be avoided because the resultant dermatitis may compromise a suitable injection site (Fig. 49.5).

Intermittent anti-inflammatory therapy can be used in combination with long-term administration of disease modifying osteoarthritic agents such as polysulfated glycosaminoglycans (PSGAGs), pentosan polysulfate, glucosamine and chondroitin sulfate. Although definitive evidence with regard to their cost benefits, ideal dosing and efficacy is still lacking, subjective evaluation indicates that continual short interval (5–7 days intramuscular and daily oral agents) dosing is optimal for Thoroughbreds with osteoarthritis while in training.

Surgical management of joint injury and disease

The primary aim of surgery is to return the joint to non-painful function and limit the formation and progression of osteoarthritis. Surgery is occasionally indicated in order to salvage an animal for breeding or retirement. Before deciding if surgery is indicated, careful consideration must be given to the prognosis, expected rehabilitation time and economics. In many cases surgery assists the diagnostic process and may more accurately determine the prognosis and post-surgical management. Horses occasionally perform successfully with intra-articular lesions that may be addressed surgically, and weighing up the long-term benefits of surgery against the potential short-term economic losses can be difficult, particularly during the high earning stages of horses' careers. A good working relationship with a surgeon experienced in treating joint disease in Thoroughbred race horses will facilitate the decision-making process. Importantly only horses not at risk of breakdown should continue to train and should be monitored for evidence of progression.

Osteoarthritis

Early osteoarthritis can be managed with medical therapy and rest when indicated. The progression of osteoarthritis is often difficult to predict accurately. Despite this, initial and subsequent joint radiography provides valuable assessment of disease progression, in conjunction with regular lameness examinations and assessment of response to therapy. Complete rest for long periods in older horses with osteoarthritis can often be contraindicated with regard to racing longevity, since retraining often places demands on the arthritic joints that they cannot accommodate. Alternatively, maintaining such horses in lower-intensity modified training regimens which include swimming, longer intervals between high speed work combined with intermittent anti-inflammatory therapy, physical therapy and continual use of disease-modifying osteoarthritis agents may assist in prolonging their racing longevity. Advancing osteoarthritis requires continual monitoring, particularly for evidence of subchondral bone injury that may propagate to complete fracture. Eventually a stage is reached where the level of osteoarthritis becomes incompatible with safe and economic training and racing, and in these cases clinical findings combined with appropriate diagnostics support advice for retirement.

Bone-related injuries and diseases

Non-adaptive exercise-induced bone remodeling and incomplete stress fractures are reported in a variety of bones

including the third metacarpal bone, tibia, humerus, pelvis, sacrum, lumbar vertebrae and scapula. These manifestations of bone fatigue have been postulated in some instances as precursors to complete spontaneous fractures.[24,32,36,74–79] Similarly, osteochondral fractures have been proposed to be associated with cyclic loading and bone adaptation responses.[80]

Training modifications

Training protocols appear to directly influence bone-related injuries and disease. Changes in training intensity induce bone adaptation via altered forces and fatigue damage, with initial bone weakening due to increased bone porosity.[81] The decreased mineral content is thought to impact significantly on bone strength around 3 weeks after an alteration in training,[82,83] and it may take up to 3–4 months or longer to replace the lost bone, during which time the bone is weaker.[82–84] It is the bone adaptation process itself that appears the more important component of bone weakening, rather than the fatigue damage.[85] Two-year-old horses appear to be at greatest risk of adaptive bone pathology as their skeleton models and remodels in response to race training. The lowest bone mineral density in these horses occurs at 2–3 months after entering race training.[84,86] Significant decreases in bone mineral content detrimental to bone strength occur during periods of inactivity,[87] and are likely to result from a decrease in bone strains leading to extensive bone remodeling and increased porosity.[81] A greater risk of bone fatigue related injuries has been associated with return to work after periods of inactivity or lay-up.[79,88]

Since horses training at slow speeds adapt their bones to that particular speed, the introduction of higher speed pace work ('breezing') results in altered loads and bending forces requiring a further bone adaptation response, making bone susceptible to fatigue injury during this adaptation period.[81,89] A study examining gait and speed as risk factors for fatigue injury of the third metacarpal bone in 2-year-old Thoroughbred race horses recommended training modifications to reduce the incidence of 'bucked shins' consisting of reducing the extent of the low-speed long-distance work and increasing the frequency of the short-interval high-speed work.[90] Therefore, allocating less training time to long-distance slow exercise and the introduction of earlier more frequent short-distance fast exercise affords bone more time to adapt to race speeds.[79] Problems that may be encountered include the inability to control young poorly educated horses, and the uninvestigated effects of this training protocol on other structures, particularly tendons and ligaments. The most appropriate training regimens to obtain optimal remodeling and modeling responses of bone that will best accommodate forces associated with racing and training are yet to be determined.[91]

Dorsal metacarpal disease

Dorsal metacarpal disease manifesting as 'bucked or sore shins' is one of the most common causes of lost training days in 2-year-old Thoroughbreds; one survey reported it as affecting 70% of Thoroughbreds, with increased risk of third metacarpal stress fracture within 6–12 months.[81,92,93] Deciding if affected horses can continue training will depend on the severity of the condition as determined by regular palpation of shins, lameness examination and radiographic evaluation. Early identification of disease through palpation and detection of subtle lameness allows early treatment and the majority of horses to remain in training. Treatment should include immediate modifications to the training program and aggressive anti-inflammatory therapy. Monitoring the horse's gait during exercise and the level of pain on palpation of shins are useful in assessing the response to therapy. Swimming can be used to augment fitness, with the track regimen consisting of trotting and shorter distances of pace work regularly (for example 1–2 furlongs every other day). Horses with more advanced dorsal metacarpal disease have marked pain, plus evidence of swelling or cortical lucency identified radiographically, and should be removed from training on economic grounds for at least 6 weeks. They should be returned to training with suitable modifications to the training regimen as discussed above for horses with adaptive bone pathology.

Third metacarpal dorsal cortical stress fractures

Conservative management typically requires a minimum of 7 months' rest with a variable degree of success in achieving healing.[94,95] Surgery offers an advantage and the combination of osteostixis and screw fixation is reported to be more reliable than osteostixis alone, with healing and screw removal at 2 months after surgery, followed by resumption of training within 1 month of screw removal.[54,55]

Stress fractures at other sites

Stress fractures may be seen at a variety of sites (third metacarpal bone, tibia, humerus, pelvis, sacrum, lumbar vertebrae and scapula) and periods of reported rest for these fractures vary; there is no clear consensus on an appropriate duration of stress fracture rehabilitation.[96] Provided the stress fracture is not at risk of propagation to a complete fracture, general recommendations include: stall rest with hand walking (the horse should be offered approximately 10 minutes hand walking twice daily, doubling weekly) until the horse is sound at the trot in a straight line. The horse should be evaluated for lameness after 2–4 weeks, first at the walk and if appropriate at the trot. Once sound at the trot, access to a small yard (20 feet square) for a further month is followed by a month of pasture release prior to return to training. A more rapid rehabilitation plan can be instituted under direct veterinary supervision with gradual introduction to low level trot work after the month of stall rest and walking. However, such a program requires regular lameness and radiographic evaluation to monitor healing and possibly follow-up scintigraphic evaluation. This protocol can minimize time of maximal exercise restriction but return to high-speed training should be delayed for at least 3 months from time of stress

fracture diagnosis. Stress reactions and non-adaptive exercise-induced bone remodeling can also be managed with a similar approach.

Sclerotic subchondral bone lesions

Subchondral bone sclerosis and associated osteoarthritis occurs primarily in the carpus associated with the third carpal bone and the fetlock joint in the palmar/plantar metacarpal/metatarsal condyles and proximal sesamoid bones.[74,78,97] The pathogenesis of these injuries is poorly understood but involves disease of both the articular cartilage and subchondral bone.[80,97] Subchondral epiphyseal bone changes have been identified as potential precursors to some slab fractures of third carpal bone and condylar fractures of the cannon bone.[74,78,98]

The diagnosis and management of subchondral bone diseases is problematic and both joint and bone disease issues should be addressed. Often radiographic findings are equivocal and in these cases scintigraphy can be a useful aid in diagnosis. Determining the degree of subchondral bone injury and collapse on radiographs alone can be difficult; computed tomography and magnetic resonance imaging (MRI) are likely to enhance identification and management of subchondral bone diseases. Typically if subchondral bone damage is evident, prolonged periods of rest are usually required and surgery may be indicated, particularly if disease is involving the carpus. Many advanced subchondral bone injuries carry a guarded prognosis for future athletic performance, due to lameness.

Breakdown injury

Major breakdown injuries in racing Thoroughbreds include severe bone and ligament injuries involving the fetlock (traumatic disruption of suspensory apparatus, condylar fractures and proximal phalanx fractures) and carpus (distal or proximal row slab fractures with unstable or collapsed carpus) as well as major fractures of the humerus, tibia and pelvis. Appropriate assessment and use of coaptation for transport of major musculoskeletal injuries has been well described elsewhere and is important knowledge for any racetrack veterinarian.[99] Appropriate first-aid measures prevent further osseous and cartilage injury, maintain skin cover and prevent further damage to blood supply that may ultimately determine the ability to salvage the animal. Removal of these patients from the racetrack environment allows appropriate diagnostics, communications and decision-making to take place.

Tendon- and ligament-related injuries and diseases

The combination of training and aging may have a progressive detrimental effect on tendon strength. Micro-trauma due to accumulated submaximal strains results in alterations in tendon structure that decrease its ability to cope with cyclic strains and may ultimately result in injury.[100,101] There may be an 'optimal window' during growth and training for the development of tendon extracellular matrix that would best prepare the tendon for cyclic damage associated with race training. This timing and activity level is yet to be determined and excessive exercise at a young age may result in damage.[102] Prevention and early detection of lesions may become reality with further research into marker molecules that could allow identification of subclinical tendinitis.[103]

Tendon injuries

Superficial digital flexor tendon (SDFT) injuries are a substantial cause of wastage with a reported incidence in racing Thoroughbreds of 8–43%, and are more prevalent in horses older than 2 years of age.[22,42,104–108] Astute observations of changes in flexor tendon profile, careful palpation and ultrasonography are the essential tools for the identification, assessment of severity, prognostication and monitoring of healing in tendon injuries.[104,105,109–111]

Clinically apparent swelling, heat and pain on palpation indicate the need for careful ultrasonographic evaluation. Re-evaluation of a tendon at 1–3 weeks after injury may provide a more accurate indication of lesion severity and is particularly important when a lesion is suspected but not well defined on the initial examination.[104,105,109,110] Peritendinous inflammation ('bandage bow') is typified by apparent tendon swelling with less intense pain on palpation when compared with tendinitis. Ultrasound conformation of the diagnosis is required and treatment consists of aggressive anti-inflammatory therapy and cessation of pace work until all inflammation has resolved.[111,112] Slow resolution of inflammation or residual thickening should prompt follow-up ultrasonographic examination.

Ultrasonographic monitoring of healing allows alterations to be made in the rehabilitation program and examinations are advised prior to any major increase in the level of exercise intensity.[110,113,114] Clinical reassessment during rehabilitation is also important and changes should prompt ultrasonography. Blisters are not advised since they affect both the clinical and ultrasonographic assessment of a tendon and have no documented benefits.[107,115] The prognosis for SDFT injuries in the Thoroughbred is reported to range from 20 to 60% of horses returning to successful racing and up to 80% sustaining a reinjury.[105,116–119] Continuing to train with a mild lesion in a Thoroughbred race horse results in progression to a more severe lesion. This is seldom economically or clinically successful and carries the risk of a catastrophic breakdown.

Controlled exercise rehabilitation programs may improve results, with 71% of horses treated with a graded exercise program racing at least once compared with 25% of horses subjected to pasture rest alone.[120] The decision to embark on a rehabilitiation program should take economics into consideration, particularly the costs and benefits.[110,113] Regardless of the level of rehabilitation undertaken, initial management involves cessation of training and aggressive anti-inflammatory therapy. The value of additional medical management procedures including intralesional or

peritendinous sodium hyaluronate, polysulfated glycosaminoglycans and beta-aminoproprionitrile furmarate has not been well defined.[106,107] Surgical intervention has been suggested to improve prognosis with tendon splitting in the acute phase often combined with superior check ligament desmotomy.[121,122] Superior check ligament desmotomy has a reported prognosis of 68–88% for returning horses to racing, with 52–56% racing at least five times after surgery.[108,123,124] These results are similar to reports of conservative therapy alone.[108,118] Furthermore, superior check desmotomy may increase the risk of suspensory ligament injury.[108] Regardless of additional therapies the total time required prior to reintroduction to race training is 8–12 months; a worse prognosis is documented for horses rested for less than 6 months.[105,110,113]

Injuries of the suspensory ligament and its insertions

Training appears to have a strengthening effect on the suspensory apparatus with untrained horses more likely to experience ligament failure at smaller loads, whereas trained horses fail at greater loads with fracture of the proximal sesamoid bones.[125] The diagnostic approach is similar to that for tendon lesions although prognostication based on a lesion's ultrasonographic appearance is more difficult. Inferior ultrasonographic image quality compared with that obtained when imaging superficial digital flexor tendons and the presence of muscle fibers complicates both diagnosis and assessment of healing, particularly in the high suspensory area.[110,126] The prognosis for return to racing after suspensory desmitis has been reported to be relatively poor.[127]

Suspensory branch desmitis and sesamoiditis

Suspensory branch desmitis appears most prevalent in younger horses and particularly 2-year-olds early in their career.[128–131] Desmitis of the suspensory branches may manifest with concurrent sesamoiditis, sesamoid fractures or splint bone lesions.[128,131] Sesamoiditis on the other hand is often identified prior to training and a range of severity exists and may progress with training.[129] Management of sesamoiditis is difficult and can be frustrating as recurrence with resumption of higher intensity exercise is common. Initial therapy consists of local application of cold therapy, pressure bandaging and administration of systemic anti-inflammatory agents. Long-term rest up to 6 months is important to allow bone maturity and prevent fracture. Despite the benefits of long-term rest the radiographic appearance of the lesions seldom makes an appreciable improvement. The long-term effect on the horse's career is not clear. However, it appears that the severity and presence of additional pathology such as enthesiophytes impact on both racing longevity and earning potential.[132,133]

Suspensory branch and body

Horses developing small lesions of the suspensory branch early in training often only require 4–6 months of rest and have a fair to good prognosis. In contrast, lesions in older horses, more advanced lesions, or those slow to resolve ultrasonographically, have only a poor to fair prognosis and require prolonged periods of rest up to 12 months. A higher incidence of recurrence is seen in these horses, the desmitis behaving similarly to that described in show and dressage horses.[134] Rehabilitation is the same as for tendons, with a graded exercise program and ultrasonographic monitoring of healing combined with attention to foot balance, particularly avoiding excessive heel length. There are anecdotal reports of horses with mild lesions remaining in training and racing, particularly if speed work is limited to race starts only. However, there is a risk of progressive damage or complete failure.[134]

Lesions of the suspensory body are dealt with using similar methods as discussed for tendon injuries. The presence of concurrent splint bone lesions should be ruled out. Typically, management and the prognosis for return to racing is determined by the lesion severity and assessment of the healing response. At least 8–12 months is usually necessary prior to returning to training.

Proximal suspensory and its attachment

Lameness associated with the proximal suspensory ligament and its attachment is relatively common in Thoroughbred race horses.[135] Diagnosis can be difficult because of the variety of ligament or bone lesions seen separately or together, with a wide range of clinical severity.[136] In addition, the intimate association of the carpometacarpal joint and proximal suspensory ligament limits the specificity of diagnostic anesthesia to identify lameness arising from the proximal suspensory area and the carpometacarpal and middle carpal joints.[131,134,137] Clinical differentiation of high suspensory pain and third carpal bone disease can be difficult.[134]

Horses identified with primary ligament lesions are managed similarly to tendon injuries. Those with primary bone damage may have non-adaptive bone remodeling 'stress reaction', longitudinal or avulsion fracture of the palmar cortex of the third metacarpal.[138–140] Management of bone injuries has been discussed and typically at least 3–6 months is required depending on the specific lesion.

Nuclear scintigraphy may be particularly useful in assessing the relative contribution of bone and ligament pathology causing lameness. Mild lameness of short duration often responds to medical management. A combination of NSAIDs, infiltration of the proximal suspensory area with a corticosteroid, correction of dorsopalmar foot balance and modifications to training mimicking that advised for horses with bone remodeling problems, have provided success in treating approximately half these cases. Horses are limited to a low-intensity workload until the lameness has resolved, typically within a 5-day period. Persistent lameness indicates the need for further diagnostics. Extracorporeal shock wave therapy may be useful for treatment of proximal suspensory ligament injury as well as having potential for treatment of other tendon, ligament or insertional injuries.[141,142]

Foot-related injuries and shoeing

The foot is a common site of lameness and poor foot conformation is a common Thoroughbred trait, particularly underrun heels and long toes that may predispose to injury.[3,6,30,143,144] Foot balance in the dorsopalmar or plantar plane appears important. Excessive heel length or wedging and the resultant high hoof angles preferentially load the suspensory ligament and SDFT predisposing these structures to injury.[145–148] Suspensory apparatus failure has been associated with underrun heels (difference in toe and heel angles) and low toe angles have been associated with an increased risk of catastrophic injury. Decreasing the difference between toe and heel angle and increasing the toe angle alone may reduce injury risk.[29,149,150] Toe grabs have been associated with an increased incidence of injury.[30,150]

Overreach injuries are typically high impact, with deep tissue damage usually greater than is initially apparent. Rarely do they initially cause a significant lameness unless there is major tissue trauma. These injuries can become a site of lamina detachment and if overlooked result in pocketing of dirt and subsequent infection, manifesting as lameness 3–7 days after the initial injury (Fig. 49.6). Prevention of this sequela requires excision of the separated tissue back to lamina attachment combined with bandaging while avoiding sand and dirt from gaining entry to the lamina–wall interface. Repetitively injured horses can be managed with 'bell boots' and shoeing changes.

Corns are a common cause of lameness and appear to be more commonly associated with flat sole, low heel and long toe conformations increasing weight bearing in the caudal aspect of the foot.[151] Addressing foot balance combined with light paring of sole over the bruising and application of a seated-out heart-bar shoe combined with 2–3 days of low-intensity exercise are generally adequate to resolve lameness. In some cases it may be necessary to 'float' the affected heel off the shoe. Hoof treatments are initially aimed at reducing inflammation through magnesium sulfate foot soaking and poulticing coupled with anti-inflammatory agents. These modifications combined with low-impact work including walk, trot, swimming are undertaken until there is resolution of inflammation and lameness. Use of heart-bar or egg-bar shoes and correction of foot balance by removal of excess toe provides more support for the caudal third of the foot. Time is necessary for dissipation of interstitial fluid and re-cornification of the bruised solar tissue. Once the pain is resolved, hardening of the new sole can be achieved by applying diluted iodine solution (2%) or formalin (10%).

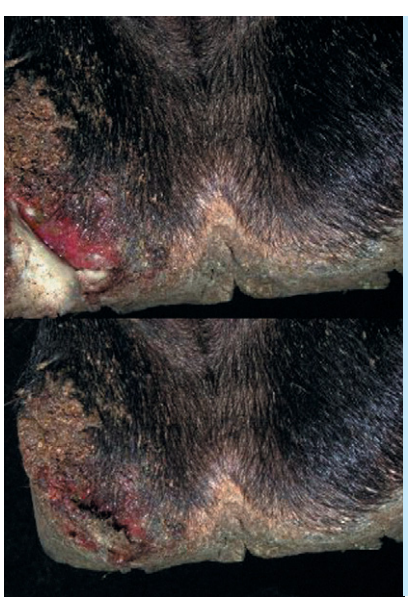

Fig. 49.6 Overreach injury to the lateral heel of a left forelimb above. The picture below demonstrates the lamina detachment that can be present with these injuries.

Quarter cracks are manifestations of shear forces within the hoof wall and laminae. Some cases may be associated with hoof imbalance and excessive wall length in the affected quarter.[152] Cracks may be identified prior to lameness, providing an opportunity to prevent crack propagation and lameness by corrective trimming/shoeing and modified exercise regimens. Depending on size, stability and the extent of propagation many smaller stable cracks can be debrided and patched. This combined with rasping of the quarter, attention to foot balance and application of a bar shoe all assist in stabilizing the crack.[153] Unfortunately many cracks in Thoroughbreds involve the heel or caudal aspect of the quarter and are not readily amenable to repair. These caudal cracks, and cracks with coronary band involvement often require stripping of the hoof wall to allow regrowth of stable horn tissue.

Pedal osteitis, pedal bone 'rim' fractures, sole bruises and other injuries secondary to solar concussion are often accentuated by exercise on sand tracks. Management includes sole pads, wide web seated-out shoes and egg-bar shoes. Discrete sole lesions can be covered temporarily with a small welded plate to protect the area, while still allowing access of topical treatment.

High nails or 'nail presses' can be overlooked during lameness examinations. Nail and/or hematoma pressure may result in persistent lameness without evidence of infection. Evaluation of clinch heights and sequential application of hoof testers to each nail will facilitate their identification. If identified before the onset of infection, the nail can be removed and iodine solution flushed down the nail hole to disinfect and facilitate drying. If infected, soaking the foot in Epsom salts, poulticing and debridement are indicated.

Interference injuries

Interference injuries can result from one or a combination of factors including conformation, shoeing, soundness and immaturity (Fig. 49.7). Identifying the cause of the interference is necessary in order to develop a plan aimed at resolving the problem. The presence of neurologic disease should be ruled out. If necessary, identification of the source of interference can be determined by applying chalk to the affected area to identify the limb and area causing the interference. Resolution requires ideal foot balance and in younger horses time is needed to learn and achieve balance on the straight before high-speed work around turns is introduced. Protective bandaging and bell boots minimize trauma while

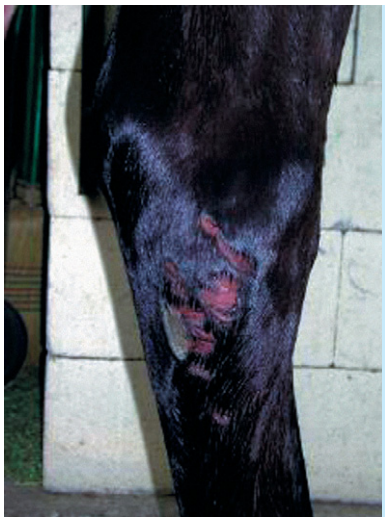

Fig. 49.7
Multiple interference injuries on the medial aspect of this Thoroughbred's left hock. This type of interference is commonly referred to as 'hock hitting' or 'speedy cutting'.

attempts are made to resolve a problem. Lighter shoes, partial shoes ('tips') and 'safing' (rounding) of edges resolve many problems.

'Going down on bumpers' or 'running down behind' describes excoriation typically of the plantar fetlock in the hindlimbs and occasionally in the forelimbs (Fig. 49.8). This can be multifactorial and may be associated with fatigue, shoeing, or compensation for lameness. At times this may be severe and result in the removal of full thickness skin cover. If no lameness problems are identified and if the problem continues with a temporary decreased intensity of training, the application of extended heel- or egg-bar shoes and correction of dorsoplantar foot balance can assist resolution. Recurrently injured horses often require taping of the fetlocks with protective padding such as orthopedic felt or other padding. All interference injuries should be treated as contaminated wounds with potential for infection.

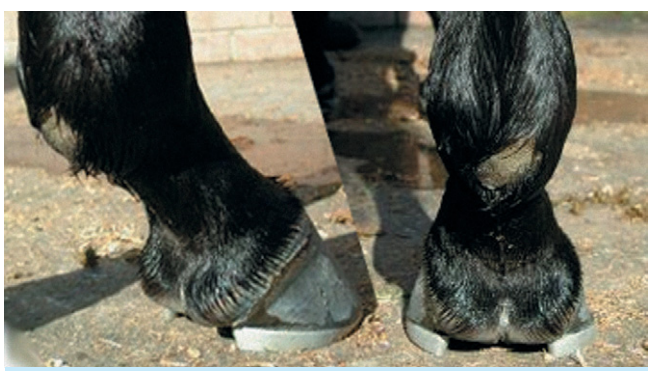

Fig. 49.8
An example of 'running down behind' or 'going down on the bumpers' chronic excoriation seen here on the plantar aspect of the right hind fetlock in this Thoroughbred race horse. Note also the slightly wedge heeled shoe that has been applied in an attempt to reduce the ongoing trauma to the area.

Muscle-related injuries and disease

Recurrent exertional rhabdomyolysis (RER)

Most commonly seen in 2-year-old fillies RER is reported to affect approximately 5% of racing Thoroughbreds.[154,155] The quantitative correlation between muscle enzymes and severity of clinical signs is poor and elevation of muscle enzymes after exercise does not always indicate clinical rhabdomyolysis; conversely, clinically affected horses may have delayed peaks and more prolonged elevations of enzyme activity in serum.[154,156] Horses exhibiting elevated muscle enzymes and minimal clinical signs warrant further investigation and management changes, since the effect on ultimate performance is unknown.[156] Serial monitoring of muscle enzymes is a reasonable tool to determine responses to management changes and therapy. Cases responding poorly warrant further diagnostic evaluation.[156]

Management issues that can be manipulated include diet, exercise schedules and potential stressors.[157,158] Minimizing stressors by maintaining a regular daily work schedule and quieter stall location remote from major traffic areas in the stable are recommended. Benefit can be gained from different exercise prior to track work, including extensive walking, swimming or 'ponying'. Tranquilization can also assist, with low doses of acepromazine (5–10 mg intramuscularly 60 min prior to work) effective in some cases. Reduction of the amounts of digestible carbohydrate in the diet can be achieved by reduction of the quantity of grain or substitution of a less digestible carbohydrate source replacing oats with corn,[159] while adding fat to maintain dietary calories.[157] Dietary change may be more important in modulating the degree of nervousness and excitability rather than playing a direct role in the pathogenesis of the disease.[158] While the use of progestagens is often advocated, no association in elevation of muscle enzymes was seen in fillies associated with their estrous cycle, controlling estrus behavior may still act to minimize stress levels in some individuals.[154] Electrolyte, and vitamin E and selenium supplementation may also be of benefit.[156]

Avoiding 'days off' and substituting different forms of exercise on days that horses are not worked, combined with reduction or complete removal of grain from the diet on these rest days is indicated. A slow introduction of high-intensity work coupled with a gradual increase in carbohydrates which follows increased workloads limits subclinical elevations in muscle enzymes. Cases responding poorly to other management changes may respond to administration of muscle relaxants such as methocarbamol, dantrolene and phenytoin.[156,160] Use of oral branch chain amino acid preparations prior to exercise has been reported anecdotally to reduce the magnitude of muscle enzyme elevations.

Treatment of acute cases includes immediate cessation of exercise and administration of polyionic fluids (either intravenous or oral depending on severity) to achieve rehydration and promote diuresis, combined with administration of NSAIDs (flunixin meglumine or phenylbutazone). Acepromazine appears efficacious in calming these horses and may facilitate resolution of RER. Occasionally extremely

uncomfortable horses may require α-2 sedatives and opiates for analgesia.

Muscle strains and tears

Primary muscle injuries are difficult to verify as a source of lameness and usually require exclusion of skeletal lesions. Swelling, asymmetry and pain on deep palpation may be apparent in some cases. Measurement of muscle enzymes is of limited value as elevated enzyme levels are generally not a consistent finding with isolated muscle tears. Lameness is typically the most obvious at the walk and swing phase of the trot. Muscles commonly identified include semimembranosus, semitendinosus and brachiocephalicus. Accompanying bone lesions may be present and are seen most commonly at the tuber ischii with tears of the semimembranosus and semitendinosus. Muscle tears generally require a rest period of 2–3 weeks to resolve if no bony involvement is present,[157] but brachiocephalicus tears require 3–6 weeks of rest.

Back and wither injuries

Withers are a common site of injury due to saddle rubs or falls. These are susceptible to rubbing, hematoma formation and infection. They are best managed by avoiding saddle contact until completely healed and exercise may continue with use of military saddles or swimming and 'ponying'. Padding in most cases is inadequate due to the propensity to rub.

Diagnosis of back injuries and related pain is often difficult. Typically pain is muscular in origin and may be associated with an underlying lameness. The presence of bony pathology such as vertebral stress fractures and overriding spinous processes may be demonstrated with radiology or nuclear scintigraphy.[161,162] Treatment is directed at identifying the underlying cause coupled with temporary cessation of pace work, anti-inflammatories and local therapy.[163]

Infections of the musculoskeletal system

High-intensity exercise, close horse-to-horse and horse-to-handler interaction, confined surroundings and veterinary intervention contribute to Thoroughbred race horses commonly experiencing a variety of musculoskeletal infections. Cellulitis is common and generally seen in the lower limb. Occasionally idiopathic peri-articular tarsal infections are seen.[164] Traumatic injury leading to osseous infection is common. Although rare, clinicians should be observant for signs of septic arthritis given the frequency of intra-articular therapy and the repercussions of this complication. There are rare reports of idiopathic synovial infections of horses in training[165] (Sykes and Lumsden, unpublished data).

Successful treatment is facilitated by rapid identification and institution of appropriate antimicrobial therapy, adequate wound therapy, clean bandaging and avoiding areas of contamination, such as sand rolls, water activities, and the hands of the stable staff. Antibiotic selection should take into consideration the high concentrations of horses interacting in a common environ coupled with intense human contact and frequent use of antimicrobials. It is likely that individual racetrack environments will establish predominant pathogens with specific sensitivities akin to a hospital environment.

Respiratory diseases

Lower respiratory disease

Respiratory disease is a major cause of wastage for horses in race training, and lower respiratory diseases in particular appear to contribute most significantly.[166–169] An appropriate diagnostic workup consisting of a clinical examination and use of clinical pathology (hematology, transtracheal aspirate (TTA) and bronchoalveolar lavage (BAL)), endoscopy, ultrasonography and radiography, when indicated to allow appropriate management and prognostication.[170]

Coughing horses and inflammatory airway disease (IAD)

Horses suffering from IAD typically present as otherwise apparently healthy young horses usually 2 or 3 years old that have been in the stable environment for a couple of weeks or longer and present primarily for 'coughing'.[166–168,171–173] The presence of a nasal discharge may be variable. Endoscopic evaluation typically reveals a mucopurulent tracheal exudate containing elevated numbers of neutrophils. Excessive coughing is stimulated by laryngotracheal palpation, auscultation with the aid of a rebreathing bag or passing an endoscope into trachea.[166–168,171–173]

Historically, viral respiratory infections have been implicated as the major cause of lower respiratory disease in young race horses.[174,175] Recent studies suggest that a variety of pathogens including bacteria, mycoplasma and non-infectious agents contribute to IAD.[176–180] The role that bacteria isolated from transtracheal aspirates play in this syndrome is unclear. Their quantity, location (whether extra- or intracellular) and species (*Streptococcus*, *Pasteurella* and *Bordetella* spp.) have all been considered as characteristic of IAD.[173] The role of antibiotics in treating IAD has yet to be established.

The environment appears to be an important component of IAD, triggering allergic or non-allergic airway inflammation.[171,181,182] Air quality improvements can be made by minimizing feed dust with low dust or wet feeds, soaking hay and feeding on the ground. Housing changes including improving ventilation by use of yards or pens and reviewing choice of bedding avoiding straw and dusty beddings in favor of wood shavings or clean sand.[183] Minimizing noxious gases by regular stall cleaning and minimizing dust production by avoiding sweeping and mechanical 'blowers' in favor of hosing also improve air quality. Quarantine of cases may reduce risks if an infectious cause is suspected because of the sudden onset of multiple cases.

Pharmacologic therapy for IAD includes systemic or inhaled mucolytics, bronchodilators and corticosteroids. The presence of mast cells in BAL fluid may indicate the presence of immune-mediated airway disease. In such cases use of a short course of systemic corticosteroids and an inhaled mast cell stabilizer (sodium cromoglycolate) may be indicated.[182,184,185]

Exercise-induced pulmonary hemorrhage (EIPH)

Exercise-induced pulmonary hemorrhage (EIPH) is thought to occur due to high transmural alveolar capillary pressures,[186,187] and numerous factors may contribute to the severity of hemorrhage including exercise intensity, distance, age, upper respiratory obstruction, heterogeneous ventilation, hemorrheological factors, small airway disease and lower airway inflammation.[188–193]

The reported prevalence of EIPH depends on the criteria used, with epistaxis occurring in approximately 1–2% of race starters.[188,194] After high-intensity exercise (30–90 min) there is endoscopic evidence of EIPH in approximately 75% of horses.[188,189] Bronchoalveolar lavage (BAL) is a more sensitive means of documenting EIPH and has demonstrated its presence in nearly all racing Thoroughbreds. Furthermore, BAL may better correlate with severity and chronicity.[195]

Identification and appropriate treatment of IAD combined with the use of bronchodilators and furosemide (frusemide) prior to exercise are still the popular mainstays of EIPH therapy. Furosemide is administered to the majority of Thoroughbred race horses prior to racing in the USA and Canada, although efficacy in reducing EIPH has not been definitively demonstrated.[196,197] Even in jurisdictions where furosemide is not allowed on race day it can be incorporated in the training program and used prior to high-intensity training. The furosemide dosage (150–250 mg) is typically given intravenously or intramuscularly 2–4 hours prior to work.[197–199] One study suggested administration 30 minutes prior to exercise was superior to administration 240 minutes prior to exercise.[200]

The association with the high work intensity makes training modifications difficult; slower longer duration work may decrease severity of EIPH, since the disease has been documented with greater incidence in racing distances less than a mile.[193] Blood in the airway incites an inflammatory response and complete erythrophagocytosis takes up to 2 weeks.[201,202] Management should be aimed at minimizing high-intensity exercise during the inflammatory period, and treating airway inflammation. Response to therapy can be assessed with a follow-up BAL. Recently investigation of the FLAIR nasal strip (CNS Inc, Minneapolis, MN) has shown potential benefits in upper airway mechanics and a reduction of EIPH. However, controversy and conflicting results exist with its use.[203–206]

Upper respiratory diseases

Upper respiratory diseases commonly manifest as poor performance, and in most cases are associated with abnormal upper respiratory noise. Upper airway abnormalities have a prevalence of approximately 10% in racing populations.[207,208]

Detailed investigation of an upper respiratory abnormality should include a thorough accurate history aimed at characterizing the noise and determining if there is an effect on performance. Track visits or the use of 'sound spectrum analysis' assist noise characterization.[209] Diligent and systematic clinical examination is indicated particularly with respect to palpation of the larynx, nasal septum, jugular veins and assessment of facial symmetry, previous surgical scars and airflow from each nostril. Resting upper airway endoscopic examination should document nasal passages, nasopharynx, trachea and guttural pouches as well as dynamic function by induced swallowing response and nasal occlusion. Further diagnostics such as high-speed treadmill endoscopy, radiography and oropharyngeal examination may be indicated.

Left laryngeal hemiplegia (LLHP)

Once diagnosed the prognosis and suitability for surgery should be determined. Potential diagnostic oversights include previous surgery, arytenoid chondritis, fourth branchial arch defects, or the presence of another upper airway problem in conjunction with the LLHP. Presence of these abnormalities will negatively impact on the surgical prognosis. The level of arytenoid function should be determined and horses with grade III/IV hemiparesis, or those likely to be suffering from an additional upper respiratory problem, warrant endoscopic examination at high speed on a treadmill.[210,211] If arytenoid abduction at maximal exercise is judged better than would be obtained with surgery, continued training and racing with regular monitoring may be indicated; surgery may be required if there is progressive loss of function. This assessment is important since horses with grade III/IV movements may be less successful candidates for a laryngoplasty.[211] Prior to embarking on surgery, an assessment of the horse's athletic ability and evaluation of other performance-limiting conditions may be better assessed by continued training and racing over 5–6 furlongs if the degree of airway compromise permits. Prognosis for laryngoplasty has been reported over a wide range from 48% to 85% for successful outcome with horses able to return to training within 2 months.[212,213] Complications of surgery, such as coughing and aspiration, can be managed by dampening feed at ground level, avoiding feeding prior to work and long-term treatment with mucolytics, antibiotics and mucociliary transport mechanism stimulants.

Neuromuscular pedicle grafting has been reported to provide a similar prognosis. However, it appears best applied to horses identified with hemiparesis and younger than 2 years old due to the prolonged rehabilitation time (6–12 months). Laryngoplasty can be performed after neuromuscular pedicle grafting if reinnervation is unsuccessful.[214,215] Other management options include short-distance racing with the expected decrease in performance – these horses are usually only competitive over less than 6 furlongs. Furthermore, permanent tracheostomy or

temporary tracheotomy are both alternatives if sanctioned by racing authorities.

Intermittent dorsal displacement of the soft palate (IDDSP)

Diagnosis is based on a combination of appropriate history and endoscopic examination, subjective judgment of laryngopalatal instability and/or presence of soft palate ulceration.[216] Evidence of epiglottic flaccidity, dysfunction or hypoplasia may warrant further diagnostics including radiography and treadmill endoscopy. Ensuring IDDSP is a repeatable phenomenon is essential before embarking on exhaustive diagnostics and management changes.

Medical management may include continued training as the condition may resolve with increased fitness and weight loss, or rider and gear changes. Inexperienced riders can often encourage the likelihood of displacement by taking too heavy a hold on the reins. Gear changes including tongue ties and figure-8 nosebands used individually or combined can be effective. Medical management of upper airway inflammation (pharyngitis) may be beneficial when neuritis of the pharyngeal branch of the vagus nerve accompanies upper airway inflammation.[217] Anti-inflammatory therapy, both systemic and local pharyngeal spray, may benefit these horses.[218,219]

Immature horses should be given time to mature, as many resolve their tendency for IDDSP. When medical management fails surgery is indicated and a variety of procedures have been described.[216] The combined sternothyrohyoideus myectomy, tenectomy and staphylectomy appears to have gained most support as a surgical procedure. The procedure requires only a short time out of training, approximately 14 days with reintroduction back to fast work after approximately 3–4 weeks.[216] Epiglottic augmentation may assist horses with an apparently hypoplastic epiglottis in which the above surgery is unsuccessful; this procedure does require approximately 2–3 months out of training.[220] The prognosis for resolution of IDDSP is similar regardless of type of therapy pursued, with approximately 60% of horses improving.[216]

Arytenoid chondritis

Small mucosal lesions noted on the axial surface of arytenoids in the absence of arytenoid thickening are encountered infrequently and generally heal without complication. However, rarely these mucosal lesions have been seen to progress to chondropathy in yearlings (Kelly and Lumsden, unpublished data, 2001). Therefore, endoscopic monitoring of arytenoid mucosal lesions appears appropriate, and if indicated medical management consisting of cessation of high-intensity training, parenteral and topical antibiotics and anti-inflammatory agents.

Arytenoid chondropathy identified in the acute stages with only mild cartilage thickening may be managed with cessation of training and medical therapy. Periarytenoid inflammation with minimal cartilage involvement may be arrested medically and may allow continued training if mucosa is intact and abductor function and airway are judged as adequate. Cases with minimal cartilaginous distortion, granulation tissue on the axial surface and complete arytenoid cartilage abduction capability may be managed with a combination of medical therapy, surgical debridement of granulation tissue and draining tract and short-term rest.[221,222] Horses failing to respond to the above approaches or those with moderate to severe cartilage thickening are candidates for partial arytenoidectomy. This procedure is associated with a longer convelescence (3–4 months) and the reported success rate for horses returning to racing following partial arytenoidectomy is approximately 60%.[223] Despite this, a drop in class is anticipated, which may be minimized in horses racing over shorter distances and where residual cricoarytenoideus dorsalis muscle function exists.

Other upper respiratory problems

Other regularly recognized upper respiratory problems that can be managed with minimal lost training time and while the horse remains in the stable include uncomplicated epiglottic entrapment and subepiglottic cysts. Problems that often require 2–4 weeks out of training for surgery include alar fold flutter, axial deviation of aryepiglottic folds and atheromas. Pharyngeal collapse, fourth branchial arch defects, septal abnormalities and advanced sinus cysts limiting airflow carry a poor prognosis even with appropriate surgery if indicated.

Gastrointestinal diseases

Parasite prophylaxis programs are best coordinated with the spelling facilities. Mouth cuts in the commissures are often encountered and may be overlooked in a horse 'hanging' on a rein. Management involves ruling out a musculoskeletal problem and minimization of the trauma by using topical medical therapies, changing to a thicker or rubber bit, using cheekers or ponying without a bit until healed.

Gastric ulceration

Gastric ulceration in Thoroughbred race horses is reported to affect between 66 and 93% of the population, increasing to 80–100% for horses in advanced training or racing.[224–227] The disease most commonly manifests in racing Thoroughbreds as a decrease in feed intake, and conformation of ulceration is achieved via endoscopy. However, a poor correlation exists between clinical signs and the severity of ulceration.[228] Risk factors include the stable environment, periods of no feed intake and administration of NSAIDs and corticosteroids.[225,226,229,230]

Feed management in horses with gastric ulceration should focus on regular feeding with multiple daily meals and constant access to hay in order to avoid any prolonged periods that horses are not eating.[229] Pharmacologic anti-ulcer therapy (H2 blockers or proton pump inhibitors) in most

cases improve appetite within 1–2 weeks of commencing therapy. Failure to improve may indicate need for further investigation and management changes. Because the prevalence of ulceration is high in the racing Thoroughbred population and the severity of ulcers in our experience does not seem well correlated with clinical signs, a therapeutic trial may be indicated if gastric endoscopy is not available. Horses that respond to therapy should be maintained on therapy while in training. An oral formulation of ranitidine (L Begg, unpublished data, 2002) has been shown to be effective at healing ulcers while horses remain in training. Similarly other reports suggest only omeprazole is effective in achieving healing of ulcers while in training.[231]

Colic

Typically the incidence of colic is low in racing populations. Swimming activity is noted occasionally to cause colic in some individual horses; in this capacity it is typically seen within 2 hours of a swimming episode. The etiology of swimming-associated colic is undetermined but is typically associated with gaseous distension of the large bowel, which usually responds to medical therapy. Individuals that seem predisposed to recurrent bouts require swimming to be removed from their training schedule.

Diarrhea

Severe enterocolitis needs to be recognized and treated immediately with aggressive medical therapy. Prophylaxis involves avoiding unnecessary use of antimicrobials. Use of specific antimicrobial agents appears to be associated with an increased frequency of enterocolitis. Inclusion of metronidazole in therapy may be indicated if diarrhea is associated with antimicrobial use. Concerns of potential salmonellosis warrant some form of isolation of these cases.

Cardiovascular diseases

Cardiovascular diseases, with the exception of atrial fibrillation, are relatively rare in race horses. However, functional and anatomic cardiac abnormalities should not be overlooked as potential causes of poor performance.

Veins (septic and non-septic thrombophlebitis)

Typically associated with intravenous injections, thrombophlebitis can be very debilitating to a Thoroughbred race horse. Once a vein is inflamed it should be avoided as a site of venepuncture until inflammation is completely resolved. Cessation of high-intensity activity combined with hot packing and antimicrobials may hasten resolution. Progressive sepsis or thrombosis of both veins can become career threatening. The risks of thrombophlebitis may be decreased by use of a disposable 1.5 inch 18-gauge catheter instead of a needle for administration of all agents that may incite an inflammatory response if delivered perivascularly.

Cardiac abnormalities

The most common indication for investigation of cardiac function in racing Thoroughbreds is poor or decreased performance. The most commonly identified pathologic arrhythmia is atrial fibrillation.[232] Atrial fibrillation is typically associated with a marked reduction in high-speed performance and may be noted after a race or strenuous exercise. Atrial fibrillation may be paroxysmal, resolving within 24–48 hours of its identification after exercise, and diagnosis may be difficult if the arrhythmia resolves before it is documented.[233,234] Cases with persistent atrial fibrillation require treatment to achieve conversion; the presence of a preexisting cardiac lesion as a contributing factor should be ruled out as this will negatively impact long-term athletic prognosis.[232,234,235]

Heart murmurs have been documented in a large portion of the population of racing Thoroughbreds. One study identified murmurs in 81% of 846 Thoroughbred race horses and no association was found between racing performance and murmurs.[236] Investigation of cardiovascular function via Doppler echocardiography may be indicated if a murmur not typical of a functional systolic murmur is identified or in horses with poor performance not attributable to the respiratory or musculoskeletal systems. Documentation of apparently pathologic murmurs in young untrained horses warrants documentation and monitoring over time, since mitral and tricuspid regurgitant murmurs have been demonstrated to progress with training.[237]

References

1. Anon. www.horseracingintfed.com
2. Bourke JM. Wastage in Thoroughbreds. In: Proceedings of the Annual Seminar of the Equine Branch New Zealand Veterinary Association 1995; 107–119.
3. Bailey CJ, Reid SW, Hodgson DR, et al. Factors associated with time until first race and career duration for Thoroughbred racehorses. Am J Vet Res 1999; 60(10):1196–1200.
4. Physick-Shead PW. Career profile of the Canadian Standardbred. Can J Vet Res 1986; 50:449–456.
5. Gabel AA, Spencer CP, Pipers FS. A study of correlation of closure of the distal radial physis with performance injury in the standardbred. J Am Vet Med Assoc 1977; 170(2): 188–194.
6. Jeffcott LB, Rossdale PD, Freestone J, et al. An assessment of wastage in Thoroughbred racing from conception to 4 years of age. Equine Vet J 1982; 14(3):185–198.
7. Rossdale PD, Hopes R, Wingfield Digby NJ, et al. Epidemiological study of wastage among racehorses 1982 and 1983. Vet Rec 1985; 116:66–69.

8. Lindner A, Dingerkus A. Incidence of training failure among Thoroughbred horses at Cologne, Germany. Prev Vet Med 1993; 15:85–94.
9. Perkins N. Wastage in NZ Thoroughbred racing industry: An epidemiological investigation. In: Proceedings of the Annual Seminar of the Equine Branch New Zealand Veterinary Association 1999; 103–112.
10. Kobluck CN, Robinson RA, Clanton CJ, et al. Comparison on the exercise level and problem rate of 95 Thoroughbred racehorses. Proc Am Assoc Equine Pract 1990; 36:471–475.
11. Bailey CJ, Reid SW, Hodgson DR, et al. Impact of injuries and disease on a cohort of two- and three-year old Thoroughbreds in training. Vet Rec 1999; 23:487–493.
12. Haynes PF, Robinson RA. Racetrack breakdown pilot study summary. Proc Am Assoc Equine Pract 1988; 340:673–676.
13. Bathe AP. 245 Fractures in Thoroughbred Racehorses: Results of a 2-year prospective study in Newmarket. In: Proceedings of the 40th Annual AAEP Convention 1994; 175–176.
14. Estberg L, Stover SM, Gardner IA, et al. High-speed exercise history and catastrophic racing fracture in Thoroughbreds. Am J Vet Res 1996; 57(11):1549–1555.
15. Bailey CJ, Reid SW, Hodgson DR, et al. Flat, hurdle and steeple racing: risk factors for musculoskeletal injury. Equine Vet J 1998; 30(6):498–503.
16. Kobluk CN. Epidemiologic study of racehorse injuries. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:564–569.
17. Cohen ND, Mundy GD, Peloso JG, et al. Results of physical inspection before races and race-related characteristics and their association with musculoskeletal injuries in Thoroughbreds during races. J Am Vet Med Assoc 1999; 215(5):654–661.
18. Ueda Y. Preventing accidents in racehorses: studies and measures taken by the Japan Racing Association. In: Report of the committee on the prevention of accidents to racehorses. Japan Racing Association, 1991.
19. Peloso JG, Mundy GD, Cohen ND. Prevalence of, and factors associated with, musculoskeletal racing injuries of Thoroughbreds. J Am Vet Med Assoc 1994; 204(4):620–626.
20. McKee SL. An update on racing fatalities in the UK. Equine Vet Educ 1995; 7:202–204.
21. Estberg L, Stover SM, Gardner IA, et al. Fatal musculoskeletal injuries incurred during racing and training in Thoroughbreds. J Am Vet Med Assoc 1996; 208:92–96.
22. Wilson JH, Robinson RA, Jensen RC, et al. Equine soft tissue injuries associated with racing: descriptive statistics from American racetracks. In: Dubai International Equine Symposium Proceedings: 'The equine athlete: tendon, ligament and soft tissue injuries' 1996; 1:1–21.
23. Mohammed HO, Hill T, Lowe J. Risk factors associated with injuries in Thoroughbred horses. Equine Vet J 1991; 23:445–448.
24. Stover SM, Johnson BJ, Daft BM, et al. An association between complete and incomplete stress fractures of the humerus in racehorses. Equine Vet J 1992; 24:260–263.
25. Stover SM, Ardans AA, Read DH, et al. Patterns of stress fractures associated with complete bone fractures in racehorses. Proc Am Assoc Equine Pract 1993; 39:131–132.
26. Poole RR, Meagher DM. Pathologic findings and pathogenesis of racetrack injuries. Vet Clin North Am Equine Pract 1990; 6(1):1–30.
27. Clanton C, Kobluk CN, Robinson RA, et al. Monitoring surface conditions of a Thoroughbred racetrack. J Am Vet Med Assoc 1991; 198:613–620.
28. Bailey CJ, Reid SW, Hodgson DR, et al. Risk factors associated with musculoskeletal injuries in Australian Thoroughbred racehorses. Prev Vet Med 1997; 32:47–55.
29. Kane AJ, Stover SM, Gardner IA, et al. Horseshoe characteristics as possible risk factors for fatal musculoskeletal injury of Thoroughbred racehorses. Am J Vet Res 1996; 57(8):1147–1152.
30. Kane AJ, Stover SM, Gardner IA, et al. Hoof size, shape, and balance as possible risk factors for catastrophic musculoskeletal injury of Thoroughbred racehorses. Am J Vet Res 1998; 59(12):1545–1552.
31. Johnson B, Ardens A, Stover SM, et al. California racehorse postmortem program: A 4 year overview. Proc Am Assoc Equine Pract 1994; 40:167–169.
32. Mackey VS, Trout DR, Meagher DM, et al. Stress fractures of the humerus, radius and tibia in horses. Vet Radiol 1987; 28:26–31.
33. McIlwraith CW, Yovich JV, Martin GS. Arthroscopic surgery for the treatment of osteochondral chip fractures in the equine carpus. J Am Vet Med Assoc 1987; 191:531–540.
34. Kawcak CE, McIlwraith CW. Proximodorsal first phalanx chip fragmentation in 336 horses. Equine Vet J 1994; 26(5):392–396.
35. Moore RM, Schneider RK. Arthroscopic findings in the carpal joints of lame horses without radiographically visible abnormalities: 41 cases (1986–1991). J Am Vet Med Assoc 1995; 206(11):1741–1746.
36. Spike DL, Bramlage LR, Embertson RM, et al. Tibial stress fractures in 51 racehorses. Proc Am Assoc Equine Pract 1996; 42:280–281.
37. Colon JL, Bramalge LR, Hance SR. Qualitative and quantitative documentation of the racing performance of 461 Thoroughbred racehorses after arthroscopic removal of dorsoproximal first phalanx osteochondral fractures 1986–1995. Equine Vet J 2000; 32(6):475–481.
38. Buchner HH, Kubber P, Zohmann E, et al. Sedation and antisedation as tools in equine lameness examination. Equine Vet J 1999; Suppl 30:227–230.
39. Wilson JH, Robinson RA. Risk factors for equine racing injuries. Comp Cont Educ Pract Vet 1996; 18:682–690.
40. Moyer W, Spencer PA, Kallish M. Relative incidence of dorsal metacarpal disease in young Thoroughbred racehorses training on two different surfaces. Equine Vet J 1991; 23(3):166–168.
41. Cheney JA, Shen CK, Wheat JD. Relationship of racetrack surface to lameness in the Thoroughbred racehorse. Am J Vet Res 1973; 34(10):1285–1289.
42. Rooney JR, Genovese A. Survey and analysis of bowed tendon in Thoroughbred racehorses. J Equine Vet Sci 1981; 1:49–53.
43. Zebarth BJ, Sheard RW. Impact and shear resistance of turf grass racing surfaces for Thoroughbreds. Am J Vet Res 1985; 46(4):778–784.
44. Pratt GW. Racing surfaces a survey of mechanical behavior. Proc Am Assoc Equine Pract 1984; 30:321–331.
45. Kai M, Takahashi T, Aoki O, et al. Influence of rough track surfaces on components of vertical forces in cantering Thoroughbred horses. Equine Vet J 1999; Suppl 30:214–217.
46. Fredrickson I, Dalin G, Drevmo S, et al. Ergonomic aspects of poor racetrack design. Equine Vet J 1975; 7(2):63–65.
47. Oikawa M, Ueda Y, Inada J, et al. Effect of restructuring a racetrack on the occurrence of racing injuries in Thoroughbred horses. J Equine Vet Sci 1994; 14:262–268.

48. Evans DL, Walsh JS. Effect of increasing the banking of a racetrack on the occurrence of injury and lameness in Standardbred horses. Aust Vet J 1997; 75(10):751–752.
49. Eaton MD, Evans DL, Hodgson DR, et al. Effect of treadmill incline and speed on metabolic rate during exercise in Thoroughbred horses. J Appl Physiol 1995; 79(3):951–957.
50. Grant BD. Rest, exercise, and physical therapy programs. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse: Philadelphia: WB Saunders; 1996:217–223.
51. Miyata H, Sugiura T, Kai M, et al. Muscle adaptation of Thoroughbred racehorses trained on a flat or sloped track. Am J Vet Res 1999; 60(12):1536–1539.
52. Ratzlaff MH, Hyde ML, Grant BD, et al. Measurement of vertical forces and temporal components of the strides of horses using instrumented shoes. J Equine Vet Sci 1990; 10:23–35.
53. Palmer S. Prevalence of carpal fractures in Thoroughbred and Standardbred racehorses. J Am Vet Med Assoc 1986; 188:1171–1173.
54. Cervantes C, Madison JB, Ackerman N, et al. Surgical treatment of dorsal cortical fractures if the third metacarpal bone in Thoroughbred racehorses: 53 cases (1985–1989). J Am Vet Med Assoc 1992; 200(12):1997–2000.
55. Dallap BL, Bramlage LR, Embertson RM. Results of screw fixation combined with cortical drilling for treatment of dorsal cortical stress fractures of the third metacarpal bone in 56 Thoroughbred racehorses. Equine Vet J 1999; 31(3):252–257.
56. Hubbell JA, Hinchcliff KW, Muir WW, et al. Cardiorespiratory and metabolic effects of walking, standing and standing with a splint during the recuperative period from maximal exercise in horses. Am J Vet Res 1997; 58(9):1003–1009.
57. Ridgeway K, Harman J. Equine back rehabilitation. Vet Clin North Am Equine Pract 1999; 15(1):263–280.
58. Misumi K, Sakamoto H, Shimazu R. The validity of swimming training for 2-year old Thoroughbreds. J Vet Med Sci 1994; 56(2):217–222.
59. McIlwraith CW, Frisbie DD, Kawcak CE. Current treatments for traumatic synovitis, capsulitis, and osteoarthritis. Proc Am Assoc Equine Pract 2001; 47:180–210.
60. Tokuriki M, Ohtsuki R, Kai M, et al. EMG activity of the muscles of the neck and forelimbs during different forms of locomotion. Equine Vet J Suppl 1999; 30:231–234.
61. Knight PK, Sinha AK, Rose RJ. Effects of training intensity on maximal oxygen uptake. In: Persson SG, Lindholm A, Jeffcott LB, eds. Equine exercise physiology, vol 3. Davis CA: ICEEP Publications; 1991:77–82.
62. Art T, Lekeux P. Training induced modifications in cardiorespiratory and ventilatory measurements in Thoroughbred horses. Equine Vet J 1993; 25:532.
63. Tyler CM, Golland LC, Evans DL, et al. Changes in maximum oxygen uptake during prolonged training, overtraining, and detraining in horses. J Appl Physiol 1996; 81(5):2244–2249.
64. Burks RT, Bean BG, Marcus R, et al. Analysis of athletic performance with prophylactic ankle devices. Am J Sports Med 1991; 19:104–106.
65. Kobluk CN, Martinez del Campo L, Harvey-Fulton KA, et al. A kinematic investigation of the effect of a cohesive elastic bandage on the gait of the exercising Thoroughbred racehorse. Proc Am Assoc Equine Pract 1988; 34:135–148.
66. Crawford W, Vanderby R, Neirby D, et al. The energy absorbing capacity of equine support bandages. I Comparison between bandages placed in various configurations and tensions. Vet Comp Othop Trauma 1990; 1:2–9.
67. Crawford W, Vanderby R, Neirby D, et al. The energy absorbing capacity of equine support bandages II. Comparison between bandages of different materials. Vet Comp Othop Trauma 1990; 1:2–9.
68. Wilson AM, Goodship AE. Exercise-induced hyperthermia as a possible mechanism for tendon degeneration. J Biomech 1994; 27(7):899–905.
69. Birch HL, Wilson AM, Goodship AE. The effect of exercise induced hyperthermia on tendon cell survival. J Exp Biol 1997; 200(11):1703–1708.
70. Porter M, Kobluk CN. Physical therapy and rehabilitation for equine athletes. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:553–561.
71. Kaneps AJ. Tissue temperature response to hot and cold therapy in the metacarpal region of a horse. Proc Am Assoc Equine Pract 2000; 46:208–213.
72. Palmer JL, Bertone AL. Joint biomechanics in the pathogenesis of traumatic arthritis. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia: WB Saunders; 1996:104–119.
73. Pool RR. Pathologic manifestations of joint disease in the athletic horse. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia: WB Saunders; 1996:87–104.
74. Young A, O'Brien TR, Pool RR. Exercise related sclerosis in the third carpal bone of the racing Thoroughbred. Proc Am Assoc Equine Pract 1988; 34:339–346.
75. Pilsworth RC, Sheperd MC, Herinckx BM, et al. Fracture of the wing of the ileum, adjacent to the sacroiliac joint, in Thoroughbred racehorses. Equine Vet J 1994; 26:94–99.
76. Seeherman HJ. Clinical applications of bone scanning. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:592–605.
77. Stover SM. Stress fractures. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:451–459.
78. Riggs CM, Whitehouse GH, Boyd A. Pathology of the distal condyles of the third metacarpal and third metatarsal bones of the horse. Equine Vet J 1999; 31:140–148.
79. Shepherd MC. Stress fractures. Equine Vet Educ 2002; 14(2):75–76.
80. Kawcak CE, McIlwraith CW, Norrdin RW, et al. The role of subchodral bone in joint disease: a review. Equine Vet J 2001; 33(2):120–126.
81. Nunamaker DM. Metacarpal stress fractures. In: Nixon AJ, ed. Equine fracture repair. Philadelphia: WB Saunders; 1996:195–199.
82. Rodan GA. Introduction to bone biology. Bone 1992; 13:S3–S6.
83. Anderson MW, Greenspan A. Stress fractures. Radiology 1996; 199(1):1–12.
84. Riggs CM. Implications of bone adaptation in the Thoroughbred racehorse. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:99–103.
85. Martin RB, Gibson VA, Stover SM, et al. Residual strength of equine bone is not reduced by intense fatigue loading: implications for stress fracture. J Biomech 1997; 30(2):109–114.
86. Neilsen BD, Potter GD, Morris EL, et al. Changes in the third metacarpal bone and frequency of bone injuries in young quarter Horses during race training – observations and theoretical considerations. J Equine Vet Sci 1997; 17(10):541–548.

87. Porr CA, Kronfeld DS, Lawrence LA, et al. Deconditioning reduces mineral content of the third metacarpal bone in horses. J Anim Sci 1998; 76(7):1875–1879.
88. Carrier TK, Estberg L, Stover SM, et al. Association between long periods without high-speed workouts and risk of complete humeral or pelvic fracture in Thoroughbred racehorses: 54 cases (1991–1994). J Am Vet Med Assoc 1998; 212(10):1582–1587.
89. Nunamaker DM, Butterweck DM, Provost MT. Fatigue fractures in Thoroughbred racehorses: relationship with age, peak bone strain and training. J Orthop Res 1990; 8:604–611.
90. Boston RC, Nunamaker DM. Gait and speed as exercise components of risk factors associated with onset of fatigue injury of the third metacarpal bone in 2-year-old Thoroughbred racehorses. Am J Vet Res 2000; 61(6):602–608.
91. Riggs CM. Fractures – a preventable hazard of racing Thoroughbreds. Vet J 2002; 163(1):19–29.
92. Norwood GL. The bucked shins complex in Thoroughbreds. Proc Am Assoc Equine Pract 1989; 35:319–336.
93. Sullins K. Third metacarpal stress fractures. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:460–463.
94. Copelan RW. Incidence, location, and principles of treatment of stress fractures of the 3rd metacarpal bone. Proc Am Assoc Equine Pract 1979; 25:159–162.
95. Richardson DW. Dorsal cortical fractures of the equine metacarpus. Comp Cont Educ Pract Vet 6:S248–265.
96. Pilsworth R, Shepherd M. Stress fractures. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:104–111.
97. Pool RR. Pathologic manifestations of joint disease in the athletic horse. In: McIlwraith CW, Trotter GW, eds. Joint disease in the horse. Philadelphia: WB Saunders; 1996:87–104.
98. De Haan CE, O'Brien TR, Koblik PD. A radiographic investigation of third carpal bone injury in 42 racing Thoroughbreds. Vet Radiol 1987; 28:88–92.
99. Bramlage LR. First aid and transportation of fracture patients. In: Nixon AJ, ed. Equine fracture repair. Philadelphia: WB Saunders; 1996:36–42.
100. Patterson-Kane JC, Wilson AM, Firth EC, et al. Exercise-related alterations in crimp morphology in the central regions of superficial digital flexor tendons from young Thoroughbreds: a controlled study. Equine Vet J 1998; 30:61–64.
101. Patterson-Kane JC, Firth EC, Parry DA, et al. Effects of training on collagen fibril populations in the suspensory ligament and deep digital flexor tendon of young Thoroughbreds. Am J Vet Res 1998; 59(1):64–68.
102. Cherdchutham W, Meershoek LS, vanWeeren PR, et al. Effects of exercise on the biomechanical properties of the superficial digital flexor tendon in foals. Am J Vet Res 2001; 62(12):1859–1864.
103. Oikawa M, Goodship AE. Clinical and investigational advances in the prevention of tendinitis. Equine Vet J 1999; Suppl 30:640–641.
104. Genovese RL, Rantanen NW, Simpson BS, et al. Clinical experience with quantitative analysis of superficial digital flexor tendon injuries in Thoroughbred and Standardbred racehorses. Vet Clin North Am Equine Pract 1990; 6:129–147.
105. Genovese RL. Prognosis of superficial flexor tendon and suspensory ligament injuries. Proc Am Assoc Equine Pract of the 39th Annual AAEP Convention 1993; 39:9–10.
106. Goodship AE. The pathophysiology of flexor tendon injury in the horse. Equine Vet Educ 1993; 5:23–29.
107. Dowling BA, Dart AJ, Hodgson DR, et al. Superficial digital flexor tendinitis. Equine Vet J 2000; 32(5):369–378.
108. Gibson KT, Burbridge HM, Pfeiffer DU. Superficial digital flexor tendinitis in Thoroughbred racehorses: outcome following non-surgical treatment and superior check desmotomy. Aust Vet J 1997; 75(9):631–635.
109. Marr CM, McMillan I, Boyd JS, et al. Ultrasonographic and histopathological finding in equine superficial digital flexor tendon injury. Equine Vet J 1993; 25(1):23–29.
110. Genovese RL, Reef VB, Longo KL, et al. Superficial digital flexor tendinitis – long term sonographic and clinical study of racehorses. In: Dubai International Equine Symposium Proceedings: 'The equine athlete: tendon, ligament and soft tissue injuries' 1996; 187–205.
111. Reef VB. Musculoskeletal ultrasonography. In: Equine diagnostic ultrasound. Philadelphia: WB Saunders; 1998:39–186.
112. Romero JM, Dyson SJ. The diffusely filled limb. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:23–27.
113. Gillis C. Tendon and ligament rehabilitation. In: Dubai International Equine Symposium Proceedings: 'The equine athlete: tendon, ligament and soft tissue injuries' 1996; 417–421.
114. Marr CM. Advances in equine ultrasound. Vet Clin North Am Equine Pract 2001; 17(2):305–317.
115. Rantanen NW. Principles of ultrasonographic examination of tendons and ligaments. Proc Am Assoc Equine Pract 1993; 39:9–10.
116. Silver IA, Brown PN, Goodship AE, et al. A clinical and experimental study of tendon injury, healing and treatment in the horse. Equine Vet J 1983; Suppl 1:1–43.
117. Bramlage LR. Superior check ligament desmotomy as treatment for superficial digital flexor tendinitis: initial report. Proc Am Assoc Equine Pract 1986; 365.
118. Sawdon H, Yovich JV, Booth T. Superficial digital flexor tendinitis in racehorses. Long term follow up of conservatively managed cases. Aust Equine Vet 1996; 14:21–25.
119. Genovese R, Longo K, Berthold B, et al. Quantitative sonographic assessment of superficial digital flexor injuries in Thoroughbred racehorses. Proc Am Assoc Equine Pract 1997; 43:285–290.
120. Gillis CL. Rehabilitation of tendon and ligament injuries. Proc Am Assoc Equine Pract 1997; 43:306–309.
121. Henniniger RW. Superficial digital flexor tendinitis. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:341–347.
122. Henninger RW, Bramlage LR, Schneider R. Short-term effects of superior check ligament desmotomy and percutaneous tendon splitting as a treatment for acute tendinitis. Proc Am Assoc Equine Pract 1990; 36:539–540.
123. Bramlage LR, Rantanen NW, Genovese RL, et al. Long-term effects of surgical treatment of superficial digital flexor tendinitis by superior check desmotomy. Proc Am Assoc Equine Pract 1988; 34:655–666.
124. Fulton IC, MacLean AA, O'Reily JL, et al. Superior check ligament desmotomy for treatment of superficial digital flexor tendinitis in Thoroughbred and Standardbred horses. Aust Vet J 1994; 71(8):233–235.

125. Bukowiecki CF, Bramlage LR, Gabel AA. In vitro strength of the suspensory apparatus in training and resting horses. Vet Surg 1987; 16(2):126–130.
126. Wilson DA, Baker GJ, Pijanowski GJ, Boero MJ, et al. Composition and morphologic features of the interosseous muscle in Standardbreds and Thoroughbreds. Am J Vet Res 1991; 52(1):133–139.
127. Colbourne CM, Yovich JV. Suspensory ligament injuries in racing horses: ultrasonographic diagnosis and long term follow-up. Aust Equine Vet 1994; 12(3):119–128.
128. O'Brien TR, Morgan JP, Wheat D, et al. Sesamoiditis in the Thoroughbred: a radiographic study. J Am Vet Rad Soc 1971; 12:75–87.
129. Hardy J, Marcoux M, Breton L. Clinical relevance of radiographic findings in proximal sesamoid bones of two-year-old standardbreds in their first year of training. J Am Vet Med Assoc 1991; 198(12):2089–2094.
130. Bertone AL. The fetlock. In: Stashak TS, ed. Adams' Lameness in horses, 5th edn. Baltimore: Lippincott, Williams and Wilkins; 2002:768–782.
131. McIlwraith CW. Diseases of joints, tendons, ligaments and related structures. In: Stashak TS, ed. Adams' Lameness in horses, 5th edn. Baltimore: Lippincott, Williams and Wilkins; 2002:459–644.
132. Spike DL, Bramlage LR, Howard BA, et al. Radiographic proximal sesamoiditis in Thoroughbred sales yearlings. Proc Am Assoc Equine Pract 1997; 43:132–133.
133. Kane AJ, McIlwraith CW, Park RD, et al. The effect of radiographic changes in Thoroughbred yearlings on future racing performance. Proc Am Assoc Equine Pract 2000; 46:370–374.
134. Dyson SJ, Arthur RM, Palmer SE, et al. Suspensory ligament desmitis. Vet Clin North Am Equine Pract 1995; 11(2):177–215.
135. Cowles RR. Proximal suspensory desmitis – a qualitative survey. Proc Am Assoc Equine Pract 2000; 46:143–144.
136. Dyson SJ. Proximal suspensory desmitis in the forelimb and the hindlimb. Proc Am Assoc Equine Pract 2000; 46:137–142.
137. Ford T, Ross M, Orsini P. A comparison of methods for proximal palmar metacarpal anesthesia in horses. Vet Surg 1988; 18:146–150.
138. Bramlage LR, Gabel AA, Hackett RP. Avulsion fractures of the origin of the suspensory ligament of the horse. J Am Vet Med Assoc 1980; 176(10 Pt1):1004–1010.
139. Lloyd KC, Koblick P, Ragle C, et al. Incomplete palmar fractures of the proximal extremity of the third metacarpal bone in horses: ten cases (1981–1986). J Am Vet Med Assoc 1988; 192(6):798–803.
140. Ross MW, Ford TS, Orsini PG. Incomplete longitudinal fracture of the proximal palmar cortex of the third metacarpal bone in horses. Vet Surg 1988; 17(2):82–86.
141. Boening KJ. Radial extracorporeal shock wave therapy for chronic insertional desmopathy of the proximal suspensory ligament. Proc Am Assoc Equine Pract 2000; 46:203–205.
142. McClure S. Extracorporeal shock wave therapy: What is it? What does it do to equine bone? Proc Am Assoc Equine Pract 2000; 46:197–199.
143. Cannon J. Common hoof conditions observed in racetrack practice. Proc Am Assoc Equine Pract 1979; 24:311–315.
144. Balch OK, Butler D, Collier MA. Balancing the normal foot: hoof preparation, shoe fit and shoe modifications in the performance horse. Equine Vet Educ 1997; 9(3):143–154.
145. Stephens PR, Nunamaker DM, Butterweck DM. Applications of a Hall-effect transducer for measurement of tendon strain in horses. Am J Vet Res 1989; 50:1089–1095.
146. Denoix J. Functional anatomy of tendons and ligaments in the distal limbs. In: Dubai International Equine Symposium Proceedings: 'The equine athlete: tendon, ligament and soft tissue injuries' 1996; 23–53.
147. Reimersma DJ, van de Bogert AJ, Jansen MO, et al. Influence of shoeing on ground reaction forces and tendon strains in the forelimbs of ponies. Equine Vet J 1996; 28:133–138.
148. Clayton HM. Effects of hoof angle on locomotion and limb loading. In White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:504–509.
149. Kobluk CN, Robinson RA, Gordon BJ, et al. The effect of conformation and shoeing: A cohort study of 95 Thoroughbred racehorses. Proc Am Assoc Equine Pract 1989; 35:259–274.
150. Balch OK, Helman RG, Collier MA. Underrun heels and toe-grab length as possible risk factors for catastrophic musculoskeletal injuries in Oklahoma racehorses. Proc Am Assoc Equine Pract 2001; 47:334–335.
151. Barrey E. Investigation of the vertical hoof force distribution in the equine formlinb with an instrumented horseboot. Equine Vet J 1990; Suppl 19(9):35–38.
152. Young J. Hoof balance: methods and assessment. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:510–512.
153. Goodness P. Composite repair of hoof injuries. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:516–518.
154. Frauenfelder HC, Rossdale PD, Ricketts SW. Changes in serum muscle enzyme levels associated with training schedules and the oestrus cycle in Thoroughbred racehorses. Equine Vet J 1986; 18(5):371–374.
155. MacLeay JM, Sorum SA, Valberg SJ, et al. Epidemiologic analysis of factors influencing exertional rabdomyolysis in Thoroughbreds. Am J Vet Res 1999; 60(12): 1562–1566.
156. Beech J. Chronic exertional rhabdomyolysis. Vet Clin North Am Equine Pract 1997; 13(1):145–168.
157. Valberg SJ. Muscular causes of exercises intolerance in horses. Vet Clin North Am Equine Pract 1996; 12(3):495–515.
158. MacLeay JM, Valberg SJ, Pagan JD, et al. Effect of diet on Thoroughbred horses with recurrent exertional rhabdomyolysis performing a standardized exercise test. Equine Vet J 1999; Suppl 30:458–462.
159. Meyer H, Radicke S, Kienzle E, et al. Investigations on preileal digestion of starch from grain, potato and manioc in horses. J Vet Med Assoc 1995; 42:371–381.
160. Beech J, Fletcher JE, Lizzo F, et al. Effect of phenytoin on the clinical signs and in vitro muscle twitch characteristics in horses with chronic intermittent rhabdomyolysis and myotonia. Am J Vet Res 1988; 49(12):2130–2133.
161. Jeffcott LB. Historical perspective and clinical indications. Vet Clin North Am Equine Pract 1997; 15(1):1–12.
162. Haussler KK, Stover SM. Stress fractures of the vertebral lamina and pelvis in Thoroughbred racehorses. Equine Vet J 1998; 11(1):374–381.
163. Marks D. Medical management of back pain. Vet Clin North Am Equine Pract 1999; 15(1):179–194.
164. Pilsworth RC, Head MJ. A study of ten cases of focal peritarsal infection as a cause of severe lameness in the Thoroughbred racehorse: clinical signs, differential

diagnosis, treatment and outcome. Equine Vet J 2001; 33(4):366–370.
165. Schneider RK, Bramlage LR, Moore RM, et al. A retrospective study of 192 horses affected with septic arthritis/tenosynovitis. Equine Vet J 1992; 24(6):436–442.
166. Burrel M. Endoscopic and virological observations on respiratory disease in a group of young Thoroughbred horses in training. Equine Vet J 1985; 17:99–103.
167. MacNamara B, Bauer S, Iafe J. Endoscopic evaluation of exercise induced pulmonary hemorrhage and chronic obstructive pulmonary disease in association with poor performance in racing Standardbreds. J Am Vet Med Assoc 1990; 196:443–445.
168. Sweeney C, Humber K, Roby K. Cytological findings of tracheobronchial aspirates from 66 Thoroughbred racehorses. Am J Vet Res 1992; 53:1172–1175.
169. Burrel MH, Wood JL, Whitwell KE, et al. Respiratory disease in Thoroughbred horses in training: the relationship between disease and viruses, bacteria and environment. Vet Rec 1996; 139:308–313.
170. Cannon JH. Practical respiratory diagnosis. In: Dubai International Equine Symposium Proceedings: 'The diagnosis and treatment of respiratory disease' 1997; 315–320.
171. Moore BR, Krakowka S, Robertson JT, et al. Cytological evaluation of bronchoalveolar lavage fluid obtained from Standardbred racehorses with inflammatory airway disease. Am J Vet Res 1995; 56:562–567.
172. Christley RM, Hodgson DR, Rose RJ, et al. Coughing in Thoroughbred racehorses: risk factors and tracheal endoscopic and cytological findings. Vet Rec 2001; 148:99–104.
173. Christley RM, Hodgson DR, Rose RJ, et al. A case-control study of respiratory disease in Thoroughbred racehorse in Sydney, Australia. Equine Vet J 2001; 33(3):256–264.
174. Mumford JA, Rossdale PD. Virus and its relationship to the 'poor performance' syndrome. Equine Vet J 1980; 12:3–9.
175. Christley RM, Hodgson DR, Rose RJ, et al. Attitudes of Australian veterinarians about the cause and treatment of lower respiratory tract disease in racehorses. Prev Vet Med 2000; 46:149–159.
176. Wood JL, Burrell MH, Roberts CA, et al. Streptococci and Pasteurella spp. associated with disease of the equine lower respiratory tract. Equine Vet J 1993; 25:314–318.
177. Wood JL, Chanter N. An outbreak of respiratory disease in horses associated with *Mycoplasma felis* infection. Vet Rec 1997; 140:388–391.
178. Moore BR. Lower respiratory tract diseases. Vet Clin North Am Equine Pract 1996; 12:457–472.
179. Wood JL, Newton JR, Chanter N, et al. A longitudinal epidemiological study of respiratory disease in racehorses: disease definitions; prevalence and incidence. In: Werney U, Wade JF, Munford Kaaden JO, eds. Equine infectious diseases VIII: Proceedings of the 8th International conference of equine infectious diseases. Newmarket: R and W Publications; 1999:64–70.
180. Chapman PS, Green C, Main JP, et al. Retrospective study of the relationships between age, inflammation and the isolation of bacteria from the lower respiratory tract of Thoroughbred horses. Vet Rec 2000; 146:91–95.
181. Moore BR, Krakowka S, McVey DS, et al. Inflammatory markers in bronchoalveolar lavage fluid of Standardbred racehorses with inflammatory airway disease: response to interferon alpha. Equine Vet J 1997; 29:142–147.
182. Viel L. Lower airway inflammation in young performance horses. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:426–427.
183. Clarke AF. Stable dust–threshold limiting values, exposure variables and host risk factors. Equine Vet J 1993; 25(3):172–174.
184. Thompson JR, Mcpherson EA. Prophylactic effects of sodium cromoglycate on chronic obstructive pulmonary disease in the horse. Equine Vet J 1981; 13(4):243–246.
185. Derksen FJ. Inhalation therapy for the treatment of lower airway disease. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997; 429–431.
186. West JB, Mathieu-Costello O. Stress failure of pulmonary capillaries as a mechanism for exercise induced pulmonary hemorrhage in the horse. Equine Vet J 1994; 26:441–447.
187. Langesetmo I, Fedde MR, Meyer TS, et al. Relationship of pulmonary arterial pressure to pulmonary hemorrhage in exercising horses. Equine Vet J 2000; 32(5):379–384.
188. Pascoe JR, Ferraro GL, Cannon JH, et al. Exercise induced pulmonary hemorrhage in racing Thoroughbreds: a preliminary study. Am J Vet Res 1981; 42:703–707.
189. Raphael CF, Soma L. Exercise induced pulmonary hemorrhage in Thoroughbreds after racing and breezing. Am J Vet Res 1982; 46:1123–1127.
190. Weiss DJ, Smith CM. Haemorrheological alterations associated with competitive racing activity in horses: implications for exercise induced pulmonary hemorrhage (EIPH). Equine Vet J 1998; 30:7–12.
191. Pascoe JR. Exercise induced pulmonary hemorrhage. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:441–443.
192. Roberts CA, Erickson HH. Exercise induced pulmonary hemorrhage workshop. Equine Vet J 1999; Suppl 30:642–644.
193. Takahashi T, Hiraga A, Ohmura K, et al. Frequency of and risk factors for epistaxis associated with exercise induced pulmonary hemorrhage in horses: 251,609 race starts (1992–1997). J Am Vet Med Assoc 2001; 218(9):1462–1464.
194. Bourke JM. Exercise induced pulmonary hemorrhage – the Australian situation. Proceedings of the 9th International Conference of Racing Analysts and Veterinarians, New Orleans 1992; 115–119.
195. Meyer TS, Fedde MR, Gaughan EM, et al. Quantification of exercise induced pulmonary hemorrhage with bronchoalveolar lavage. Equine Vet J 1998; 30(4):284–288.
196. Gross DK, Morley PS, Hinchcliff KW, et al. Effect of furosemide on performance of Thoroughbred horses racing in the United States and Canada. J Am Vet Med Assoc 1999; 215:664–669.
197. Hinchcliff KW. Effects of furosemide on athletic performance and exercise-induced pulmonary hemorrhage in horses. J Am Vet Med Assoc 1999; 215(5):630–635.
198. Manohar M, Hutchens E, Coney E. Pulmonary hemodynamics in the exercising horse and their relationship to exercise induced pulmonary hemorrhage. Br Vet J 1993; 149:419–428.
199. Manohar M, Goetz TE, Sullivan E, et al. Pulmonary vascular pressures of strenuously exercising Thoroughbred horses after administration of phenylbutazone and frusemide. Equine Vet J 1998; 30:158–162.
200. Lester G, Clarke C, Rice B, et al. Effect of timing and route of administration of furosemide in pulmonarly hemorrhage and pulmonary arterial pressure in exercising Thouroughbred racehorses. Am J Vet Res 1999; 60(1):22–28.
201. McKrane SA, Slocombe RF. Sequential changes in bronchoalveolar cytology after autologous blood inoculation. Equine Vet J 1999; Suppl 30:126–130.

202. Erickson HH, Kindig CA, Poole DC. Role of the airways in exercise induced pulmonary haemorrhage. Equine Vet J 2001; 33(6):537–539.
203. Geor RJ, Ommundson L, Fenton G, et al. Effects of an external nasal strip and frusemide on pulmonary hemorrhage in Thoroughbreds following high intensity exercise. Equine Vet J 2001; 33(6):577–584.
204. Goetz TE, Manohar M, Hassan AS, et al. Nasal strips do not affect pulmonary gas exchange, anerobic metabolism, or EIPH in exercising Thoroughbreds. J Appl Physiol 2001; 90(6):2378–2385.
205. Kindig CA, McDonough P, Fenton G, et al. Efficacy of nasal strip and furosemide in mitigating EIPH in Thoroughbred horses. J Appl Physiol 2001; 91(3):1396–1400.
206. Holcombe SJ, Berney C, Cornelise CJ, et al. The effect of commercially available nasal strips on airway resistance in exercising horses. Am J Vet Res 2002; 63(8): 1101–1105.
207. Raphel CF. Endoscopic findings in the upper respiratory tract of 479 horses. J Am Vet Med Assoc 1982; 181(5):470–473.
208. Seeherman HJ. Left recurrent laryngeal neuropathy. In: Robinson NE, ed. Current therapy in equine medicine, 4th edn. Philadelphia: WB Saunders; 1997:404–407.
209. Derksen FJ, Holcombe SJ, Hartmann W, et al. Spectrum analysis of respiratory sounds in exercising horses with experimentally induced laryngeal hemiplegia or dorsal displacement of the soft palate. Am J Vet Res 2001; 62(5):659–664.
210. Rakestraw PC, Hackett RP, Ducharme NG, et al. Arytenoid cartilage movement in resting and exercising horses. Vet Surg 1991; 20(2):122–127.
211. Hammer EJ, Tulleners EP, Parente EJ, et al. Videoendoscopic assessment of dynamic laryngeal function during exercise in horses with grade-III left laryngeal hemiparesis at rest: 26 cases (1992–1995). J Am Vet Med Assoc 1998; 212(3):399–403.
212. Tulleners EP, Stick JA. Laryngoplasty and repeat laryngoplasty. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:137–142.
213. Russell AP, Slone DE. Performance analysis after prosthetic laryngoplasty and bilateral ventriculectomy for laryngeal hemiplegia in horses: 70 cases (1986–1991). J Am Vet Med Assoc 1994; 204(8):1235–1241.
214. Fulton IC, Derksen FJ, Stick JA, et al. Treatment of left laryngeal hemiplegia in Standardbreds, using nerve muscle pedicle graft. Am J Vet Res 1991; 52(9):1461–1467.
215. Fulton IC. Treating equine laryngeal paralysis and paresis using a nerve muscle pedicle graft. In: Proceedings of the Veterinary Comparative Respiratory Society: Melbourne 2000. Online: http://tvms.tufts.edu/vcrs/2000/present.htm.
216. Robertson JT. Dorsal displacement of the soft palate. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:131–135.
217. Holcombe SJ, Derksen FJ, Stick JA, et al. Pathophysiology of dorsal displacement of the soft palate in horses. Equine Vet J 1999; Suppl 30:45–48.
218. Tulleners E. Epiglottiditis. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:135–137.
219. Holcombe SJ, Robinson NE, Jackson C, et al. Stabling, airway inflammation, and dorsal displacement of the soft palate in young horses. Proc Am Assoc Equine Pract 2000; 46:254–255.
220. Tulleners E, Stick JA, Leitch M, et al. Epiglottic augmentation for treatment of dorsal displacement of the soft palate in racehorses: 59 cases (1985–1994). J Am Vet Med Assoc 1987; 211(8):1022–1028.
221. Hay W, Tulleners E. Excision of intralaryngeal granulation tissue in 25 horses using a Nd:YAG laser (1986–1991). Vet Surg 1993; 22:129–134.
222. Sullins KE. Minimally invasive laser treatment of arytenoid chondritis in 5 horses. Proc Am Assoc Equine Pract 2001; 47:120–122.
223. Tulleners EP, Harrison IW, Raker CW. Management of arytenoid chondropathy and failed laryngoplasty in horses: 75 cases (1979–1985). J Am Vet Med Assoc 1988; 192(5):670–675.
224. Hammond CJ, Mason DK, Watkins KL. Gastric ulceration in mature Thoroughbred horses. Equine Vet J 1986; 18:284–287.
225. Murray MJ. Gastic ulceration in horses with colic: 91 cases (1987–1990). J Am Vet Med Assoc 1992; 195:1135–1138.
226. Murray MJ, Schusser GF, Pipers FS, et al. Factors associated with gastric lesions in Thoroughbred racehorses. Equine Vet J 1996; 28:368–374.
227. Johnson JH, Vatistas N, Castro L, et al. Field survey of the prevalence of gastric ulcers in Thoroughbred racehorses and on response to treatment of affected horses with omeprazole paste. Equine Vet Educ 2001; 13:221–224.
228. Andrews FM, Nadueau JA. Clinical syndromes of gastric ulceration in foals and mature horses. Equine Vet J 1999; Suppl 29:30–33.
229. Murray MJ, Eichorn ES. Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. Am J Vet Res 1996; 57:1599–1602.
230. Collier D. Gastric ulceration: a response to an unnatural environment. Equine Vet J 1999; Suppl 29:5–6.
231. Vatistas NJ, Snyder JR, Neito J, et al. Acceptability of a paste formulation and efficacy of high dose omeprazole in healing gastric ulcers in horses maintained in race training. Equine Vet J 1999; Suppl 29:71–76.
232. Begg LM, Hutchins DR, Suann CJ. Atrial fibrillation.
233. Holmes JR, Henigan M, Williams RB, et al. Paroxysmal atrial fibrillation in racehorses. Equine Vet J 1986; 18(1):37–42.
234. Mitten LA. Cardiovascular causes of exercise intolerance. Vet Clin North Am Equine Pract 1996; 12(3):473–494.
235. Marr CM Equine cardiology
236. Kriz NG, Hodgson DR, Rose RJ. Prevalence and clinical importance of heart murmurs in racehorses. J Am Vet Med Assoc 2000; 216(9):1441–1445.
237. Young LE, Wood JL. Effect of age and training on murmurs of atrioventricular valvular regurgitation in young Thoroughbreds. Equine Vet J 2000; 32(3):195–199.

CHAPTER 50

Veterinary aspects of racing and training Standardbred race horses

Kenneth W. Hinchcliff and Michael Hamlin

The breed and racing

Standardbred

Origins of the breed

The Standardbred racehorse, sometimes referred to as the American Trotter, originated in the USA and Canada in the early 1800s, with the breed society being formed in 1871.[1] Standardbred horses all trace their male lineage to Messenger, a Thoroughbred foaled in England in 1780 and exported to the USA, and to his four sons: George Wilkes, Dictator, Happy Medium, and Electioneer.[2] However, although mainly derived from Thoroughbred stock, Morgan and Hackneys also contributed to the Standardbred gene pool.[1] The Standardbred name derived from the requirement that, in order to be entered into the register of the new breed, Trotters had to complete a mile in a prescribed (standard) time.

Standardbreds are divided into two groups based on gait while racing, although a small number (~ 2%) use both gaits at some stage in their racing career.[3] There is a strong influence of gait on breeding in that most horses race at the gait used by their sire. Approximately 20% of offspring sired by Trotters register as pacers, whereas only 1% of offspring sired by pacers are registered as Trotters.[4] The extent of the genetic difference between Standardbred Trotters and pacers is as great or greater than that seen between some distinct horse breeds.[4]

Subsequent to its development in North America, Standardbreds and harness racing were exported to many countries. The Standardbred (American Trotter) is the origin of the Danish Trotter, Romanian Trotter, Swedish Standardbred Trotter, and the Russian Trotter.[1] The Coldblooded Trotter of parts of Scandinavia is not related to the Standardbred, being derived from the Dole Horse.[5] Trotters in Scandinavia derived approximately 94% of their genetic make-up from North American Standardbreds, with the remainder coming from French horses.[6] Presently, at least 24 countries, including countries in Scandinavia, Europe, and Australasia, have active organizations that promote Standardbred racing. The centers of Standardbred racing are the Midwest and East Coast of the USA, eastern Canada, Scandinavia, Australia, and New Zealand.

Although the Standardbred was derived from Thoroughbreds and in many respects resembles that breed, there are readily apparent differences. Stardardbreds are often not as tall as are Thoroughbreds, being 15 to 16 hands at the withers, are more heavily muscled and tend to be longer in the body. A prominent aspect of many Standardbreds is the presence of a Roman nose and large head. The predominant colors are bay, brown, and black, although gray horses do occur. Regional variations in the breed occur, with Finland having its own variation of the Standardbred.

Genetic aspects of performance

The population of Standardbred race horses has been subjected to strong selection pressure based on racing performance for most of the duration of the breed. The relative consistency of the type of racing, including use of the 1 mile (1640 m) race, has facilitated this selection. A consequence of this strong selection pressure, and other factors such as improved training methods, equipment and racing facilities, has been a progressive reduction in racetimes.[6] The decrease in race time has been well documented for Swedish Trotters (Fig. 50.1).[6] The reduction is exponential and appears to be approaching an asymptote, which is predicted to occur in 2015.[6]

Whereas it is well recognized that many non-genetic factors influence racing ability and, in particular, the speed over any one race, the ability to detect effects of selective breeding relies on identifying methods to compare horses to a common standard. The concept of the 'race pace' has

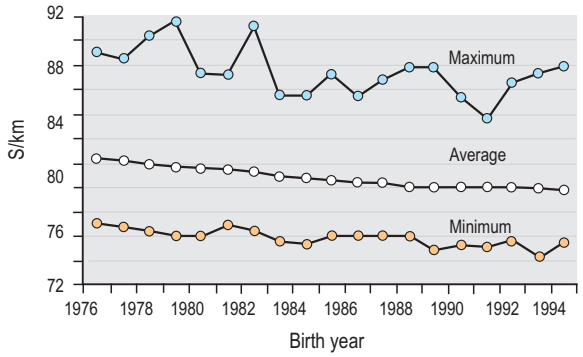

Fig. 50.1
Racing times of Swedish Standardbred trotters demonstrating progressive reduction in race time over an 18-year period. (Reproduced with permission from Arnason.[6])

therefore evolved. The 'pace' of a race is the speed of the winning horses. Performance of non-winning horses is then standardized by linear regression to this 'pace', thereby removing the influence of environmental factors.[7] Using this and similar approaches, heritability of speed was 0.31 ± 0.3 for pacers and 0.16 ± 0.09 for Trotters.[7] Heritability of speed was lower for 3 years than for 2-year-olds (0.25 ± 0.03 versus 0.44 ± 0.07, respectively) and may be due to culling.[7] Similarly, the heritability of earnings, average time and best time for Trotters was 0.20, 0.32, and 0.25, respectively.[8] The heritability of best time for a pacer was 0.23.[8]

Gait and racing

Gait

Standardbreds are raced both under saddle and pulling a light cart (sulky) upon which the driver sits. Racing under saddle is uncommon and mainly of novelty value. Almost all Standardbred racing involves the horse pulling a cart (sometimes referred to as a racebike or 'bike').

Standardbreds race using either of two gaits – trotting or pacing (Fig. 50.2). While within the one racing jurisdiction horses can use either gait, pacers always compete against pacers and Trotters always compete against Trotters. Pacing is the faster gait, with pacers completing 1 mile approximately 3.5 s faster than Trotters.[9]

Trotters move with a diagonal gait such that the left front and right rear legs are advanced simultaneously, as are then the right front and left rear. Trotters are either line-gaited or passing-gaited. Line-gaited Trotters move their ipsilateral limbs in the same sagittal plane whereas passing-gaited Trotters move their limbs in different sagittal planes. The limbs of passing-gaited horses pass each other during the gait whereas those of the line-gaited horse come together (Fig. 50.3). Pacers move in a lateral gait with the legs on one side of their body advancing simultaneously such that the left front and rear, and then the right front and rear, are advanced at the same time (see Fig. 50.2).

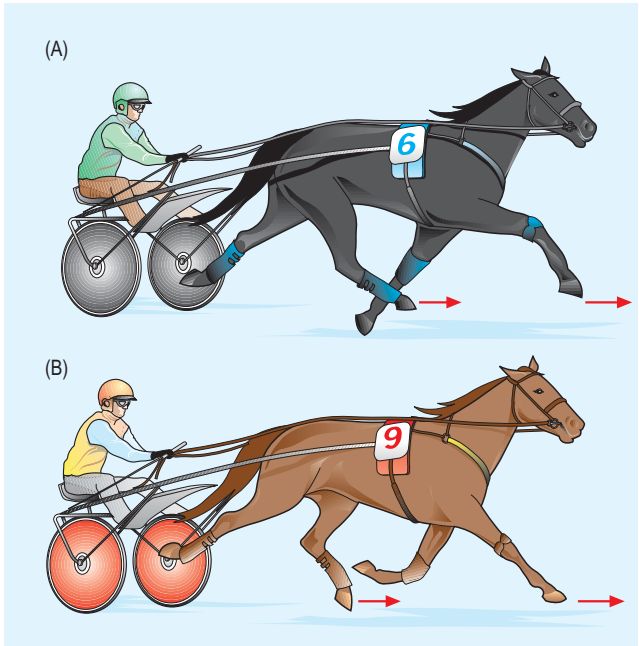

Fig. 50.2
(A) A horse pacing. (B) A horse trotting. Reproduced with permission of the United States Trotting Association.

Gait abnormalities – interference

Aspects of lameness in Standardbreds are discussed in detail later in this chapter. However, the gait of both Trotters and pacers predisposes them to problems arising from interference. Interference is the term used to describe a horse hitting one leg with the hoof of another leg, or, in the case of elbow interference, the same leg.

Interference in Trotters involves the hoof of the forelimb on one side striking parts of the ipsilateral hindlimb (Fig. 50.4). Scalping, speedy-cutting, shin-hitting, and hock

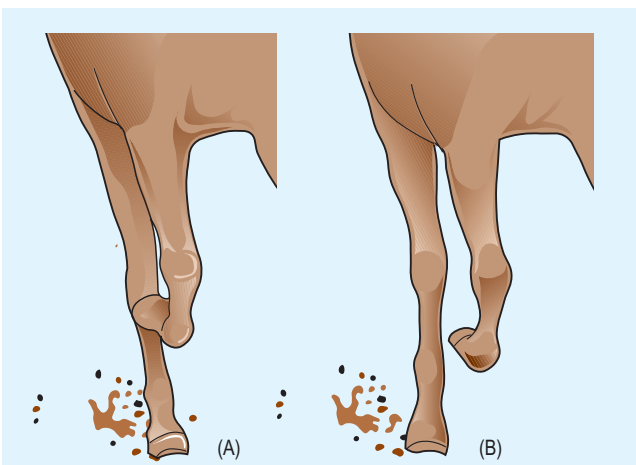

Fig. 50.3
Drawing of leg positions of a line-gaited (A) and passing-gaited (B) Trotter. (Redrawn with permission from Sylvester.[35])

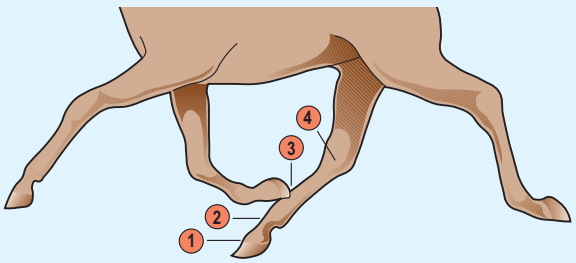

Fig. 50.4
Sites of interference in a trotting horse: (1) scalping, (2) speedy-cutting, (3) shin-hitting (as illustrated), and (4) hock hitting. (Redrawn with permission from Haughton.[36])

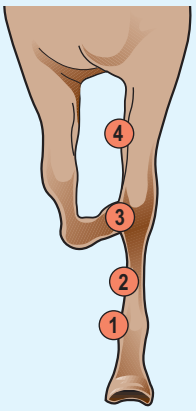

Fig. 50.7
Interference, in which the foot of one forelimb strikes the opposite forelimb, occurs at several levels: (1) the fetlock, (2) the medial metacarpus, (3) the medial carpus, and (4) the medial antebrachium. (Redrawn with permission from Haughton.[36])

hitting can all occur. Injuries are usually mild but can be sufficiently painful for the horse to be hesitant in trotting or pacing, or to not want to race at top speed. Interference in Trotters can result in the horse stumbling and breaking gait. Among pacers, interference is between the forelimb and contralateral hindlimb and is termed 'crossfiring' (Fig. 50.5). Striking of the sole of the forefoot by the ipsilateral hind foot is referred to as 'forging' (Fig. 50.6). Injuries to the fetlock, metacarpus, carpus, and medial antebrachium occur when the contralateral hoof hits one of these areas (Fig. 50.7). Interference can be minimized by changes in shoeing, including the use of weighted shoes, and equipment. Injuries resulting from interference can be minimized by application of protective boots and bandages (see below).

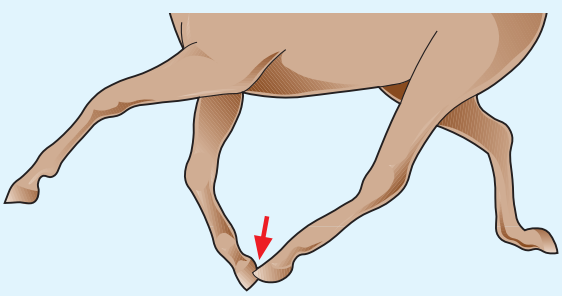

Fig. 50.5
Crossfiring, in which one hind foot hits the contralateral forefoot, occurs in pacers. (Redrawn with permission from Haughton.[36])

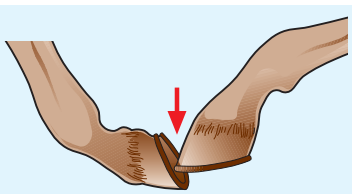

Fig. 50.6
Forging, in which the hind foot hits the ipsilateral forefoot, occurs in Trotters. (Redrawn with permission from Haughton.[36])

Equipment

Standardbreds wear a wide range of equipment when training and racing. The equipment is used to assist the horses maintain the desired gait, attach the horse to the sulky or cart, and permit the driver to maintain control and direct the horse.[10] Pacers are aided in maintaining their gait by light hobbles (Fig. 50.8), which they wear whenever they race, whereas Trotters only occasionally wear trotting hobbles. The hobbles are usually made of light plastic and have a length of 50–60 inches (112–135 cm), which is adjusted depending on the size of the horse and the length of the track. Shorter hobbles are used on smaller (e.g. half mile) than on larger (e.g. 1 mile) tracks.[11] Horses are more likely to 'break' if the hobble is too long, whereas a hobble that is too short limits performance.[11]

The harness consists of a girth, backstrap and crupper, pads, and breast collar. The shafts of the sulky or cart are connected to the harness. The tail is placed through the crupper, which is attached to the backstrap. The backstrap prevents the harness from sliding forward on the horse. The breast collar prevents the harness from slipping back.

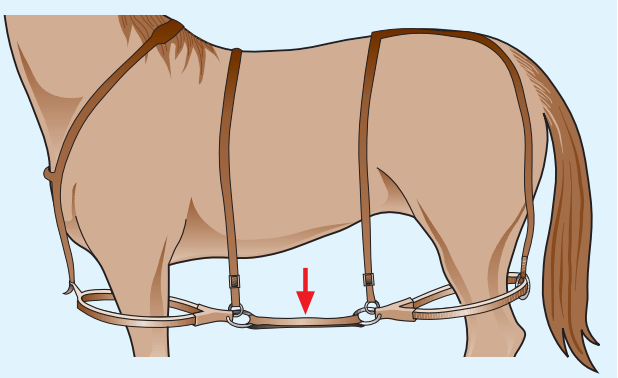

Fig. 50.8
Hobbles used to assist pacers in maintaining their gait while racing and training. (Redrawn with permission from Haughton.[36])

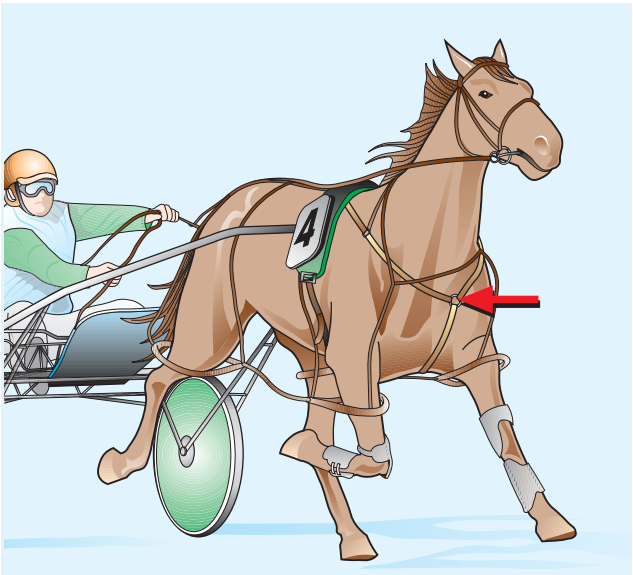

Fig. 50.9
Buxton martingale (arrow) used in place of a chest strap to maintain the correct position of the harness. (Redrawn with permission from Haughton.[36])

The breast strap is occasionally replaced with a Buxton martingale (Fig. 50.9).

Martingales, which usually run from the girth to the halter, are used to keep the horse's head in position and in particular to prevent it throwing or tossing its head. There are several different designs of martingale (Fig. 50.10).

Horses also wear any one of a variety of bridles (which might include 'blinders') designed to limit the visual field (Fig. 50.11). Bridles are selected based on the horse's temperament and handling characteristics. Bits, which are used to direct the horse and to maintain its head position, vary widely in design (Fig. 50.12). Check bits are used with a check rein to prevent the horse excessively flexing its neck and 'choking down'. The check rein is attached to the check bit over the nose and then runs up between the ears before attaching to the girth strap over the horse's back.

Horses can wear a variety of boots to protect against the effects of interference (Fig. 50.13). Boots that cover the dorsal metatarsus and fetlock protect against interference in these areas. Other variations on this boot include an attachment that protects the speedy-cut area of the dorsal pastern. Yet other boots extend proximally to protect the hock. A shorter boot protects just the distal metatarsus and fetlock. Bell boots and scalpers provide protection for the proximal hoof and coronary band.

Racing statistics

Standardbreds are bred with the intention of having them race, although not all foals born and registered eventually race. There were 11 332 registered Standardbreds in North America (the USA and Canada) in 2002.[12] These horses started 39 600 times at 288 tracks for a total purse of $US 500 724 338.[12] This compares with 17 637 registered horses in 1986 starting 57 021 times at 464 tracks for $US 387 474 745.[12] In Australia in 2001 there were 13 552 horses that had 14 471 starts in 15 558 races for a total stakemoney of $71 500 000.[13] Sweden, which permits only Trotters to race, has 31 harness tracks at which approximately 10 000 races are held with 110 000 starters each year.[14] The total prize money annually is 700 000 000 crowns.[14]

Most Standardbreds are eligible to first race as 2- or 3-year-olds. Although information regarding age at first start is

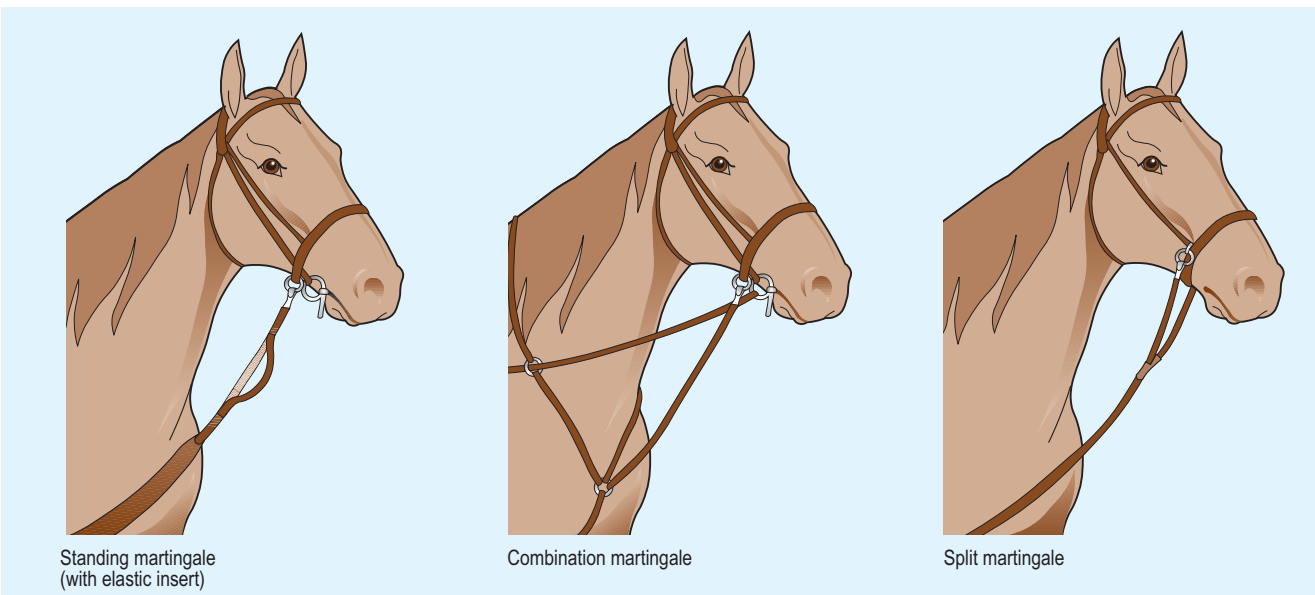

Fig. 50.10
Martingales used on harness horses. (Redrawn with permission from Haughton.[36])

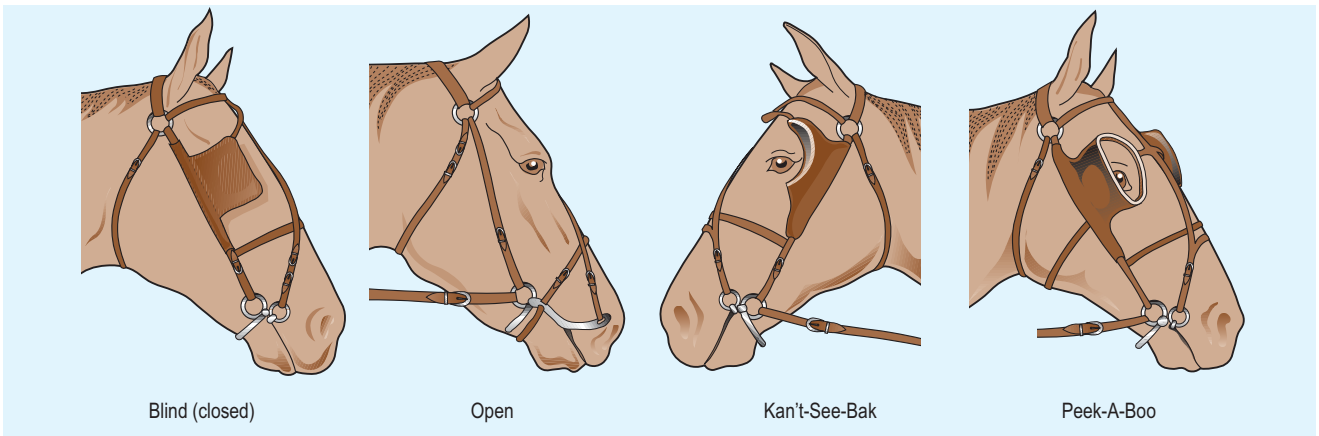

Fig. 50.11
Bridles used on Standardbred race horses. (Redrawn with permission from Haughton.[36])

not available for all regions in which Standardbreds race, in Canada the average age at the time of the first race for horses born in 1972 was 3.4 ± 0.5 years,[3] although the age at which horses first race has likely decreased since that time. For foals born in 1972 in Canada, 67% eventually raced, with approximately 17% having their first race as 2-year-olds, 48% as 3-year-olds, and 22% as 4-year-olds.[3] This is similar to the situation with Dutch trotters.[15] Horses that first raced as 2-year-olds had longer racing careers than horses first raced as 3-year-olds (5.1 versus 4.4 years).[3] Horses older at the time of their first race had progressively shorter racing careers. The racing life ranged from < 1 to 10 years, with an average of 4.1 ± 0.1 years. There is no difference in racing life span of trotters and pacers.[3]

There are important differences among sexes in the proportion of horses that race – 78% of male (colt and stallion), 88% of geldings, and 54% of fillies born in 1972 raced at some time.[3] The smaller proportion of fillies that eventually race is likely related to their tractability in early training, and opportunities for breeding when health and management problems related to training or racing are encountered.

Among Standardbreds born in Canada in 1972, 80% won at least one race during their career.[9] The number of starts during the horses career ranged from 1 to 347, with the 95% confidence interval for number of starts being 21 to 70 races. Thirty percent of horses had fewer than 20 starts and 29% raced more than 100 times.[9] The average horse had its best racing performance (fastest race) 2.55 years after its first race at a mean age of 5.27 years.[9]

Training the Standardbred

General principles

Most human sporting performances are governed by three general factors: technique, physiological fitness, and mental toughness. Standardbred race horses are no different, they require all three factors, but in particular physiological fitness and physical training, although a smooth economical pacing or trotting gait and a tough mental attitude to training and racing will also help. Consequently, one of the major elements to a successful Standardbred race horse is the trainer's ability to enhance physical fitness.

Training can be explained as a systematic and controlled application of a stimulus (stress) above that normally encountered by the animal, which forces the body to reorganize itself and thereby adapt. These overloading stimuli are normally given in a slowly progressive manner to enable the gradual adaptation of the animal to the training stress. In the case of race horses, the aim is to give the appropriate amount of training stimulus to realize the horse's full racing potential.

A major consideration when training horses is the energy requirements needed during the actual racing event. Standardbred race horses generally race over distances of 1600–3200 m (1–2 miles), which usually takes approximately 2:00–4:20 minutes to complete. Although there is some disagreement over the exact proportion of energy supplied by the aerobic and anaerobic pathways, it is generally considered that Standardbred race horses gain the majority of their energy during a race from the aerobic pathway (~60–90%) while the anaerobic pathways contribute a smaller but still important proportion (10–30%).[16] For that reason, training the Standardbred should focus on stressing both the aerobic and anaerobic energy pathways, as both respond to training,[17] however the majority of work should be aerobic in nature.

Training programs

Traditional training programs

Traditionally training programs for Standardbreds have incorporated three or four basic phases:

- *Phase 1. The Initial or Foundation Phase*: The aim of this phase of training is to develop aerobic fitness and decrease bodyweight, strengthen the muscles and joints, improve

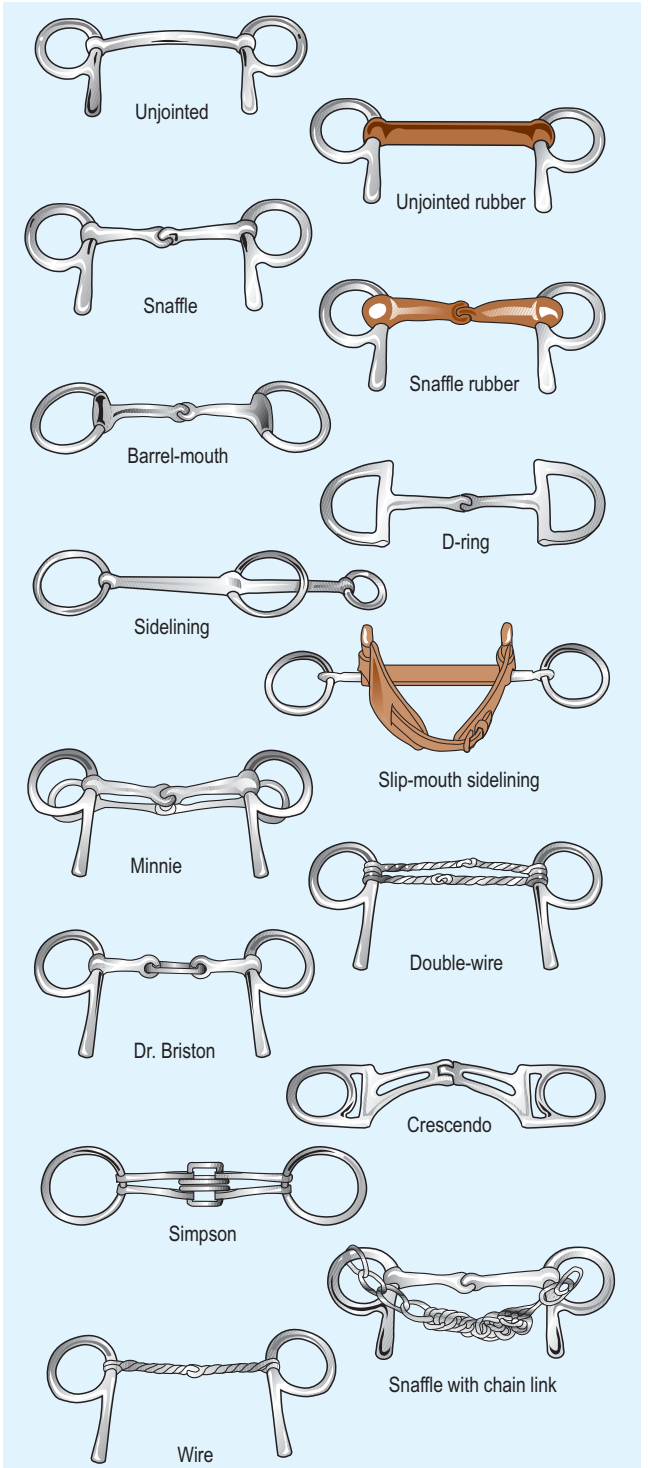

Fig. 50.12
Bits used in Standardbred race horses. (Redrawn with permission from Haughton.[36])

joint mobility and establish good training habits. Training during this phase usually consists of low-intensity moderate-duration exercise. For the Standardbred this usually incorporates slow jogging.

- *Phase 2. Preparation Phase*: This phase is usually separated into a number of subphases but overall the trainer is trying to increase the efficiency of the energy system(s) predominant in the event – namely the aerobic system. The trainer is also attempting to develop and maximize the components of fitness required by the Standardbred during racing, which includes strength, speed, power and flexibility. Training during this phase is usually characterized by alternate days of low-intensity jogging and higher-intensity gallop, pace, or trotting work.
- *Phase 3. Competition or Racing Phase*: The aim of this phase of training is to maintain rather than improve appropriate energy systems and fitness components required by the Standardbred during racing. Training during this phase is characterized by similar training to the final preparation phase, however, it will often involve a reduction in the high-intensity exercise, especially if competing regularly.
- *Phase 4. Rest or Lay-off Phase*: During this phase of training the horse is spelled, usually in a paddock, and given complete rest from any training. To decrease expenses during this phase the horse is normally transported back to the owners. This phase allows the horse to recover both physically and mentally from the racing season.

Standardbreds in Australiasia typically race over distances ranging from 1600 to 3200 m whereas Standardbreds in North America tend to race over the shorter distances of 1600–2200 m. Although current practices of New Zealand trainers, and an example of a more scientific approach from an Australian trainer have been published recently, similar training information from American trainers is difficult to find.[18,19] Sherman & Hopkins (1995)[18] investigated the training practices used by New Zealand's top 100 trainers of Standardbred maiden pacers and revealed that most trainers tend to give their horses very similar types of training. They reported that most New Zealand trainers separated their training into three preparation phases and a racing phase. The initial preparation phase is similar to the foundation phase described above and consisted mainly of jogging the horses at a steady pace (see Table 50.1) for 5–6 weeks with one rest day per week. The middle preparation phase followed and signaled the start of fast work. Fast work normally involved the horses being harnessed-up into their hobbles and pulling the racing cart. The final preparation phase, which lasted about 4 weeks, then followed. In the racing or competition phase, the majority of New Zealand trainers continued a similar pattern of training, however, about one-third of the trainers incorporated one or more 'strong' workouts (galloping rather than pacing in the cart).

Sherman and Hopkins[18] found that the intensity of the fast work increased during training but, interestingly, the intensity of the jog work remained unchanged throughout training. The speed at which horses were jogged remained at about 19 km/h whether they were in the initial preparation phase or the racing phase of training. The intensity of jog work described in the training program by Lovel[19] was almost the same as that described by Sherman and Hopkins.[18] However, the horses in Lovell's program started

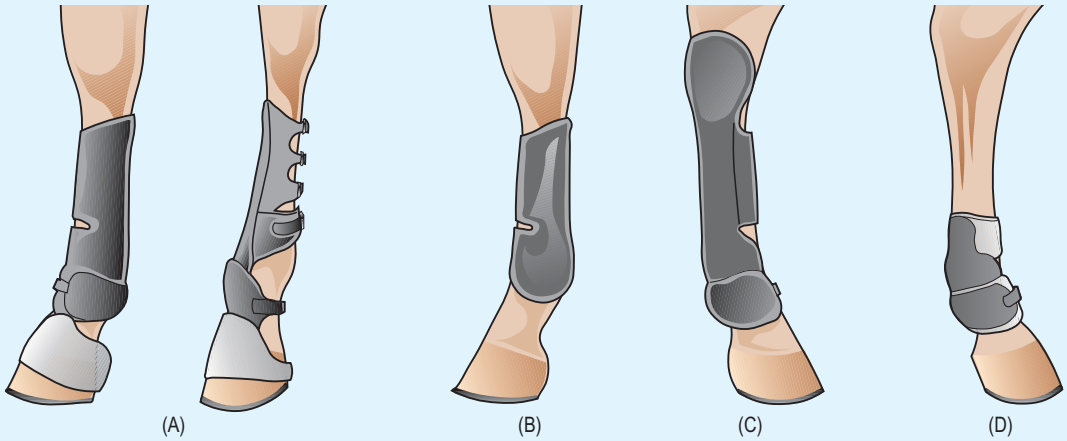

Fig. 50.13
Protective boots worn on the hind limbs by trotters. (A) The standard hind shin boot with speedy-cut attachment and a low scalper (left, side view; right, front view). (B) The standard hind shin boot. (C) Standard hind shin boot with speedy-cut attachment and hock protection. (D) Hind ankle boot with speedy-cut attachment. (Redrawn with permission from Haughton.[36])

Table 50.1 Training phases for maiden pacers of a typical top trainer In New Zealand[18]

Training phase	Training day	Type	Distance (m)	Speed (km/h)	Intensity (%)	Duration (min:s)
Initial preparation						
Weeks 1–5	Mon–Sat	Jog	12400	19.6	44.9	38:20
	Sun	Off				
Mid-preparation						
Weeks 6–10	Mon, Wed, Fri	Jog	11900	19.1	43.7	37:40
	Tue, Thu, Sat	Fast	4500	32.3	74.0	10:00
	Sun	Off				
Final preparation						
Weeks 11–14	Mon, Wed, Fri	Jog	12800	19.5	44.6	39:20
	Tue, Thu, Sat	Fast	3200	40.0	91.6	4:50
	Sun	Off				
Racing						
Two-weekly	Sat	Race				
	Sun	Off				
	Mon	Jog	11800	19.6	44.9	36:40
	Tue	Jog	11800	19.6	44.9	36:40
	Wed	Jog	11800	19.6	44.9	36:40
	Thu	Fast	3000	41.6	95.3	4:30
	Fri	Jog	11800	19.6	44.9	36:40
	Sat	Fast	3000	41.6	95.3	4:30
	Sun	Off				
	Mon	Jog	11800	19.6	44.9	36:40
	Tue	Fast	3000	41.6	95.3	4:30
	Wed	Jog	11800	19.6	44.9	36:40
	Thu	Fast	3000	41.6	95.3	4:30
	Fri	Jog	11800	19.6	44.9	36:40
	Sat	Race				

The means for 26 trainers (mid-preparation phase) or 94 trainers (all other phases). Workout intensities are percentages of qualifying pace, which was calculated from the average qualifying time for a maiden pacer over 2400 m, which was 3:18 min:s.

with much less jog work, which was quickly increased to be approximately the same as that described by Sherman and Hopkins by week 5 of the program (Table 50.2). Both training programs introduced fast work at about the same time (week 5) and typically trained the horses with alternating fast and slow days. Lovell's program is slightly more scientific in that the work intensities are calculated from a standard fitness test, which he suggests should be carried out every 2

Table 50.2 Suggested training for a mature Standardbred that has raced before but has been turned out for a prolonged rest[19]

Training phase	Training day	Type	Distance (m)	Speed (km/h)	Intensity (% V_{HRmax})
Pretraining					
Week 1	Mon, Tue	Jog	5000	19.0	
	Wed–Sat	Jog	6000	19.0	
	Sun	Off			
Week 2	Mon–Sat	Jog	8000	19.0	
	Sun	Off			
Week 3	Mon–Sat	Jog	10000	19.0	
	Sun	Off			
Week 4	Mon–Fri	Jog	13000	19.0	
	Sat	V_{HRmax}	4000	37.5	
	Sun	Off			
Foundation training					
Week 5	Mon, Wed, Fri	Jog	10000	19.0	
	Tue, Thu	Fast	2 × 1000		90%
	Sat	Fast	3 × 1000		90%
	Sun	Off			
Week 6	Mon, Wed	Jog	10000	19.0	
	Tue, Thu, Sat	Fast	3 × 1000		90%
	Fri	V_{HRmax}	4000	37.5	
	Sun	Off			
Week 7	Mon, Wed, Fri	Jog	10000	19.0	
	Tue, Thu, Sat	Fast	3 × 1000		90%
	Sun	Off			
Week 8	Mon, Wed	Jog	10000	19.0	
	Tue, Thu, Sat	Fast	3 × 1000		90%
	Fri	V_{HRmax}	4000	37.5	
	Sun	Off			
Racing					
Week 9	Mon, Wed, Fri	Jog	6–10000	19.0	
	Tue, Thu	Fast	1 × 1600		90%
	Sat	Fast	1 × 1600		first 1200 at 90% last 400 at 110%
	Sun	Off			
Week 10	Mon, Wed	Jog	6–10000	19.0	
	Tue	Fast	1 × 1600		90%
		Fast	1 × 1600		first 1200 at 90% last 400 at 110%
	Thu	Fast	1 × 1600		90%
		Fast	1 × 1200		90%
		Fast	1 × 400		110%
	Fri	V_{HRmax}	4000	37.5	
	Sat	Fast	1 × 1600		90%
		Fast	1 × 1600		800 at 90% next 400 at 110% last 400 in 30 s
	Sun	Off			

V_{HRmax} is an exercise test that uses four bouts of 1000 m at increasingly higher speeds to calculate the velocity at which the horse's heart rate reaches maximum. Overall the horse covers 4000 m during this exercise test, at an average speed of 37.5 km/h. Intensity is given as a percentage of the velocity reached at heart rate maximum during the V_{HRmax} test. Prior to all fast work sessions and exercise tests, horses should be given a warm-up consisting of a jog for 3000 m at a speed of 19 km/h.

weeks or so. Basically, the test uses heart-rate measurements during a series of 1000 m trials at specific speeds to calculate the velocity at which the horse's heart rate reaches maximum. As the horse becomes fitter the speed at which it can travel at maximum heart rate increases, thereby allowing the adequate planning of appropriate training intensities. However, most trainers do not have access to heart-rate monitors and therefore plan their training intensity around distance and time.

As the two training programs demonstrate, there is an increase in intensity of fast work approaching the final preparation and racing phases and a slight reduction in fast work volume. The higher training intensities during these phases are designed to stress the horses in a way that is similar to the actual race. Neither training program actually asks the horses to complete time trials or to train at race pace for any length of time.

Interval and tapered training programs

A relatively new type of training that attempts to improve performance by introducing training that is close to or even above race pace is interval training. Interval training for the race horse has been discussed by Tom Ivers in his book *The Fit Racehorse*.[20] In his book, Ivers outlines the general concept and proposed benefits of interval training and gives examples of structured interval training sessions.

Interval training involves bouts of exercise alternated with periods of relief (or rest) and has been shown to be an effective way to train the appropriate energy systems in human and equine athletes.[21,22] Interval training decreases fatigue and allows for a greater amount of high-intensity work to be performed than if work was carried out in one continuous stretch. For example, suppose you exercised your horse continuously as hard as you could for 3 min, then on another occasion suppose you ran the horse intermittently, exercising the horse just as hard as you did continuously, but for only 30 s at a time with 2 min of rest between each run. If you repeat this six times you would have completed the same amount of work but the degree of fatigue following the intermittent or interval exercise would be considerably less. After the continuous exercise the horse would be extremely fatigued and tired compared with the horse after the interval training session. Essentially, with interval training the recov-

Table 50.3 Sample interval training programme for Standardbred horses[23]

Aim: Able to pace 1600 m in 1:57 (1000-m track).
Required base: At least 400 km in previous 84 days.
Frequency: Every 4 days.
Rest-period criteria: Heart rate 110 or less within 5 min of completing the interval.
Interval criteria: If time greater than 1.5 s outside scheduled time, session halted. Only proceed to next step if all criteria for previous level have been met.

Training level	Distance (m)	Repetitions (number of heats)	Work interval time (min:s)	Rest interval time (min:s)
1	600	2	0:56	5:00
2	800	2	1:15	5:00
3	1000	2	1:35	5:00
4	600	3	0:53	5:00
5	800	3	1:10	5:00
6	1000	3	1:28	5:00
7	1200	2	1:45	5:00
8	600	4	0:50	5:00
9	800	4	1:07	5:00
10	1000	4	1:25	5:00
11	1200	3	1:42	5:00
12	800	4	1:05	5:00
13	1000	4	1:23	5:00
14	1200	3	1:40	5:00
15	800	4	1:03	5:00
16	1000	4	1:20	5:00
17	1200	3	1:38	5:00
18	800	3	1:00	5:00
19	600	4	0:44	5:00
20	1000	2	1:18	5:00
21	800	2	0:58	5:00
22	600	3	0:42	5:00
23	1000	1	1:15	5:00
24	800	2	0:57	5:00
25	600	2	0:41	5:00

ery period allows for replenishment of stored energy in the muscles, removal of lactic acid, and recovery from the exercise bout. Therefore the horse is less fatigued when it starts its next bout of exercise, and the quality of training is better than if the horse completed the exercise continuously.

Normally, in training for middle- to long-distance events, the exercise intensity is set around the anaerobic threshold to improve aerobic capacity without producing too much lactic acid and consequently fatigue. However, trainers should also think about training at intensities over the anaerobic threshold to help train the anaerobic energy system that is also required during a race. Shorter, very-high-intensity sprint intervals might also help at improving speed.

When constructing an interval training program the following terms are used:

- *Work interval*: the length of time the horse is exercising (sometimes expressed as the distance covered, e.g. 1000 m).
- *Rest or Relief interval*: the time between work intervals in a set. The relief interval can consist of light activity such as walking or mild to moderate exercise such as jogging.
- *Repetition*: the number of work intervals per set.
- *Sets*: A group of work and relief intervals.

An example of an interval training program can be seen in Table 50.3. In this program the recovery time has been set randomly at 5 min, during which time the horse walks. As can be seen from the table, the trainer who developed this program considers that the interval training should occur only every 4 days.[23] Most interval training programs allow more days between interval exercise bouts to allow for full recovery from the much higher stresses involved. Horses would normally be given slow work between the interval training days. Because of the high stresses involved, interval training is not recommended until a sound fitness base has been established.

Some trainers prefer to use heart-rate measurements when programming exercise intensity for interval training, rather than strict performance times that can be influenced by track and weather conditions. If using the heart-rate monitor the aim at the start of interval training would be to get the horses' heart rate up to about 180–200 bpm (approximately anaerobic threshold). With a gradual increase in fitness this target can be progressively increased to a heart rate of about 200 bpm or more. In most cases, however, trainers will use the heart-rate monitor to judge the recovery ability of the horses. A target of about 110–120 bpm after 5 min recovery indicates that the horse has recovered sufficiently to continue with the next bout of exercise. If the heart rate exceeds what is expected or takes much longer to recover than normal, it might be an indication that the previous exercise bout was too stressful and further work bouts should be abandoned. Unexpected high heart rates during training and recovery have also been suggested to be an early warning sign of physiological stress, possibly indicating low-grade lameness or musculoskeletal injury.[24,25]

Whereas the proposed benefits of interval training include the intense metabolic demands it produces, as well as the specific neuromuscular and fiber-type activation that is needed during a race, disadvantages include the time-consuming nature of the training compared to conventional training, and an increased risk of injury. In a recent study, interval training was used in an attempt to increase time trial performance in a number of Standardbred race horses over a prolonged period of time.[26] Horses were given a series of 2-weekly taper training programs. The taper is a training technique used in human athletes to optimize performance

Table 50.4 Two-week training cycles for the conventional and taper groups. Numbers in parentheses are training pace as a percentage of pace over the last 1200 m of the most recent 2400 m time trial[26]

Day	Conventional training	Taper 1	Taper 2	Taper 3
1	Rest	Jog 50 min (40%)	Fast 2400 m (89%)	Fast 3000 m (92%)
2	Jog 40 min (40%)	Fast 3000 m (90%)	Jog 50 min (50%)	Jog 50 min (50%)
3	Fast 2400 m (86%)	Jog 50 min (40%)	Fast 2400 m (89%)	Fast 3000 m (92%)
4	Jog 40 min (40%)	Fast 3000 m (90%)	Jog 50 min (60%)	Jog 50 min (50%)
5	Fast 2400 m (86%)	Jog 50 min (40%)	Fast 2400 m (89%)	Fast 3800 m (90%)
6	Jog 40 min (40%)	Fast 3800 m (90%)	Jog 50 min (60%)	Jog 40 min (50%)
7	Fast 3200 m (86%)	Jog 40 min (40%)	5 × 800 m intervals (100%)	Fast 1800 m (94%)
8	Jog 40 min (40%)	Rest	4 × 800 m intervals (100%)	Jog 30 min (50%)
9	Rest	Fast 1800 m (95%)	3 × 800 m intervals (100%)	Fast 1200 m (100%)
10	Fast 2400 m (86%)	Jog 30 min (40%)	2 × 800 m intervals (100%)	Jog 20 min (50%)
11	Jog 40 min (40%)	Fast 1200 m (100%)	1 × 800 m intervals (100%)	Fast 1200 m (100%)
12	Fast 2400 m (86%)	Jog 20 min (40%)	Walk	Walk
13	Jog 40 min (40%)	Walk	Walk	Walk
14	Time trial	Time trial	Time trial	Time trial

All fast work was completed with the horses harnessed up into their hobbles. Horses were only introduced to the above training programs after 8 weeks of foundation training. As an example of intensity the jog at 40% time trial pace was approximately 19 km/h. The relief period between interval repetitions was set at 5 min, during which the horses walked.

by allowing adequate recovery from hard training prior to competition. During the second week of one of the taper programs (see taper 2 in Table 50.4) the researchers used a series of progressively shorter intervals to reduce duration but maintain adequate training intensity. They found a significant improvement in the horse's speed during the taper programs (particularly taper 1), compared to the conventional training, however, there was also an increase in the number of injuries reported in the taper group using the interval training. Also note that the high-intensity interval training days during taper 2 were not separated by recovery or rest days, possibly leading to inadequate recovery, which might have caused the injury problems.

The main objective of any training program is to enhance performance while keeping the animal free from injury and disease. During training, stress in the form of exercise initiates changes within the horse's structural and biochemical make-up. These exercise-induced changes cause adaptation and improved performance if sufficient recovery is allowed. On the other hand, excessive stress due to inappropriate training or insufficient recovery produces maladaptation and poor performance.

Overtraining

A recent study on Standardbred maiden pacers found some useful indicators of overtraining, which might help trainers detect and possibly prevent overtraining.[27] One of the major indicators of overtraining was a drop in bodyweight. The body condition of the horses declined and they lost weight. In addition, heart rate during exercise was elevated in the overtrained horses. In other words, the horses had to work harder to maintain speed during pace work. The increased stress was highlighted further when blood tests after exercise revealed a significant increase in lactate levels. Blood lactate is a normal byproduct from the breakdown of sugar by muscle cells, so an increase during overtraining suggests more muscular work was required by the overtrained horses to maintain speed.

During conventional training, horses are usually able to consume an appropriate amount of food to fuel the energy requirements needed. Horses that become overtrained might lack sufficient carbohydrates to meet the demands of their excessive training. Possible reasons include an inadequate diet, decreased hunger drive, or a problem within the muscle cells themselves. As a result, there is a depletion of carbohydrate stores and weight loss. Ordinarily, when the body's stores of carbohydrates decrease below normal, more can be formed by the breakdown of protein and fat, which requires the hormone cortisol. During overtraining, however, something goes wrong with the hormonal control system, resulting in a decreased magnitude of the cortisol response to exercise. Consequently, a further reduction in the availability of fuel to the working muscle cells can occur, resulting in force loss and poor performance.

Signs of overtraining

Signs of overtraining include:

- Slower split times
- Unexplained drop in form
- A decrease in bodyweight ≥ 6 kg
- Horse might leave feed
- Decreased enthusiasm to train
- Horse might become moody and lethargic
- Increased heart rate during exercise and possibly slower recovery heart rate
- An increase in blood lactate concentration between 8 and 16% after pace and fast work.

Treatment and prevention

The recommended treatment for overtraining is usually a dramatic reduction in the volume, intensity or frequency of workouts or an increase in the time between workouts. Fast workouts should be dropped and only light jogging continued. If the horse doesn't show improvement within 2–3 weeks it should be spelled in the paddock and brought back up again after a few months rest.

The best treatment of all, however, is prevention. The challenge for trainers is to detect the subtle changes in the horse's response and attitude to training that might indicate too much training. After all, unlike a human athlete the horse cannot tell you about problems that arise during training. Training logs with details of training volume, intensity, and recovery should be kept, with regular changes in bodyweight, food intake and behavior noted. Of course, a major difficulty in measuring bodyweight is access to appropriate scales, however, regular weighing remains a cheap and easy way to monitor the effects of exercise training. Regular performance tests can also be helpful, for example timing horses over set distances. As both the sprinting and staying ability of the horse is affected by overtraining, these performance tests should include a measurement of all-out speed and overall speed. If the horse takes longer to complete the test and seems tired, this might be an indication that more recovery is required. If time and equipment allow, a measurement of heart rate and blood lactate during and after exercise would also be useful. Above all, trainers need to be able to judge when the results of the training program are being threatened by too much exercise.

Veterinary problems of Standardbreds

Respiratory abnormalities

Whereas gait and respiration are linked in a 1:1 fashion in cantering or galloping horses, respiration is not linked to gait in pacing or trotting horses.[28] However, abnormalities of the respiratory tract are an important cause of poor performance

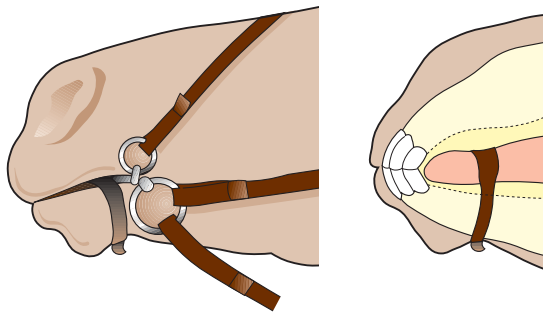

Fig. 50.14
Tongue-tie used to prevent horses from 'choking down' during racing. The tongue-tie should not interfere with the driving bit or overcheck bit. (Redrawn with permission from Haughton.[36])

or reduced racing frequency in Standardbreds. Standardbreds are afflicted with respiratory tract disease in the same way as other race horses, although their gait and associated tack makes problems such as dorsal displacement of the soft palate more problematic.

Upper airway abnormalities

Standardbreds in racing or training can develop a range of upper airway abnormalities including left laryngeal hemiplegia, dorsal displacement of the soft palate, and arytenoid chondritis. The characteristics of these diseases do not differ in any substantive way from those of other athletic horses, as discussed in Chapter 27. Dorsal displacement of the soft palate is a well-recognized syndrome in racing Standardbreds. Its apparent high prevalence in this breed is perhaps related to their tendency to 'choke down' or excessively ventroflex the head during exercise. Treatments for intermittent dorsal displacement of the soft palate include application of a tongue-tie (Fig. 50.14), use of overcheck rein and bit, and surgical manipulation of the pharynx and associated musculature.

Exercise-induced pulmonary hemorrhage (EIPH) occurs in Standardbreds, as in other athletic horses that compete at high speed. The prevalence of EIPH in Standardbred race horses is assumed to be lower than in Thoroughbred race horses, with 26–34% of horses reported to have blood in the trachea after racing.[29,30] However, these studies were based on a single examination and one[29] reported as positive only those horses with blood covering more than one-half of the tracheobronchial tree. When examined after each of three races, 87% of Standardbred race horses have evidence of EIPH on at least one occasion,[31] suggesting that EIPH is as common in Standardbred race horses as it is in Thoroughbred race horses. Management of EIPH is discussed in Chapter 29.

Musculoskeletal disorders (adapted from Ref 32 with permission)

The racetrack practitioner caring for Standardbred horses frequently deals with problems and lameness requiring prompt diagnostic and therapeutic aid, which in most cases must be compatible with the season racing activity and current drug use regulations.[32]

Recognition of lameness

Lameness is the most important cause of poor racing performance in Standardbreds.[33,34] Lameness severity can range from moderate to severe, being visible at a walk or trot in hand, to subtle or mild lameness seen only at speed or while racing. A 1- to 2-s increase in the time for a mile, generally reflected in a slower last quarter-mile time, accompanies many lameness problems but might be confused with other problems such as respiratory abnormalities or recurrent exertional rhabdomyolysis. Bilateral lameness can cause a reduction in race performance without other localizing signs. Lameness is a major cause of horses making breaks (breaking stride) at high speed, although shoeing (particularly in trotters) and equipment considerations are also important contributing factors.

Horses on a line (the driver pulls harder on one line to keep a horse from bearing in or out) generally have ipsilateral lameness problems, although occasionally horses with medial foot or carpal lameness can be on the contralateral line. If on a line at all, horses with hindlimb lameness are usually on the ipsilateral line. For instance, those with left hind lameness are usually on the left line. Horses on a shaft (rear of horse closer to one shaft) generally have contralateral hindlimb lameness. Occasionally, a horse with forelimb lameness (and 'hard on the line') will be on the opposite shaft (horse with right front lameness will be on left shaft). This is usually because the driver is pulling the horse hard enough with the right line to cause it to bend its hind end to the left. These horses are often affected with lameness in more than one limb. Horses with forelimb lameness are generally worse on turns, although foot soreness and splints worsen as the mile progresses. Horses with hock lameness might be worse going into a turn or when coming out of a turn, whereas those with metatarsophalangeal joint (MTPJ) lameness will be worse around turns. Horses with left hind lameness might be able to trot or pace the turns, but those lame in the right hind will be worse in turns. Pacers with hindlimb lameness and a history of being worse when on the pace than when on the trot are usually affected with stifle lameness. Track size varies in Standardbred racing and horses that are lame in the turns are usually worse on smaller tracks. However, racing is generally slower on smaller tracks allowing lame horses, particularly those with soft-tissue injuries to compete successfully.

Breed and gait differences

There is considerable difference regarding lameness distribution and prognosis in Standardbreds as compared with Thoroughbred race horses. Gait difference between the breeds undoubtedly plays a role. The trot and pace are two-beat gaits, and there is more equal distribution of load (and lameness) between the forelimbs and hindlimbs. Fewer rota-

tional forces in certain joints of Standardbreds such as the carpus can reduce overload injury when compared with Thoroughbreds. Diseases such as suspensory disruption, catastrophic or incomplete fractures of the humerus, tibia, ilium, and third metacarpal/metatarsal, and bucked shins are much less common in Standardbreds. In general, Standardbreds have a better prognosis than Thoroughbreds for soft-tissue injuries such as suspensory desmitis and superficial digital flexor tendinitis. There appear to be differences in prognosis within the breed and, in general, prognosis in trotters is worse than in pacers. Lameness in pacers can be difficult to see, particularly in the forelimb. Pacers can usually tolerate lameness better than trotters with the exception of some hindlimb problems such as stifle lameness.

Because many Standardbred lamenesses are subtle, there is no substitute for evaluation of these horses at the track when jogging or training. It can be useful to sit behind the horse, particularly when evaluating subtle hindlimb lameness. Treadmill examination is useful in providing a consistent surface and speed for lameness evaluation but does not simulate turning or pulling weight. Unfortunately, lameness examinations cannot always be performed under ideal situations, and horses are commonly evaluated at a walk and trot in hand. Standardbreds evaluated at slow speed might not exhibit the same lameness as they do at high speed. Problems such as splints and foot soreness might surface only after training or racing, and examination at rest might be nondiagnostic. Care must be taken not to overinterpret subtle hindlimb lameness at a trot in hand. However, careful lameness examination can be useful, even in horses with subtle problems.

Lameness of the forelimb is slightly more common than that of the hindlimb, but there is a near equal distribution between hindlimb and forelimb lameness. Articular and periarticular injuries account for the majority of lameness seen in Standardbreds, whereas long-bone abnormalities are less common. The carpus is the most common articular injury and is likely the most common source of lameness overall. The MTPJ is very important in hindlimb lameness, in fact nearly equal to that of the hock, and has been underemphasized.

Forelimb lameness

Front limb lameness in the racing Standardbred can range from readily apparent lameness to subtle disturbances of gait. There are conditions in which the acute lameness requires immediate radiographic examination to rule out frequent injuries, including sagittal fractures of the proximal PI, proximal sesamoid fractures, pedal bone fractures, and, less frequently, injuries of the proximal metacarpal region. However, more commonly the complaint is a subtle to mild lameness, which can be complicated by problems affecting the hind limb. In such cases the clinician must investigate the horse's history, including the gait, shoeing, recent performance, previous lameness, when the horse becomes lame (after the race, the next day), factors that exacerbate the lameness (e.g. training clockwise or counterclockwise, on turns or on the straight, at the beginning or at the end of the race), wrong postures (horse on a line, on a shaft), and efficacy of previous treatments.

Foot The first step in diagnosis of lameness is a careful examination of the horse's conformation, especially foot conformation (club foot, toed-in, toed-out, hoof wall angle, lateral–medial balance, asymmetrical feet) and the presence of joint effusion, which is easily appreciated when affecting the fetlock and midcarpal joints. Joint distension is less obvious in the dorsal compartment of the coffin joint. The metacarpal region is frequently a site of visible abnormalities; enlargement of the body or branches of the suspensory ligament, bowed tendon, and constriction of the palmar annular ligament represent common findings.

Palpation detects areas of abnormal warmth and pain and allows evaluation of joint angles. The feet may have asymmetric warmth, increased digital pulse, and different responses to hoof testing. When possible, feet are first tested without removing the shoes, and ideally the horse should be kept shod until any examination of gait is completed. Lateral and medial quarters, lateral and medial middle sole, and lateral and medial toe are tested. Compressing the frog rarely brings useful information and squeezing the quarters might cause pain unrelated to primary lameness. The medial quarter is usually more sensitive and this finding must not be overinterpreted. Hoof or foot pain is a common occurrence, although it is often subtle.

Shoeing represents a source of useful information and should be discussed with the trainer to better understand the gait characteristics. For horses with a flat sole, overzealous padding can add to, rather than relieve, pressure on the sole. Wide-web shoes with leather or rubber padding are useful in cases of pain originating from the distal interphalangeal (DIP) joint. Bar shoes are now less commonly used and may exacerbate coffin and fetlock joint problems, by limiting the natural slipping of the landing foot.

Corrective shoeing provides a solution for problems located in the hoof. This pain must be distinguished from problems related to osteoarthritis (OA) of the DIP joint. In this case, flexion of the distal limb frequently elicits pain. The final diagnosis of OA of the DIP is the result of different investigations including history (the horse frequently gets worse at the end of the race and is on a line), conformation (foot smaller than the contralateral club foot), palpation (some pain may be elicited by deep palpation of the dorsal joint capsule, the dorsal wall and/or heels are warmer), diagnostic analgesia (being aware that this problem is not always resolved by intra-articular anesthesia and that the latter may abolish pain originating from the navicular area and from the sole), and exclusion of other sites of pain in the distal limb, especially the fetlock.

Pastern and fetlock The radiographic examination may reveal a prominent osteophyte on the distal aspect of the middle phalanx associated with a variable degree of remodeling of the proximal aspect of the distal phalanx. OA of the DIP joint is frequently bilateral.

The metacarpophalangeal joint is frequently involved in front limb lameness. Survey radiographs may detect dorsoproximal fragmentation of the proximal phalanx and osteochondrosis of the proximal sagittal ridge on the dorsodistal metacarpus. These lesions are frequently diagnosed in yearlings and treated by arthroscopic surgery.

Acute synovitis of the metacarpophalangeal joint is observed in young horses when the training is intensified, especially on hard tracks. The horse appears moderately lame and sensitive to deep palpation of the dorsal joint capsule and to flexion test. Intra-articular anesthesia is usually diagnostic. In older horses, chronic thickening of the dorsal synovial pad (villonodular synovitis) is suspected when the latero-medial radiographic view shows flattening or osteolysis of the proximal aspect of the dorsal sagittal ridge and contrast radiography evidences a filling defect corresponding to the soft tissue mass. Ultrasonography may be used to measure the thickness of the synovial pad.

The palmar aspect of the front limb fetlocks in Standardbreds is characterized by problems affecting the proximal sesamoid bones and adjacent soft tissues. Sesamoiditis in young horses has the typical radiographic feature of radiolucent lines in the palmar abaxial aspect of the bone. Scintigraphic findings are indicative of increased bone metabolism, but radiographic changes are seen in only 50% of Standardbreds with increased radioisotope uptake. In older horses, the radiographic changes include radiolucent lines in the proximal one-half of the bone, irregular palmar/abaxial radiographic outline, enthesophytes, and mineralization of the intersesamoidean ligament. When affecting the base of the sesamoid bone, the presence of enthesophytes is more properly considered distal sesamoidean desmitis.

Desmitis and tendinitis The insertion of the suspensory branch on the proximal sesamoid bone becomes irregular and ultrasonography provides the most accurate diagnostic tool. Suspensory branch desmitis is frequently associated with sesamoiditis. It may be caused by lateral-to-medial hoof imbalance, training over uneven track surfaces, strains, and fractures of the splint bone(s). Acute desmitis may be associated with metacarpophalangeal joint effusion. Ultrasonography is performed to assess the degree of ligament damage with enlargement and loss of definition of the margins of the branch, focal hypoechoic areas, diffuse loss of echogenicity, and hyperechoic foci in horses with chronic desmitis being the most frequent findings. The corresponding splint bone may deviate abaxially, and radiographic monitoring may allow early diagnosis of secondary distal splint bone fracture.

Desmitis of the proximal insertion of the suspensory ligament is commonly diagnosed and carries a better prognosis than desmitis affecting the body or branches of the ligament. When the proximal aspect of the suspensory ligament is affected, the clinician must differentiate pain originating from the carpal joint and perform a local block (subcarpal block, axially to the origin of the splint bones, or direct infiltration over the proximal suspensory ligament). In cases of positive block, ultrasonography is used to assess damage to the suspensory ligament and bone remodeling of the palmar proximal metacarpus; a dorsopalmar radiographic view is used to assess the presence of palmar sclerosis of the third metacarpal (MCIII) in chronic cases.

Superficial digital flexor tendinitis represents a frequent indication for ultrasonographic examination of the distal limb of Standardbred race horses. Most of the lesions are located in the middle and distal third of the tendon. A core lesion located in the palmarolateral border of the tendon characterizes over 30% of the lesions. Central core lesions are uncommon. Chronic recurrent lesions have the typical pattern of diffuse tendinitis. When the lesion affects the distal aspect of the tendon, the digital tendon sheath may be distended, and the typical notch of palmar annular ligament constriction is visible in the palmar outline.

Carpus With the exception of foals and yearlings, lesions are rarely located on the proximal front limb of Standardbreds, and nearly invariably lesions affecting the elbow and shoulder regions are the result of direct trauma.

The midcarpal joint represents a predilection site of lameness in race horses, especially young Standardbreds and Thoroughbreds. Typically, horses affected by midcarpal joint pain tend to trot with a wide-based gait, abducting the affected leg or legs in an attempt to minimize carpal flexion. Visual inspection reveals various degrees of joint effusion, especially on the dorsomedial aspect of the carpus. Palpation may elicit pain over the dorsal aspect of the carpus. The flexion test is positive and intra-articular analgesia abolishes the lameness in the majority of horses. A negative result from intra-articular analgesia does not necessarily exclude pain in this joint because subchondral bone damage under a relatively normal cartilage may cause pain that is difficult to abolish with intra-articular analgesia.

Radiographic examination includes six basic views and a variable number of extra views: dorsopalmar (DP), flexed lateral–medial (LM), dorsolateral to palmaromedial oblique (DLPMO), dorsomedial to plamarolateral oblique (DMPLO), and 33° and 55° skyline views (dorsoproximal–palmarodistal skyline). The latter two views must be of excellent quality because it has been shown that a large number of injuries (especially affecting the third carpal bone) can be diagnosed only on the skyline view.

Treatment depends on the type and degree of injury. Young racing horses without radiographically visible abnormalities (a more sensitive diagnostic tool is represented by scintigraphy, which may reveal increased radionuclide uptake in the early phase of the disease) are best rested and treated with non-steroidal anti-inflammatory drugs, especially polysulfated glycosaminoglycans. Training modulation allows in most of the cases time for bone remodeling and prevents the progress of bone injuries.

When chip fractures are diagnosed, arthroscopic surgery represents the best option and carries a fair to good prognosis. In cases of third carpal bone slab fractures, internal fixation via arthroscopy is the preferred technique and offers good results.

More subtle cases, characterized by mild radiographic changes, may be good candidates for diagnostic arthroscopy. Irregular areas of radiolucency on the radial fossa of the third carpal bone and loss of density on the dorsal distal medial aspect of the radial carpal bone are suggestive of more serious injuries and may be indicative of incomplete fractures. Arthroscopic curettage of the main lesion, frequently associated with curettage of the corresponding 'kissing' lesion on the opposite articular surface, carries a better prognosis than conservative management in selected cases.

Arthroscopic findings in horses with lameness located in the midcarpal joint but no radiographic findings include sinking and discoloration of articular cartilage, loss of articular cartilage in focal areas of the third and radial carpal bone, and rupture of the medial palmar intercarpal ligament. The devitalized cartilage is debrided and the underlying bone may be foraged using micropick technique, which augments cartilage repair. Rupture of the medial palmar intercarpal ligament is less common, and the treatment involves arthroscopic trimming and 4 to 6 weeks rest followed by 4 to 6 weeks of walking exercise. The same postoperative protocol is used for routine arthroscopic surgery, whereas internal fixation of C3 slab fractures is followed by 8 weeks of rest, radiographic control, and 4 weeks of walking exercise. There is usually no need for removal of the screw.

Hindlimb lameness

Careful palpation of all anatomic structures, including static flexion and extension of all joints, should be performed. Frequently overlooked sites of inflammation (in both the forelimb and hindlimb) include the dorsal aspect of the proximal phalanx (P-I, [incomplete midsagittal or dorsal frontal fractures]), proximal sesamoid bones (sesamoiditis, fractures, avulsion injury associated with the suspensory attachment), and carpus and proximal aspect of third metacarpal (MCIII) (avulsion or longitudinal fractures of MCIII, proximal suspensory desmitis, dorsomedial articular fracture, incomplete C-3 chip fractures), proximal plantar third metatarsal (MTIII) region (proximal and midbody suspensory desmitis, pain along medial and lateral splint bones associated with hock lameness), and the MTPJ. In the hindlimb, it is easy to overlook subtle swelling of the suspensory origin and body, because these portions of the ligament are buried beneath the second and fourth metatarsal bones. Hoof tester examination should be performed in all horses because foot soreness is common. Foot soreness is less common in the hindlimb than in the forelimb, but does occur, as do OA of the DIP joint and navicular disease or fracture (rare). Secondary back, gluteal, and trochanteric pain are common and treatment of these areas is often recommended along with therapy of concomitant hindlimb lameness. Back pain in Standardbreds is usually the result of muscle pain, rather than impingement or overriding of dorsal spinous processes. Scintigraphic evaluation has failed to identify a single Standardbred race horse with increased radioisotope uptake involving the dorsal spinous processes, whereas this scintigraphic abnormality is common in horses that are ridden.

Intra-articular and perineural analgesia is important in the diagnosis of Standardbred hindlimb lameness and many times is most reliably done at the track where horses can be moved and evaluated at speed. Care must be taken when incomplete fractures are suspected, particularly of the first phalanx (P-I) because comminution can occur. When performing the plantar digital block, the clinician must keep in mind that pain associated with proximal P-I can be abolished. In these horses, the clinician inadvertently diagnoses a problem in the foot, when in reality the true source of pain is a midsagittal fracture of P-I. Because of the large number of Standardbreds with MTPJ lameness, basisesamoid or abaxial sesamoid nerve blocks are not useful. With these blocks, proximal diffusion of anesthetic occurs so frequently that misdiagnosis is common. I usually perform a plantar digital block, followed by a dorsal ring block, to desensitize the dorsal aspect of the foot. A low plantar perineural block is then performed. This technique is more successful in abolishing subchondral bone pain in the MTPJ than is the intra-articular technique, but all four nerves must be blocked (medial and lateral plantar nerve and medial and lateral plantar metatarsal nerves). Horses with incomplete fractures of MTIII, P-I, or the proximal sesamoid bones or those with non-adaptive remodeling may fail to respond or only partially improve with intra-articular analgesia but become completely sound with the low plantar block. A selective lateral plantar metatarsal block can be performed to identify those horses with stress reaction or non-adaptive remodeling of the distal aspect of MTIII. High plantar analgesia is often overlooked but is critical in the diagnosis of proximal suspensory desmitis or other avulsion injury associated with MTIII. Although all three compartments of the stifle joint should be independently blocked in horses suspected of lameness in this region, the medial femorotibial joint is most frequently affected.

Diagnostic imaging The importance of well-positioned and exposed radiographs cannot be overemphasized. Radiographic views that are extremely important in the Standardbred include:

- Foot: horizontal oblique views to evaluate the subchondral bone of the distal phalanx (P-III) for radiolucent areas or incomplete fractures.
- Tarsus: dorsomedial plantarolateral oblique view (shows most common sites for radiographic changes associated with osteochondritis dissecans, distal tarsitis, and T3 and MTIII fractures).
- MTPJ: down-angled oblique views to open up the space between P-I and the sesamoids; follow-up and down-angled DP views to rule out midsagittal P-I fractures.
- Stifle: caudocranial view to evaluate femorotibial joint space (particularly medial) and condylar lesions.

Ultrasonographic examination of soft tissues in the metatarsal region is important, particularly of the proximal suspensory region. A frequently overlooked region is the proximal plantar metatarsus. Bone scintigraphy is important in the identification of abnormal subchondral bone uptake, particularly of the foot, carpus, tarsus, and MTPJ. Standardbreds appear to be predisposed to abnormal impact loading or stress (non-adaptive) remodeling of subchondral bone.

Stifle lameness has been overemphasized. Specific hindlimb lameness is described as follows.

The hind digits The hind foot is much less commonly the cause of lameness than is the front foot but is still the source of pain in many Standardbreds. Foot abscessation, quarter cracks, hoof avulsion, distal interphalangeal osteoarthritis, P-III fractures, and chronic 'foot soreness' from poor shoeing and balance occur. P-III fractures most commonly involve the

left hind lateral and right hind medial wings of P-III, but this distribution is not as clear cut as in the forelimb. It is critical to separate pain originating from the foot from that of the MTPJ and results of diagnostic analgesia need to be interpreted carefully. Anesthetic diffusion occurs when the posterior digital block is performed, and it is relatively common to desensitize structures in the pastern and MTPJ using this block. The most common diagnoses in horses in which inadvertent analgesia of the MTPJ occurs using posterior digital anesthesia is midsagittal fracture of the proximal phalanx.

Interference is a common problem in trotters. trotters that hike behind and have what appears to be unilateral hindlimb lameness can be lame in the ipsilateral forelimb. Foot or carpal lameness can cause shortening of the ipsilateral forelimb, causing interference and what appears to be ipsilateral hindlimb lameness. Superficial skin soreness or frank osteitis can result from interference, and trotters frequently 'make breaks' as the result of the problem. Corrective shoeing and the elimination of the primary source of pain are important.

Metatarsophalangeal joint Lameness of the MTPJ region has been substantially underestimated in the past. The MTPJ is an extremely important source of hindlimb lameness and, in fact, many horses suspected of having tarsal or stifle pain will 'block out' with low plantar or intra-articular analgesia, if the techniques are routinely performed. One of the most common lameness conditions of the Standardbred race horse is subchondral bone pain of the distal, plantarolateral aspect of MTIII. This is a form of stress or non-adaptive remodeling of MTIII, an early form of OA, which is characterized by lameness most consistently abolished by low-plantar (or selective lateral plantar metatarsal) analgesia. Horses tend to have a 'stabby' hindlimb gait, will likely be on the contralateral shaft, be worse in the turns, and are often misdiagnosed as having tarsal pain. Intra-articular medication is usually ineffective and obvious signs of OA such as effusion, a positive response to flexion, or other abnormalities found on palpation are usually absent. Radiographs are initially negative or equivocal, and the diagnosis is made with scintigraphy. Bone phase scintigraphic images reveal focal radiopharmaceutical uptake of distal, plantarolateral aspect of MTIII. A continuum of stress-related subchondral bone changes results in non-adaptive remodeling, sclerosis, and later areas of necrotic subchondral bone. In older horses, radiographic evidence of subchondral bone injury is seen, but in 2- and early 3-year-olds, radiographic examination may be negative. Because this lesion is a result of a continuum of stress-related subchondral bone damage, management includes a reduction in stress. Modification in exercise intensity, corrective shoeing, swimming physiotherapy, and shock wave therapy have been used, but long-term rest may be best. Intra-articular medication, including corticosteroids, is not effective early in the disease process, presumably because pain originates from subchondral bone, and overlying cartilage damage is minimal. Later, when cartilage damage worsens and subchondral bone collapse occurs (radiolucent changes develop radiographically), injections decrease inflammation and lameness.

A common problem in Standardbreds is plantar process fragmentation of the proximal phalanx. Articular fragments, most commonly involving the medial aspect (can be biaxial and bilateral), can cause high-speed lameness and perhaps contribute to the development of OA in older horses. Currently, I recommend these fragments be removed arthroscopically, preferably before the horse enters training. Large, abaxial, non-articular fragments can also cause lameness, but conventional surgical techniques are necessary for removal.

Fractures involving the MTPJ are more common in pacers than in trotters, with the exception of fractures of the proximal sesamoid bones. Midsagittal P-I fractures are more common in the hindlimb than in the forelimb and can be difficult to diagnose. Pain from this fracture is often thought to originate from the foot because posterior digital analgesia abolishes lameness in some horses. Surgical fixation is recommended in horses with long or displaced fractures, but conservative management is successful in horses with short, midsagittal fractures. Dorsal frontal fractures of P-I occur in pacers and in trotters, are more common in the RH, can be bilateral, and heal with conservative management. Fractures of MTIII condyles occur but are less common than in Thoroughbreds and are unusual in the trotter. Medial condylar fractures tend to spiral proximally, and horses are at risk for catastrophic injury either before surgical fixation or during anesthetic recovery. Lateral apical sesamoid fractures occur commonly. Lateral sesamoiditis causes lameness in 2-year-olds trained in 2:15 to 2:18 for the mile, and prognosis is poor if substantial radiolucency exits.

Metatarsal region The most common and important condition of the metatarsal region is suspensory desmitis. This is often a career limiting or ending injury, particularly in the trotter. Proximal suspensory desmitis, avulsion fracture, or stress reaction/enthesopathy occur but can be difficult to diagnose, and high plantar analgesia is a must to differentiate pain from this areas from that of the MTPJ or tarsus.

Tarsus Distal tarsitis remains the most common lameness of the tarsus. The disease involves OA of the DIT and TMT joints, but there is a significant periarticular soft-tissue component, likely caused by sliding or shear forces, and radiographs are often negative. Osteochondritis dissecans of the tarsocrural joint is the most common surgical condition of the tarsus, is likely hereditary in the breed, and causes effusion and high-speed lameness. Surgical removal of fragments is recommended in horses with clinical signs or those sold at public auction. Tarsocrural arthropathy, an insidious disease resulting in eventual severe lameness and widespread cartilage damage, is seen in older horses. Curb, a common soft-tissue lameness, is frequently tendinitis of the superficial digital flexor tendon rather than long plantar desmitis. Third and central tarsal bone slab fractures, enthesopathy at the attachment of the collateral ligament on the distal aspect of the calcaneus, occur occasionally.

Stifle Stifle lameness has been overemphasized but is still important. The most common condition is OA of the medial femorotibial joint. This condition is difficult to diagnose radiographically because early on, the only sign is narrowing of the joint space seen on the caudocranial view. Effusion of the

medial femorotibial joint is usually present but may be a subtle clinical finding. Intra-articular injections and corrective shoeing (aluminum shoe with a toe grab) usually help. Trotters appear able to race more successfully than do pacers with this problem. Osteochondritis dissecans and osseous cyst-like lesions occur and cause lameness.

References

1. Mason I. A world dictionary of livestock breeds, types and varieties. Wallingford, UK: CAB International; 1996:116.
2. Greene C. Perspectives on bloodlines and breeding. In: Hoffman D, ed. The new care and breeding of the trotter and pacer. Columbus, OH: United States Trotting Association; 1996:12–79.
3. Physick-Sheard P. Career profile of Canadian Standardbred. I. Influence of age, gait, and sex upon chances of racing. Can J Vet Res 1986; 50:449–456.
4. Cothran E, MacCluer J, Weitkamp L, Bailey E. Genetic differentiation associated with gait within American Standardbred horses. Animal Genetics 1987; 18:285–296.
5. Bjornstad G, Roed K. Breed demarcation and potential for breed allocation of horses assessed by microsatellite markers. Animal Genetics 2001; 32:59–65.
6. Arnason T. Trends and asymptotic limits for racing speed in Standardbred trotters. Livestock Prod Sci 2001; 72:135–145.
7. Tolley E, Notter D, Marlowe T. Heritability and repeatability of speed for 2- and 3-year-old Standardbred race horses. J Anim Sci 1983; 56:1294–1305.
8. Hintz R. Genetics of performance in the horse. J Anim Sci 1980; 51:582–589.
9. Physick-Sheard P. Career profile of the Canadian Standardbred II. Influence of age, gait and sex upon number of races, money won and race times. Can J Vet Res 1986; 50:457–470.
10. Darish S, Collier M. Standardbred equipment – part 1. Mod Vet Pract 1985; 66:370–376.
11. Collier M, Darish S. Standardbred equipment – part 2. Mod Vet Pract 1985; 67:485–489.
12. Pawlak J. Trotting and pacing guide. Columbus, OH: United States Trotting Association; 2003:83.
13. Miscellaneous statistics. Australian Harness Racing Annual 2001. Melbourne: Australian Harness Racing Council; 2002:163.
14. Forssberg P. Swedish Trotting Association, Stockholm. Personal communication, 2003.
15. Minkema D. Genetic studies on performance in Dutch trotters. Proc Int Symp Genet Horse Breeding 1975:24–32.
16. Eaton MD. Energetics and performance. In: Hodgson DR, Rose RJ, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994:49–61.
17. Hinchcliff KW, Lauderdale MA, Dutson J, et al. High intensity exercise conditioning increases accumulated oxygen deficit of horses. Equine Vet J 2002; 34:9–16.
18. Sherman JP, Hopkins WG. Training of Standardbred maiden pacers. J Equine Vet Sci 1995; 16:116–119.
19. Lovell D. Training Standardbred trotters and pacers. In: Hodgson D, Rose R, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994:399–408.
20. Ivers T. The fit race horse. Cincinnati, OH: Esprit Racing Team Ltd, 1983.
21. Laursen PB, Jenkins DG. The scientific basis for high-intensity interval training: optimising training programmes and maximising performance in highly trained endurance athletes. Sports Medicine 2002; 32:53–73.
22. Tyler CM, Golland LC, Evans DL, et al. Changes in fitness during prolonged training in Standardbred horses. Pferdeheilkunde 1996; 12:480–481.
23. Bayly WM. Training programs. Vet Clin Am Eq Pract 1985; 1:597–610.
24. Erickson BK, Erickson HH, Sexton WI, Coffman JR. Performance evaluation and detection of injury during exercise training in the quarter Horse using a heart rate computer. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications, 1987:92–101.
25. Hamlin MJ, Hopkins WG. Heart rate changes as a predictor of excessive training problems in Standardbred race horses, Australian Physiological & Pharmacological Society, Brisbane, 1998. Vol. 29.
26. Sherman JP, Hamlin MJ, Hopkins WG. Effect of tapered normal and interval training on performance of Standardbred pacers. Equine Vet J 2002; 34:395–399.
27. Hamlin MJ, Shearman JP, Hopkins WG. Changes in physiological parameters in overtrained Standardbred race horses. Equine Vet J 2002; 34:383–388.
28. Evans D, Silverman E, Hodgson D, et al. Gait and respiration in Standardbred horses when pacing and galloping. Res Vet Sci 1994; 57:233–239.
29. MacNamara B, Bauer S, Iafe J. Endoscopic evaluation of exercise-induced pulmonary hemorrhage and chronic obstructive pulmonary disease in association with poor performance in racing Standardbreds. J Am Vet Med Assoc 1990; 196:443–445.
30. Speirs VC. Pulmonary hemorrhage in Standardbred race horses. Aust Vet J 1982; 59:38–40.
31. Lapointe JM, Vrins A, McCarvill E. A survey of exercise-induced pulmonary haemorrhage in Quebec Standardbred race horses. Equine Vet J 1994; 26:482–485.
32. Torre F, Ross M. Lameness in the Standardbred horse. J Equine Vet Sci 2002; 22:429–436.
33. Magnusson L, Thafvelin B. Studies of the conformational and related traits of Standardbred trotters in Sweden. J Anim Breed Genet 1990; 107:135–148.
34. Dolvik N, Gaustad G. Estimation of the heritability of lameness in Standardbred trotters. Vet Rec 1996; 138:540–542.
35. Sylvester C. Training the trotter. In: Hoffman D, ed. The new care and training of the trotter and pacer. Columbus, OH: United States Trotting Association, 1996:239.
36. Haughton T. Choosing the right equipment. In: Hoffman D, ed. The new care and training of the trotter and pacer. Columbus, OH: United States Trotting Association, 1996.

CHAPTER 51

Veterinary aspects of competing and training three-day event and dressage horses

Jonathan H. Foreman

Definitions and background

Dressage is a test of obedience, balance, and suppleness. 'The object of Dressage is the harmonious development of the physique and ability of the horse. As a result it makes the horse calm, supple, loose and flexible but also confident, attentive and keen, thus achieving perfect understanding with his rider.'[1] The goal is that the horse 'gives the impression of doing of his own accord what is required of him. Confident and attentive, he submits generously to the control of his rider, remaining absolutely straight in any movement on a straight line and bending accordingly when moving on curved lines.'[1] Examples of horses performing dressage movements on the straight and curved lines are illustrated in Figs 51.1 and 51.2, respectively.

Basic gaits at the lower dressage levels are walk, trot, and canter. The international standard requires that:

> His walk is regular, free and unconstrained. His trot is free, supple, regular, sustained and active. His canter is united, light and cadenced. His quarters are never inactive or sluggish. He responds to the slightest indication of the rider and thereby gives life and spirit to all the rest of his body.[1]

The basic gaits progress to more difficult movements at the upper levels such as extended trot or canter (Fig. 51.1), counter canter, passage, pirouette, and piaffe. Each horse and rider pair performs the same test in any given class or competition. One to five judges score each movement of the test and a composite score is calculated to determine the order of the final places. Movements are judged on 'freedom and regularity of the paces; the harmony, lightness and ease of movements; the lightness of the forehand and the engagement of the hind quarters, originating in a lively impulsion; the acceptance of the bridle, with submissiveness throughout and without any tenseness or resistance.'[1]

Internationally the sport is known as the Concours de Dressage International (CDI).[1] International dressage competitions are ranked by the Fédération Equestre Internationale (FEI) as increasing in difficulty from one (CDI*) through three-star (CDI***). The abbreviation CDIO designates an Official (Officiel) CDI to which national federations are invited to send selected representative teams and individuals, such as for the

Fig. 51.1
The 7-year-old American Thoroughbred gelding Might Tango, ridden by two-time World Champion Bruce Davidson, performing an extended canter during the Dressage Test at the 1978 World Three-Day Event Championships in Lexington, Kentucky. Note the hyperextension of the fetlocks (left fore and right hind) diagonal to the lead canter limb (right fore).

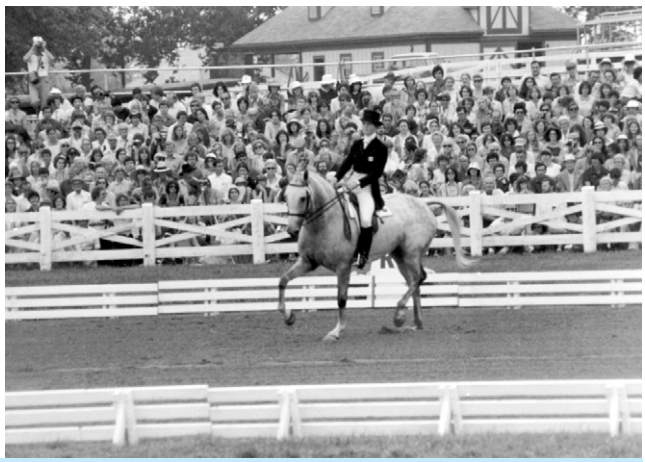

Fig. 51.2
The 14-year-old Canadian Thoroughbred mare Sumatra, ridden by team gold medallist Juliet Bishop, performing a trot circle during the Dressage Test at the 1978 World Three-Day Event Championships in Lexington, Kentucky. Note the degree of lateral bending (lateral back flexion) and impulsion necessary to trot correctly in a curving line, a movement which is required repeatedly in most dressage tests.

Fig. 51.3
The 13-year-old Thoroughbred Village Gossip, ridden by Charlie Micklem, jumping the airy Cirencester Rails over a ditch during the Cross-Country Test of the 1981 Badminton Three-Day Event. The height, spread, and lack of prominent ground lines illustrate the courage and scope required of horses jumping cross-country obstacles at the upper levels of three-day events.

Olympic Summer Games or World Equestrian Games.[2] Levels of increasing difficulty of FEI dressage competition include Prix St Georges, Intermediate I, Intermediate II, Grand Prix, and Grand Prix Special.[1,3] Freestyle is also an FEI-sanctioned competition held at either the Intermediate or Grand Prix level. Competitions sanctioned by USA Equestrian, the national equestrian federation of the USA, are progressively ranked as Training, First Level, Second Level, Third Level, Fourth Level, and Fifth Level (equivalent to international competition).[3]

Event horses are required to perform three sports in one: dressage, cross-country, and showjumping.[4] Events take place over one to three days. Complete three-day events (3DE) involve three tests on consecutive days: the Dressage Test on the first day (Figs 51.1, 51.2), the Cross-Country Test (previously termed the Speed-and-Endurance Test) on the second day (Figs 51.3, 51.4), and the Jumping Test on the third day. The cross-country portion of three-day events involves four phases. Phase A is a trotting warm-up for Phase B, the Steeplechase, in which the horse gallops over brush fences at much faster paces (Table 51.1). Phase C is designed as a cool down phase after Steeplechase. Phases A and C are known collectively as Roads and Tracks. After Phase C there is a mandatory veterinary inspection for 10–15 minutes (Phase X) to determine that the horse is sound and fit to continue (Fig. 51.5). Phase D is the Cross-Country test itself over 30–45 immovable obstacles with heights and spreads requiring speed, endurance, jumping scope, and courage on the part of both the horse and the rider (Figs 51.3, 51.4).[4] The reasoning behind the third day's test, showjumping, is to determine which horses are best able to compete further after the rigorous second day of cross-country.

Internationally the sport is known as the Concours Complet d'Equitation International (CCI).[2,4] International 3DE are ranked by the FEI as one (CCI*) through four-star

Fig. 51.4
The 11-year-old Thoroughbred-crossbred gelding Southern Comfort, ridden by Diane Hall jumping the Boathouse, a more solid obstacle than in Fig. 51.3, but with a drop down into water, during the Cross-Country Test of the 1981 Badminton Three-Day Event. The spread of the jump at the base and at the top, as well as the drop down into the water, illustrate the potential for upper hindlimb injuries from striking a large immovable fence in three-day eventing. The boat is an optical illusion in that the horse and rider would never see it on approaching the fence; it merely provides interesting detail for the photographers in the landing side of the fence.

(CCI****).[3,4] Annual CCI**** include Badminton and Burghley in the UK and Rolex Kentucky in the USA. The abbreviation CCIO designates an Official (Officiel) CCI to which national federations are invited to send selected representative teams and individuals, such as for the Olympic Summer Games or World Equestrian Games.[2,4]

Table 51.1 Speeds, times, distances, and maximum fence heights, spreads, and number of jumping efforts for FEI-sanctioned CCI after rule changes enacted in 2002[4]

Test	CCI*	CCI**	CCI***	CCI****
Cross-Country Test				
Phase A				
Speed (m/min)	220	220	220	220
Time (min)	16–20	16–20	16–20	16–20
Distance (m)	3520–4400	3520–4400	3520–4400	3520–4400
Phase B				
Speed (m/min)	640	660	690	690
Time (min)	3.0–3.5	3.0–3.5	3.5–4.0	4.0–4.5
Distance (m)	1920–2240	1980–2310	2415–2760	2760–3105
Maximum fence height (m)	1.40	1.40	1.40	1.40
Maximum no. of jumping efforts	5–7	6–8	6–8	8–10
Phase C				
Speed (m/min)	160	160	160	160
Time (min)	25–40	25–40	35–45	35–45
Distance (m)	4000–6400	4000–6400	5600–7200	5600–7200
Phase D				
Speed (m/min)	520	550	570	570
Time (min)	7–9	8–10	9–11	11–13
Distance (m)	3640–4680	4400–5500	5130–6270	6270–7410
Maximum fence height (m)	1.10	1.15	1.20	1.20
Maximum fence spread (m)	1.40	1.60	1.80	2.00
Maximum drop height (m)	1.60	1.80	2.00	2.00
Maximum no. of jumping efforts	30	35	40	45
Jumping Test				
Speed (m/min)	350	350	375	375
Time (s)	60–78	69–86	72–88	80–96
Distance (m)	350–450	400–500	450–550	500–600
Number of obstacles	10–11	10–11	11–12	11–13
Maximum fence height (m)	1.10	1.15	1.20	1.20
Maximum fence spread (m)	1.40	1.50	1.60	1.60
Maximum no. of jumping efforts	13	14	15	16

Fig. 51.5
Professor Leo Jeffcott, Foreign Veterinary Delegate, taking a facial artery pulse while examining a Danish three-day event horse between Phases C and D at the 1996 Olympic Summer Games in Atlanta, Georgia.

One- and most two-day events are usually termed horse trials and involve a Dressage Test followed by an abbreviated form of the Cross-Country Test (Phase D only) and the Jumping Test, the latter two tests in no specified order.[3] Only recently the FEI has recognized international horse trials with the designation CIC (Concours International de un jour: one- through three-star levels, Table 51.2).[4] American horse trials are sanctioned by USA Equestrian and are ranked in increasing difficulty as Novice, Training, Preliminary (comparable to CCI*), Intermediate (CCI**), and Advanced (CCI***) (Table 51.3).[3] Combined Tests usually include only two of the three disciplines on a single day.[3]

Eventing began as a cavalry competition in northern Europe and made its first appearance as an Olympic sport in Stockholm in 1912. Over the years the sport has evolved through many iterations. Prior to the 1960s, there was also a fifth phase on Cross-Country Day, Phase E, involving another warm-down Roads and Tracks phase after the cross-country phase. An additional rest stop (C Halt) became mandatory in CCI*** and CCI**** in 1999. In 2002, the recommended distances for all phases were shortened and the speed required for Phase C was decreased to allow more walking for increased recovery from Phase B (Table 51.1).[4] These changes were made in response to a spate of recent fatal rider injuries and were based in part on the results of thermoregulatory research on 3DE performed prior to the 1996 Atlanta Olympic Summer Games.[5–14] That research demonstrated that shortening Phase B,[9,10] inserting two additional rest stops (C Halt) on Phase C,[5–8] and some walking (not all trotting) on Phase C[5–8] increased recovery under hot and

Table 51.2 Speeds, times, distances, and maximum fence heights, spreads, and number of jumping efforts for FEI-sanctioned CIC after rule changes enacted in 2002[4]

Test	CIC*	CIC**	CIC***
Cross-Country Test			
Speed (m/min)	520	550	570
Time (min)			
Distance (m)	2500–3500	3000–4500	3600–5000
Maximum fence height (m)	1.10	1.15	1.20
Maximum fence spread (m)	1.40	1.60	1.80
No. of jumping efforts	25–30	30–35	35–40
Jumping Test			
Speed (m/min)	350	350	375
Time (s)	60–78	69–86	72–88
Distance (m)	350–450	400–500	450–550
Maximum fence height (m)	1.10	1.15	1.20
Maximum fence spread (m)	1.40	1.50	1.60
No. of jumps	10–11	10–11	11–12
Maximum no. of jumping efforts	13	14	15

humid conditions. Because a subcommittee of the International Olympic Committee in 2002 recommended abandoning eventing as an Olympic discipline, there is ongoing discussion about changing the Olympic CCIO format to a CICO (CIC Officiel) for safety and financial concerns.

Equestrian sports governance

The Fédération Equestre Internationale (FEI) is the international governing body for seven equestrian sports, including dressage, showjumping, eventing, driving, vaulting, endurance, and reining.[2,15] Each nation has its own national equestrian federation. Each national federation is a member of the FEI and governs competition at the national or regional level within that nation, whereas the FEI governs international competition. The national equestrian federation of the United States is USA Equestrian (USAEq), formerly known as the American Horse Shows Association (AHSA). The International Olympic Committee (IOC) oversees Olympic competition. The FEI reports to the IOC for Olympic equestrian sports, including dressage, showjumping, and eventing.

Demographics

At the introductory levels of both dressage and 3DE, innumerable different breeds are seen in competition, from ponies to Thoroughbreds and Warmbloods. In both sports, national or regional influences are seen, particularly in the use of native Warmbloods, owing to their ready availability and popularity as sport horses in any given nation. The USA lags considerably behind in a native Warmblood or sport horse

Table 51.3 Speeds, times, distances, and maximum fence heights, spreads, and number of jumping efforts for 2002 USA Equestrian horse trials[3]

Test	Novice	Training	Preliminary	Intermediate	Advanced
Cross-Country Test					
Speed (m/min)	350	420	520	550	570
Time (min)	4.0–5.0	4.5–5.5	5.0–6.0	5.5–6.5	6.0–7.0
Distance (m)	1400–2000	1890–2585	2600–3120	3025–3575	3420–3990
Maximum fence height (m)	0.90	1.00	1.10	1.15	1.20
Maximum fence spread (m)	1.00	1.20	1.40	1.60	1.80
Maximum no. of jumping efforts	18	24	28	32	36
Jumping Test					
Speed (m/min)	320	320	350	350	375
Time (s)	75–90	75–90	75–90	75–90	80–96
Distance (m)	400–480	400–480	438–525	438–525	500–600
Maximum fence height (m)	0.90	1.00	1.10	1.20	1.30
Maximum fence spread (m)	1.00	1.15	1.30	1.45	1.60
Maximum no. of jumping efforts	11	12	13	13	15

breeding and reward program compared with the European nations.

As riders progress toward upper levels, dressage horses tend more often to be Warmbloods, thus providing the size, stride length, balance, and agility required for upper level movements. According to the World Breeding Federation for Sport Horses, German Warmblood breeds routinely dominate the rankings of internationally competitive dressage horses and sires of dressage horses.[16] Hanoverians tend to be the most highly ranked dressage horses.[16] Recent gait and conformation analysis data on 3-year-old dressage horses (n = 142) have shown German Warmbloods (Hanoverians (n = 31), Westphalians (n = 16), and Oldenburgers (n = 6)) to be biomechnically superior to both Selle Français (n = 61) and purebred Spanish horses (n = 28) for use in competitive FEI dressage.[17] The superior stature and conformation of the German horses resulted in a longer stride length and decreased stride frequency. The authors concluded that the German horses had gait characteristics more adapted to dressage competition.[17]

At the upper levels of 3DE, horses are primarily Thoroughbreds or Thoroughbred crosses. The Thoroughbred influence is necessary to have the adequate fitness, stamina, and jumping ability required at the upper levels of 3DE. According to the World Breeding Federation for Sport Horses, all 10 of the top 10 sires of internationally ranked 3DE horses in 1999–2000 were Thoroughbreds.[16] Selle Français horses were also very successful in both 3DE and showjumping at the 2002 World Equestrian Games in Jerez, Spain.[18]

Dressage horses may not compete under FEI rules until they are at least 6 years old.[1,2] Horses competing in the Olympic Games or World Equestrian Games must be at least 7 years old.[2] Dressage horses may not compete in Grand Prix, Grand Prix Special, or Grand Prix Freestyle until they are at least 7 years old.[1,2]

Three-day event horses may compete in CIC* or CIC** at 5 years old.[4] They must be at least 6 years old to compete in CIC***, CCI*, or CCI**.[4] Event horses must be at least 7 years old to compete in CCI***, CCI****, the Olympic Games, or the World Equestrian Games.[2,4]

Dressage and 3DE horses have their most productive years at the upper levels between approximately 8 and 12 years of age. There are, however, always exceptions to be found, more often in older dressage horses continuing to compete at upper levels than in younger horses competing precociously. Because of the cumulative and repetitive training which must be accomplished by dressage horses to arrive at the upper levels, they tend to be somewhat older than their 3DE counterparts, who often have difficulty remaining competitively sound later in life due to the rigorous galloping and jumping required in their sport. After their peak competitiveness has passed, many older horses in both disciplines are used further to teach younger riders to compete on safer mounts as they aspire to the higher levels of competition. While these older horses are often difficult to maintain completely sound, their experience and demeanor make them invaluable mounts for upcoming young riders. They also present common challenges to practicing veterinarians who are asked to help to maintain their soundness and fitness to compete despite their advancing ages.

Due to the collection, impulsion, bending and circling (Fig. 51.2), and other types of movements required in dressage, common complaints include sore backs or hocks. Riders often complain of a horse's unwillingness to bend, perhaps worse in one direction than the other. The sore backs or hocks seen frequently in true dressage horses are often also seen in event horses, since they also must complete difficult repetitive dressage movements. Jumping and galloping cross-country (Figs 51.3, 51.4) also contribute to injuries sustained by event horses, as do the rigorous training regimens required to achieve sufficient fitness to compete at the upper levels. Bowed tendons and suspensory desmitis are common supporting leg lamenesses, especially after Steeplechase, and traumatic-origin injuries also occur during Phase D.

Veterinary services

Veterinarians are involved in both sports in various manners. Many are employed as primary healthcare providers on a daily basis. Others are secondary or tertiary healthcare providers, either in an elective or emergent manner. Elective referrals are often for more sophisticated diagnostic imaging techniques such as ultrasonography, scintigraphy, or thermography of musculoskeletal injuries. Emergent referrals are sometimes necessary for all types of emergency conditions typical in any equine practice. More recently, competitors in both sports have embraced alternative therapies, either in lieu of or in addition to conventional therapeutic measures, in an effort to maintain soundness and maximize performance in these elite equine athletes.

Many practitioners also have contact with these horses only at competitions, as treating veterinarians (the conventional 'horse show veterinarian'), team veterinarians, drug testers, or official veterinarians. Treating and team veterinarians are also healthcare providers, but in the crucible of competition. Treating veterinarians often have contact with many of the same owners, riders, and horses over the course of a horse show circuit, and develop a valid long-term doctor–client–patient relationship. Team veterinarians function as treating veterinarians but for only one team, thus allowing more focused and intensive care for a more limited number of horses. The most difficult part of the team veterinarian's job is remembering the FEI Code of Conduct,[19] which states that:

> In all equestrian sports the horse must be considered paramount. The well-being of the horse shall be above the demands of breeders, trainers, riders, owners, dealers, organizers, sponsors or officials. All handling and veterinary treatment must ensure the health and welfare of the horse,[19]

all while the team veterinarian is feeling the intense pressure of the team, governing federation, and home nation in

wanting to 'get a team through' the competition intact with sufficient competitors to achieve a composite team score.

Drug testers and official veterinarians also have as their goal the welfare of the horse, but their responsibility is more regulatory than as healthcare providers. Drug testers or medication control personnel are responsible for collection of blood and urine samples and for establishing an appropriate chain of custody to determine the validity of any evidence of wrongdoing which they may have collected.[19] Official veterinarians are responsible for the health of all the horses competing at a show or event, and make decisions appropriate for that care under the rules of that competition. The competition's Organizing Committee, with the approval of the FEI and/or the national federation, selects a Veterinary Delegate for any FEI-sanctioned competition.[19] The FEI determines the Veterinary Delegate for CCIO, CICO, or CDIO.[19] That Delegate is responsible to head the Veterinary Commission and is also responsible to the Ground Jury for veterinary matters. These responsibilities include: passport control; arrival examinations; control of veterinary practitioners within the stabling compound; recommendations to the Ground Jury about fitness to compete at official jogs or veterinary inspections (Fig. 51.5); and oversight of medication control.[19] Official veterinarians are sometimes at odds with treating or team veterinarians, but all should remember that the officials are ultimately responsible for the welfare of all the horses in the competition. The best relationships are those where the veterinary officials are somewhat flexible before the relationship becomes too adversarial. The treating veterinarians must also remember that the officials have as their primary mandate the welfare of the horse. These officials are often very experienced in their roles, and many have functioned as treating veterinarians in the past.

Common diseases and conditions

Horse competing in dressage or eventing may have all the same problems or internal diseases of any other horse. However, some conditions may be more common due to the type of activity in which they compete. As always, poor conformation also plays a significant role in many unsoundnesses. For example, post-legged or straight hindleg conformation may predispose a dressage horse to hock or stifle lameness, as will sickle hocks or the cow-hocked conformation more common in many Warmblood breeds.

Skeletal

Forelimb problems in dressage horses are less common than hindlimb problems. Improper hoof balance is not a rare problem and is best corrected with the farrier and veterinarian working together to achieve proper medial-to-lateral and left-to-right hoof balance. Because dressage does not occur at high rates of speed, supporting leg lamenesses such as bowed tendons or suspensory disease are less common than in event horses but may still occur, particularly when horses begin to attempt extended gaits (Fig. 51.1). Fetlock synovitis or arthritis is seen secondary to extended movements at upper levels (note fetlock hyperextension in Fig. 51.1), especially in former Thoroughbred race horses converted to use as dressage or event horses.

Foot balance is also of critical importance in event horses galloping over varying terrain with differing footing conditions, all possibly up, down, or sideways to the slope of the hills. Due to the repetitive stresses caused by jumping, event horses are predisposed to developing navicular disease. This predisposition is worsened by poor foot conformation, with underrun and contracted heels, common in many North American Thoroughbreds who are former race horses. Sole bruises, pedal osteitis, and other foot conditions may also be seen due to poor foot conformation, the high training mileage required to keep 3DE horses fit to perform,[20] and the varying surfaces encountered in training and in competition. Because of the high speeds and jumping at speed required in eventing, supporting leg injuries such as bowed tendons or suspensory desmitis are more common than in dressage horses. These injuries are more common as 3DE horses approach the upper levels where horses and riders must learn to negotiate steeplechase courses and fences at the required velocities.

Due to the stresses caused by the excessive hindlimb reaching required in dressage ('impulsion'), hock pain and bone spavin are common maladies of both dressage and event horses. Traumatic stifle injuries are more common in 3DE horses as they progress up the ranks, owing to the greater height and spread of obstacles (Figs 51.3, 15.4) at the upper levels (Tables 51.1–51.3).[21–23] These stifle injuries consist in increasing severity of dermal abrasions ('stifle rubs'), deeper soft tissue or patellar desmitis injuries, or patellar fractures.[21–23]

Corrective shoeing in dressage horses may be done with minimal concerns about shoe loss from over-reaching during high-intensity exercise. Event horses, however, are somewhat more restricted in the use of wedge shoes or bar shoes since they may be more prone to pulling or twisting them off while galloping and jumping cross-country. Horses in 3DE are often shod with threaded holes drilled into the heels of their shoes to allow heel caulks or studs of varying length to be changed before or even during the competition, depending upon the looseness and moisture content of the footing on the day of competition.

Muscular

Exertional rhabdomyolysis (ER), myopathy, or tying-up is not a common problem in dressage horses but is much more common in 3DE horses. This condition may be related to hereditary Thoroughbred ER[24,25] but more commonly has no apparent hereditary component.[24] Unfitness and overheating seem to play important roles in the development of ER,[8,24] as may excessive dietary carbohydrate intake.[24,26] Diets higher

in fat content have proven curative for many horses.[24] Up to 20% of the diet may be fed safely as fat, available in various commercial feed products.[27] One inexpensive and convenient manner of feeding more fat is to increase gradually the daily intake until as much as 2 cups (450 mL) of corn oil twice daily is top-dressed onto the horse's regular grain diet.[27]

Exertional rhabdomyolysis should be considered an emergency, whether it occurs during competition or training, and appropriate therapy should be instituted. Treatments should include cessation of exercise, provision of adequate cooling (oral water, water baths, shade, fans), administration of nonsteroidal anti-inflammatory drugs (NSAIDs), tranquilization (acepromazine for tranquilization and peripheral vasodilatory effects), and eventually diuresis with fluids (40–60 L i.v. of isotonic fluid per 500 kg horse over 6–12 hours).

Hyperkalemic periodic paralysis (HYPP) is a hereditary disease manifesting as muscular weakness in Quarter Horses.[28,29] All horses known to be afflicted with the disease trace their pedigree to a single Quarter Horse stallion who passed it on to his progeny as an autosomal dominant trait with incomplete penetrance.[29] Homozygous horses are more severely affected than heterozygous horses. This condition is not commonly seen in dressage or eventing horses since Quarter Horses compete in these sports less commonly than do Thoroughbred or Warmblood horses. A genetic test is available on EDTA-preserved blood.

Heavier-bodied horses such as Warmbloods tracing some of their ancestry to draft breeds may be predisposed to development of polysaccharide storage myopathy (PSSM).[24,30] This condition manifests as poor performance, tying-up, muscle weakness, or shaking or shivering. Feeding more fat and less carbohydrate as energy sources is curative in many cases.[30]

Back soreness occurs in horses competing in both of these sports, most commonly due to muscle soreness secondary to hindlimb lameness (primarily bone spavin). Back pain may also be secondary to poorly fitting or poorly stuffed saddles in some horses.[31] Less commonly back pain in horses may be due to primary back disease (Fig. 51.6),[32] comprised usually of over-riding dorsal spinous processes, and sometimes of painful spinous processes (Fig. 51.6B, C) without any actual over-riding onto adjacent vertebrae. Thermography (Fig. 51.6A) and scintigraphy (Fig. 51.6B, C) may be important adjunctive diagnostic tools in evaluating back soreness.[33,34] Acupuncture with application of needles[35,36] or cold laser[36,37] can serve as both a diagnostic and a therapeutic tool in back soreness. Massage therapy may only be palliative but can serve to assist in improving performance if the horse feels better afterward, even if only temporarily.[38–40] Chiropractic therapy is often used in horses with back soreness,[40–43] but may serve more to provide massage therapy than actual true chiropractic adjustment. Due to the size differences between patient and veterinarian, and the horse's large muscle masses, huge protected vertebral column, and flighty nature, some scientists argue that true chiropractic adjustment or manipulation of a horse's spine is virtually impossible in a standing athletic horse (LB Jeffcott, personal communication,

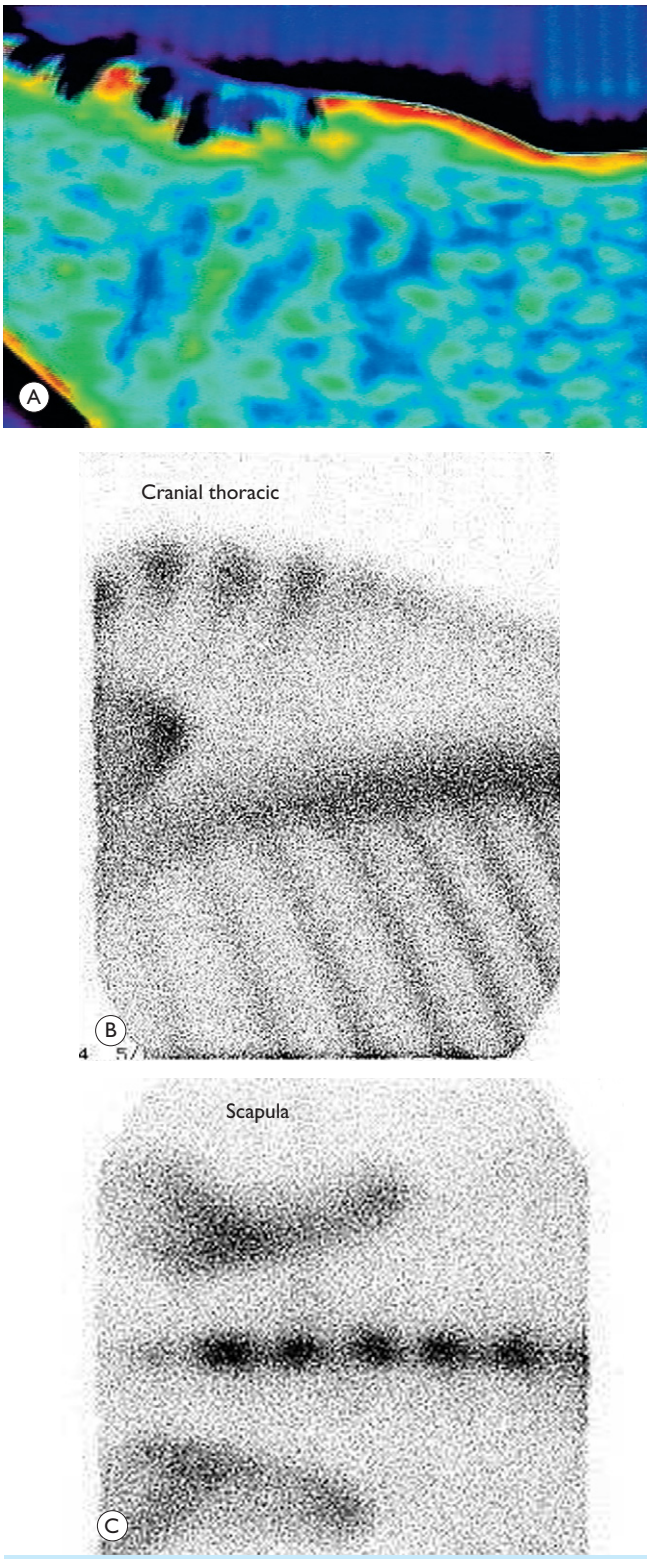

Fig. 51.6
Lateral thermograph (A) and lateral (B) and dorsal (C) scintigraphs from a dressage gelding demonstrating increased heat in the withers (A: red-to-white areas on point of withers) and abnormal radiopharmaceutical uptake (B and C: dark focal increased uptake) in the tips of the dorsal spinous processes of the withers (courtesy of Dr J. Waldsmith, San Luis Obispo, California).

1992–1996). Others feel just as strongly that spinal manipulation is possible and beneficial in athletic horses.[40–43]

Respiratory

Left laryngeal hemiplegia (LLH or 'roaring') is a common problem in both dressage and event horses because both sports emphasize the need for horses of larger stature. Both Thoroughbred and Warmblood horses are more likely to be larger and thus are more likely to be roarers. Surgery is corrective of the hemiplegia but not necessarily of the audible noise. Ironically, the pre- or postoperative LLH noise is considered a fault in the American hunter show ring, so horses that develop LLH as hunters may actually undergo lifestyle changes and become jumpers, dressage, or event horses. Other upper airway obstructions such as dorsally displaced soft palate or epiglottic entrapment may occur in horses competing in these sports but should not be considered to be more common than in other horse sports.

Sinus problems secondary to dental problems may be more common in these horses only because as they get older they are more predisposed to cheek tooth problems. Guttural pouch disease and strangles are not common occurrences in these horses because these are diseases of younger, not older, horses.

Lower respiratory tract problems may be more common in these horses owing primarily to their age and the stress of transport.[44] Depending upon the geographic location, dressage competitions may be more plentiful and require less transport distance for horses to compete. Three-day events and horse trials are much more common in the mid-Atlantic region of the eastern USA, so the distances between horse shows for both event and dressage horses are much greater in the midwestern and western USA. Pneumonia and pleuropneumonia in non-juvenile horses are clearly related to transport stress, particularly after transport greater than 500 miles.[45] Transport stress may be less of a factor in developing pleuropneumonia in European horses owing to the proximity of numerous competitions.

Exercise-induced pulmonary hemorrhage (EIPH) occurs in event horses during or after the Cross-Country Test. Epistaxis is occasionally evident at the end of Cross-Country (Fig. 51.7) but endoscopy is not used routinely for diagnosis as it is in the racing industry. EIPH is not associated with exercise intolerance as commonly in 3DE horses as it is in race horses. The industry-wide North American prophylactic treatment with furosemide (frusemide) is not possible in event horses since it is prohibited due to concern over its dilution of urine and possible masking of positive tests for other prohibited substances.

Heaves or chronic obstructive pulmonary disease (COPD) occurs sometimes in both event and dressage horses. Their occupations do not necessarily predispose them to allergic lung disease, but it is somewhat age-related in its onset and these tend to be older horses when they are at their prime competitive age. Management changes are critical but not curative since the allergy never disappears. Pasture turnout, wetting hay, and minimizing other dust exposure in bedding and diet minimizes allergen exposure and reduces the frequency and severity of exacerbations. Systemic treatment with corticosteroids and/or bronchodilators may be possible during training but is prohibited during competition.[19] Newer inhalation therapies may minimize the chances of a positive drug test but recent research with inhaled albuterol has shown that it is detectable in plasma for several hours after inhalation at therapeutic dosages.[46] Urine ELISA concentrations of inhaled albuterol are not detectable beyond 24 hours after administration, but those investigators recommended an additional 24 hours (48 hours total after the last dose) to avoid a positive urine test after use of the albuterol inhaler.[47] The best scheme should be to manage the disease as best as possible at home and to avoid therapy during competition while still maintaining exposure discipline even while away from home at a horse show or event.

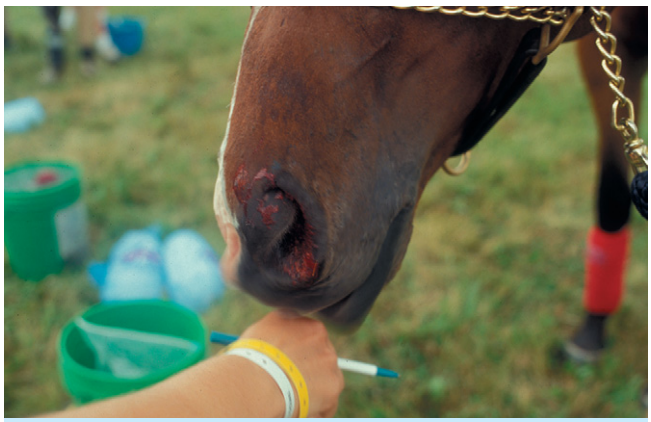

Fig. 51.7
Epistaxis secondary to exercise-induced pulmonary hemorrhage in a three-day event horse during the Cross-Country Test at the 1999 North American Young Riders Championships in Wadsworth, Illinois.

Gastrointestinal

Dental problems in dressage and event horses may predispose them to misbehavior, head-shaking, or refusal to turn in the dressage ring or refusal of jumps in the Cross-Country Test or in stadium jumping. Sharp labial points may cause pinching of the cheek or even oral ulcers which result in oral soreness and sensitivity. Ill-fitting bits may cause similar problems in the rostral mouth area close to the first cheek teeth. Wolf teeth may interfere with proper bitting. Appropriate and regular dental care should be curative. The most common error is that the teeth feel properly floated on superficial examination of the rostral labial surfaces of the first cheek teeth, but caudal enamel hooks and/or buccal points may be present and may cause misbehavior even when not interfering with the bit. Proper and complete oral examination with a speculum and a light source should make the source of the problem evident.

Gastric ulcers may be caused in these horses by a number of factors. Dietary risk factors include high grain intake and minimal pasture exposure.[48] Intense exercise and training stress may be ulcerogenic, as may transport stress. Minimizing stress is important whenever possible, and common anti-ulcer medications (cimetidine, ranitidine, omeprazole) are curative. Ranitidine (but not cimetidine) and omeprazole are approved for use during FEI competitions.[19]

Colic is another stress-related illness in dressage and event horses. Predisposing factors include minimal pasture turnout, transport stress, changes in water and dietary intake at competitions, and stress of competition itself. Cross-country exercise in particular may cause dehydration, especially at upper levels in conditions of high heat and humidity.[49,50] It has been estimated that as much as 10–15% of the horse's extracellular fluid volume may be present in the large colon, and this water reserve is the first source for the horse to mobilize in the face of dehydration.[51] This increased colonic water resorption may result in dehydration of colonic contents and impaction colic. Treatment beyond oral and intravenous fluids and possibly mineral oil may require the horse to be removed from competition.[19]

Diarrhea is another transport, dietary, and competition stress-related illness which occasionally occurs in dressage and event horses. It should be considered an emergency, and is cause for withdrawal from competition and isolation from the general population within the home or competition stable.

Cardiovascular

Cardiovascular diseases are not common in event or dressage horses but may be important when they occur. As elite athletes, these horses commonly have normal athletic arrhythmias such as second-degree atrioventricular block, sinus arrhythmia, wandering atrial pacemaker, or split first and/or second heart sounds. Murmurs should be considered pathologic when loud and systolic. Aortic insufficiency with minimal clinical implications may be ausculted in older horses as an acquired diastolic decrescendo murmur.

Atrial fibrillation (AF) occurs occasionally in 3DE horses[8] more than in dressage horses. It is ausculted as an irregularly irregular arrhythmia and is heard most during the Cross-Country Test, either during the Second Horse Inspection between Phases C and D or after completion of Cross-Country. Typical idiopathic atrial fibrillation occurs as an exercise-induced arrhythmia for no apparent reason. Three-day event horses may be more prone to atypical AF due to fluid and electrolyte loss, especially during conditions of increased heat and humidity (Fig. 51.8A).[8] For example, two horses of 99 starters during the 3DE in the 1996 Olympic Summer Games in Atlanta developed AF during the Cross-Country Test (Fig. 51.8A).[7] In these cases, isotonic fluids (60 L i.v. over 6–12 hours) were administered after exercise and were curative (Fig. 51.8B). Many horses have successfully completed the Jumping Test after developing transient fluid-responsive AF during or after the Cross-Country Test. Rest should be enforced after the competition is over, but the horse may be predisposed to subsequent episodes of AF, especially under adverse weather conditions resulting in increased fluid and electrolyte loss. Dietary supplementation of electrolytes, proper water intake, and appropriate fitness coming into the event may help to minimize the development of AF in future competitions.

Fatal arrhythmia and ruptured aorta[52] are two of the most common causes of sudden unexplained death in 3DE horses. EIPH is rarely fatal in these horses.

Neurologic

Infectious neurologic diseases (e.g. equine protozoal myelitis, West Nile virus) are not more common in dressage and event horses than in older horses performing in other sports. However, 3DE horses occasionally sustain severe neurologic trauma in jumping accidents during the Steeplechase or Cross-Country phases.[53] Fractures of the cervical vertebrae

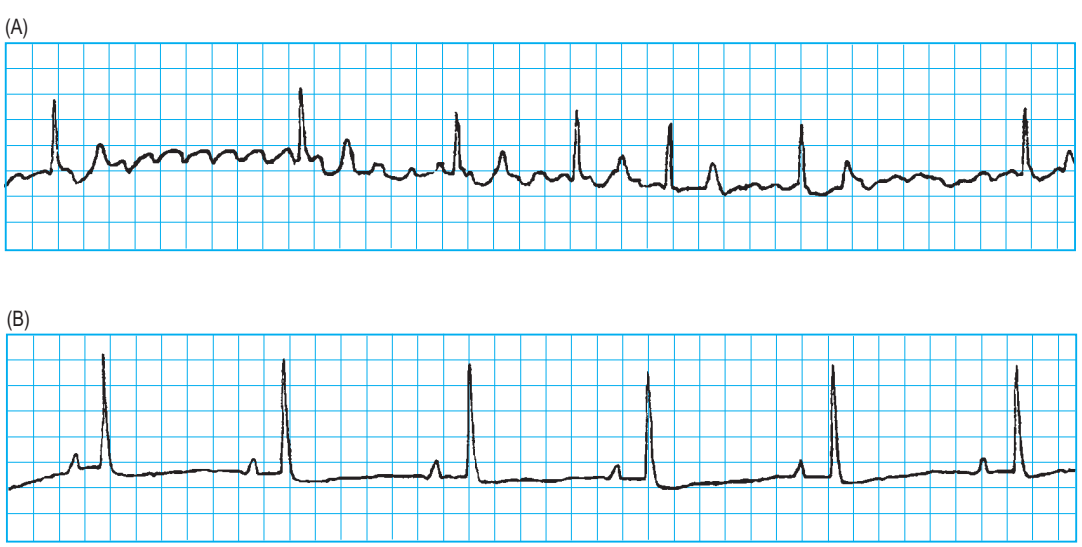

Fig. 51.8 Electrocardiograms performed after the Cross-Country Test in a three-day event horse at the 1996 Olympic Summer Games in Atlanta, Georgia (A) documenting atrial fibrillation before treatment and (B) normal sinus rhythm after intravenous treatment with 60 L of lactated Ringer's solution. Recorded at paper speed of 25 mm/s.

are generally due to falls at jumps, especially at drop fences or water jumps, and invariably prove to be fatal to the horse. Riders can sometimes be injured similarly in these falls.

Endocrine

Estrus behavior is the most common endocrine problem encountered in dressage and event horses. Cycling mares may act inappropriately during the dressage test when it is expected that they should be quiet and obedient. Altrenogest (Regumate) is currently prohibited under FEI rules[19] but not under USA Equestrian rules.[3] Judicious scheduling of competitions around heat cycles or neutering may be the only other alternatives when hormonal therapy is prohibited.

Hypothyroidism remains a controversial but often cited cause of exercise intolerance in horses.[27,54,55] Recent data have shown in a surgical model of hypothyroidism that affected horses have poor cardiac function due to poor myocardial contractility.[54] Affected mares had decreased resting heart rate and cardiac output. This effect is presumed to be due to downregulation of myocardial β-receptors evidenced by decreased cardiac responsiveness to isoproterenol. This poor cardiac function was further manifested in exercise intolerance when these same mares underwent treadmill step tests after thyroidectomy. Supplementation with thyroid hormone partially or completely reversed the various effects of hypothyroidism over one month's time. A commonly cited dose for thyroid hormone supplementation is 30 grains (1.95 g) orally twice daily, yielding approximately 2.5 μg/kg of thyroxine (T4) and 0.6 μg/kg of tri-iodothyronine (T3) with each dose.[27,54,55]

Cushing's syndrome is rare in competitive dressage and event horses because they are usually younger than the typical late-teenaged years of onset of Cushing's disease.

Dermatologic

Ringworm typically occurs in horses younger than those actively competing as dressage and event horses. Saddle-induced skin injuries are also rare as these riders usually take extra precaution to ensure that their saddles fit properly. Lacerations sustained during cross-country are common in event horses and pose particular problems since local anesthetics and sedatives are prohibited substances under all rules.[3,19] Permission may be obtained from the Veterinary Delegate and the Ground Jury for judicious use of small amounts of local anesthetic without sedation. Abrasions, or 'road rash' injuries, are also common from horses falling, slipping on wet grass or pavement, or rubbing their knees, hocks, or stifles over cross-country jumps. While the skin is raw and abraded, the concern in an unsound horse should be the probable underlying soft tissue injury such as patellar ligament pain after a stifle rub. These skin and underlying injuries are of genuine concern to the riders since they may be sufficiently painful to cause a horse to be eliminated at the Third Horse Inspection on the morning after the Cross-Country Test and before the Jumping Test. They require considerable icing therapy and possibly the use of cold lasers on underlying ligamentous pain. Use of alternative therapies such as cold lasers must be reported in writing at FEI competitions.[19]

Ocular

Ocular injuries are not common in these horses, and anterior uveitis is no more common than in other horses. Ocular disease should be investigated, however, as a possible problem whenever a horse suddenly becomes recalcitrant, unwilling to move forward or to jump as freely as usual.

Behavioral

Behavioral problems are sometimes the most difficult diagnoses, since the rider and trainer do not want to believe that it is not something physical that is causing the horse's failure to perform. Perhaps a horse and rider are simply not suited to one another. If either member of the pair is too inexperienced ('too green'), they may not be able to compete effectively despite being completely healthy physically. Some riders, in their nervousness, make certain horses more nervous and skittish than other riders. Horses often 'go better' for the trainer than for the owner/rider, and that rider simply has a difficult time dealing with the fact that he/she does not ride as well as is necessary to get the best performance out of that horse. Tack and bit problems are relatively uncommon but may be the source for some misbehaviors, as may poor dentition. The recycled Thoroughbred race horse is another problem, in that it often comes with poor foot conformation, other injuries such as bowed tendons, and racing-related inappropriate behavior for the show ring such as a frustrating willingness to be overly nervous and unwilling to quiet down at the appropriate time.[56] Some veterinary practitioners feel that acupuncture may have a calming effect in nervous horses prior to competition (A Young, personal communication, 2002).

Metabolic/heat-related

Anhidrosis is a rare problem but is sometimes seen in horses traveling to warmer climates from more temperate climates (e.g. from Chicago to Florida for the winter show circuit). Horses with anhidrosis fail to sweat effectively, although they may sweat in intermittent spotty patches but not diffusely as needed for proper thermoregulation. Diagnosis is by subcutaneous injection of epinephrine (adrenaline) followed by a failure to sweat in the injected area. Therapy is primarily by heat management (ride in cooler climates and cooler times of the day, fans on the stall, frequent baths). One commercial product (One-AC) has been touted as curative for many horses but controlled trials are not available.

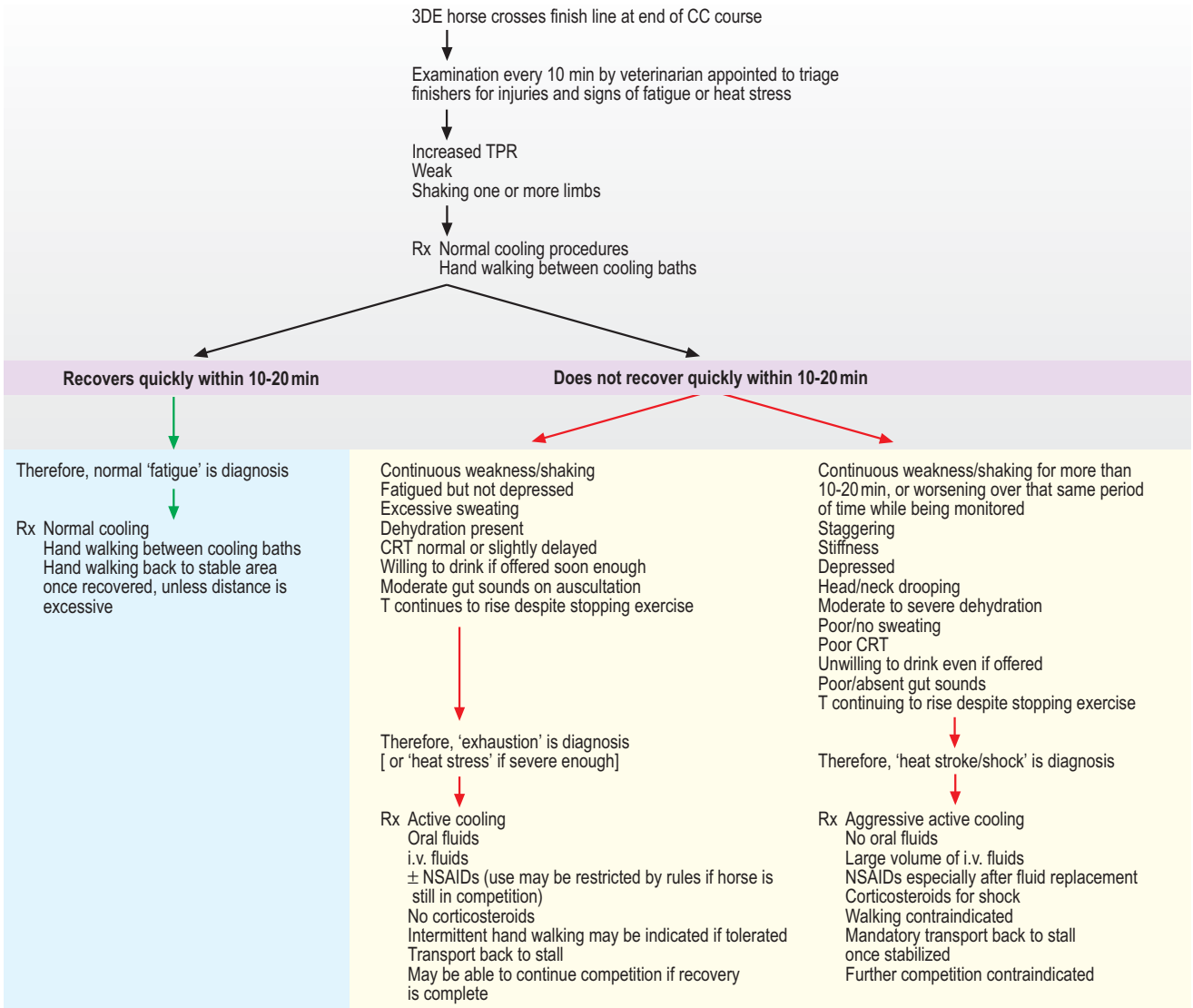

Fig. 51.9
Decision-tree for distinguishing between simple fatigue, exhaustion and heat stress, and true heat stroke. CC, cross-country; CRT, capillary refill time; NSAID, non-steroidal anti-inflammatory drug; Rx, treatment; T, temperature; TPR, temperature, pulse (heart rate), and respiratory rate.

Dehydration, fatigue, and heat-related illnesses are common in 3DE horses, especially when competing in conditions of higher ambient heat and humidity.[5–14,27,49,50,57–60] Heavily muscled dressage horses are also subject to heat-related illnesses. The most difficult decision for the practitioner examining a hot sweaty horse is distinguishing between simple fatigue, exhaustion and/or possible heat stress, and heat stroke (Fig. 51.9).[8] Fatigued horses recover in 10–30 minutes with simple bathing and voluntary water ingestion. Exhausted horses, and those with possible heat stress as part of their exhaustion, do not recover as rapidly but are still willing to drink, move around gradually, and seem moderately alert eventually.[8] Horses with heat stroke are in shock and are profoundly depressed, unwilling to eat, drink, or walk, and do not recover without intensive care in the form of large volumes of intravenous fluids and repetitive external cooling.[8]

Cooling procedures for 3DE and other hot horses have been the focus of considerable research in recent years.[5–8,13,14,61,62] A number of different studies have shown that horses may be cooled actively with large volumes of ice cold water placed repeatedly directly onto their backs and heavily exercised muscles (Fig. 51.10) without any complications such as overt tying-up or subclinical myopathy (manifested as increased plasma creatine kinase activity).[5–7,61,62] Use of this active cooling technique under conditions of adverse heat and humidity has been shown to accelerate the recovery of 3DE horses.[61,62] Shade and fans may also be used to improve heat loss, minimize radiant heat gain, and speed recovery.[5–8,63]

Fig. 51.10
Active cooling being performed on a British three-day event horse between Phases C and D at the 1996 Olympic Summer Games in Atlanta, Georgia. The team veterinarian is observing the bathing of the horse and standing by to administer additional advice or treatment if necessary.

An additional mandatory 10-minute rest stop on Phase C, now called C Halt, has been used in a number of hotter 3DE competitions since 1994 to ensure that horses are properly cooled after Steeplechase.[5–8,11–14] It was shown in the 1996 Olympic Summer Games,[13,14] and in treadmill laboratory simulations prior to Atlanta,[5–8] that C Halt was clearly beneficial to recovery after Phase B galloping in conditions of high heat and humidity. Since 1999, the FEI has mandated the use of C Halt in all CCI*** and CCI**** regardless of the weather conditions.

Horses will drink immediately after endurance exercise such as Roads and Tracks or Cross-Country, but only during approximately the first 5 minutes of recovery, so water or electrolyte water should be offered immediately.[64] If the horse fails to ingest water (i.e. it was not offered, or the horse was too exhausted to drink), water or electrolyte solutions may be administered orally via nasogastric tube (4–8 L of roughly isotonic fluid after exercise) with few complications once the horse has returned to its stall. Administration of intravenous fluids is indicated in horses with overt heat stroke, myopathy, and even simple fatigue and dehydration under severe climatic conditions (Fig. 51.9). Recommended volumes of isotonic fluid range from 10–30 L for simple fatigue and dehydration to 50–80 L over several hours for horses with more serious clinical problems.[8]

Prevention of heat-related illnesses is the purview of the treating veterinarian and should be undertaken aggressively to avoid problems during or after the competition. Horses' water intake should be monitored always, but especially after transport and when away from home. Bodyweight may be the best measure of monitoring hydration status if owners, riders, and grooms have access to a scale and are encouraged to use it.[9,11,65,66] Fluid-loading prior to competition has become more commonplace, especially prior to the Cross-Country Test.[7,8,13] Approximately 2–4 hours prior to competition, the horse may receive safely 4–8 L of oral electrolyte mixture in water (roughly isotonic) via nasogastric tube.[67–70] The only real risk from this procedure is iatrogenic epistaxis. For this reason, some riders or team veterinarians prefer to administer isotonic fluids (5–10 L) intravenously prior to exercise. Each rider must also learn to be constantly aware of his horse's performance, strength, gait pattern, forwardness, and breathing patterns to be sensitive to the possibility that the horse is not feeling well, is 'not itself', and may have some physical reason for performing poorly.[8] After exercise, proper active cooling techniques may assist in recovery and may help to prevent further possible heat-related illness (Figs 51.9, 51.10).[5–8,13,14,61–63]

Medications during competition

The different governing bodies of equestrian sport retain the right to set their own drug rules and penalties for violations. Since 1992 FEI has maintained a zero tolerance policy toward nearly all drugs, including NSAIDs, in horses in competition. The inherent philosophy is that there should be a level playing field for all horse and rider pairs, and that to allow any performance-altering drugs to be present on the day of competition might allow one competitor to have an unfair advantage over his/her counterparts by having better medication, not necessarily a better horse. There are a few substances for which FEI has set maximum allowable limits, since they can be present in horses to a slight extent due to natural exposure through feedstuffs or other environmental contamination.[19] Those substances for which maximum thresholds have been established under FEI rules include: total carbon dioxide (37 mEq/L plasma), dimethyl sulfoxide (DMSO: 15 μg/mL in urine or 1 μg/mL in plasma), hydrocortisone (1 μg/mL in urine), salicylic acid (750 μg/mL in urine or 6.5 μg/mL in plasma), theobromine (2 μg/mL in urine), total arsenic (0.3 μg/mL in urine), and the hormones nandrolone and testosterone.[19] FEI rules allow the use during competition of most antibiotics, anthelminthics, vitamins, fluids and electrolytes, ranitidine (but not cimetidine), and omeprazole.[19]

During or just prior to a competition, a horse may require treatment for any of dozens of different medical or surgical problems. In these various situations, the FEI General Regulations state:

> The Veterinary Commission/Delegate must give written approval on the appropriate form before any veterinary treatment or medication with a Prohibited Substance is administered to a horse during the entire course of an event. If during this period it is urgently necessary to treat a horse with a Prohibited Substance, the Veterinary Commission/Delegate must be informed at once and the circumstances reported to the President of the Ground Jury. Any treatment so administered must be indicated to the Veterinary Commission/Delegate by written certification. The Ground Jury must, on recommendation of

the Veterinary Commission/Delegate, decide whether the horse may take part or continue in the event, having regard to the welfare of the horse and to the possibility that the competitor may obtain an unfair advantage.[2]

Three examples of entirely different clinical circumstances follow to illustrate common but complex interpretations of FEI medication rules. (1) A horse sustains an eye injury or corneal ulcer which requires local medication but which may not require any medication that might unlevel the playing field. Systemic flunixin meglumine should be avoided in this horse but might be used in a similar injury out of competition. (2) A horse sustains a small laceration which will not prohibit further competition but which requires suturing. Judicious use of a local anesthetic might be approved by the Veterinary Commission but sedation might not be approved prior to suturing. The anesthetic will be in a small amount and should have no lasting consequence on the future of the competition. However, tranquilization might affect the competition since it might make a dressage horse, for instance, quieter for a test the following day, obviously depending upon the dose and drug used. Its legitimate use to suture the laceration might also make it more difficult to detect a second dose given illicitly the following day. Finally, (3) a horse develops colic signs severe enough to require systemic use of an NSAID. This horse should be treated and removed from competition since it (a) has a medical problem severe enough to preclude it from further competition for medical reasons alone, and (b) has received one or more doses of an NSAID which might affect the outcome of the competition since the NSAID will also have musculoskeletal effects that might benefit the horse and create an unlevel playing field.

The most commonly detected foreign substances in the FEI Medication Control Programme are analgesics (primarily NSAIDs including salicylic acid), comprising 58% of the positive samples in 1999 (AK Allen, personal communication, 2001). Corticosteroids, caffeine, theobromine, isoxsuprine, and tranquilizers are less commonly encountered. From 1990 to 1998, 79% of the positive drug tests in FEI competitions were from showjumpers, and only 9% and 8% were from 3DE and dressage horses, respectively.

USA Equestrian rules are just as restrictive as those of the FEI for most substances such as stimulants, tranquilizers, and other mood-altering drugs.[3] However, USAEq rules are much more liberal than FEI with respect to NSAIDs.[3] The philosophy simply put is that therapeutic medications allow some horses to continue to compete at an effective level over the course of a season or over the course of a long horse show. The rule specifically states, 'The full use of modern therapeutic measures for the improvement and protection of the health of the horse and/or pony is permitted'.[3] USA Equestrian rules prohibit the use of any drugs within 24 hours of competition, but they allow for fairly liberal use of five different NSAIDs up to 24 hours prior to competition. Furthermore, two different NSAIDs may be detected legally in horses in competition as long as: (1) phenylbutazone and flunixin meglumine are not detected in the same horse on the same test, and (2) each NSAID detected is below a maximum threshold established by USA Equestrian. Those maximum thresholds are set for plasma concentrations of phenylbutazone (15 μg/mL), flunixin (1 μg/mL), ketoprofen (0.25 μg/mL), meclofenamic acid (2.5 μg/mL), and naproxen (40 μg/mL).[3] Tranquilizers, cocaine, and NSAIDs above the allowable limits are the most commonly detected foreign substances under USAEq medication testing (AK Allen, personal communication, 2001).

Finally, there are innumerable unsanctioned or unrecognized horse shows that may not be subject to any drug testing by a governing body unless local law allows for testing. California law, for instance, allows state veterinarians from the California Drug and Food Administration to drug test any horse show in California, sanctioned or otherwise. Most European Union countries now have commonly restricted use of NSAIDs in horses in general, although veterinarians in the UK have fought what they see as a restriction on their ability to practice freely to promote optimal health and pain relief in their equine patients.

Depending upon the governing body, the rider may also be subject to drug testing during a competition. Any competitor identified by the national federation as an international level competitor is also subject to random, unannounced, out-of-competition drug testing by the national federation at any time.

References

1. Anonymous. FEI Rules for Dressage Events. Fédération Equestre Internationale, Lausanne, Switzerland, 1999.
2. Anonymous. FEI General Regulations. 2000. Fédération Equestre Internationale, Lausanne, Switzerland.
3. Anonymous. USA Equestrian 2002 Rulebook. USA Equestrian, Lexington, Kentucky, November 2001.
4. Anonymous. FEI Rules for Eventing. Fédération Equestre Internationale, Lausanne, Switzerland, 2003. www.horsesport.org, 3 October 2002.
5. Foreman JH. Modifications to the 1996 Olympic 3-Day-Events to optimise safety under hot and humid conditions. Pferdeheilkunde 1996; 12:397–400.
6. Foreman JH. Thermoregulation in the horse exercising under hot and humid conditions. Pferdeheilkunde 1996; 12:405–408.
7. Foreman JH. Olympic horses, heat and humidity. Atti Accademia Peloritana dei Pericolanti 1998; 84:15–32.
8. Foreman JH. The exhausted horse syndrome. Vet Clin North Am Equine Pract 1998; 14:205–219.
9. Foreman JH, Grubb TL, Benson GJ, et al. Physiological effects of shortening steeplechase in a 3-day-event. Equine Vet J 1995; Suppl 20:73–77.
10. Foreman JH, Grubb TL, Benson GJ, et al. Acid–base and electrolyte effects of shortening steeplechase in a 3-day-event. Equine Vet J 1996; Suppl 22:85–90.
11. Kohn CW, Hinchcliff KW, McCutcheon LJ, et al. Physiological responses of horses competing at a modified 1 Star 3-day-event. Equine Vet J 1995; Suppl 20:97–104.
12. Hinchcliff KW, Kohn CW, Geor R, et al. Acid:base and serum biochemistry changes in horses competing at a modified 1 Star 3-day-event. Equine Vet J 1995; Suppl 20:105–110.
13. Jeffcott L, Kohn C, Mayo J. Three-day event competition at the 1996 Olympics. The Equine Athlete 1996; 9(4):12a–12d.

14. Jeffcott LB, Kohn CW. Contributions of equine exercise physiology research to the success of the 1996 Equestrian Olympic Games: A review. Equine Vet J 1999; Suppl 30:347–355.
15. Anonymous. FEI Statutes. Fédération Equestre Internationale, Lausanne, Switzerland, 1999.
16. Anonymous. World Breeding Federation for Sport Horses. www.wbfsh.org, 12 October 2002.
17. Barrey E, Desliens F, Poirel D, et al. Early evaluation of dressage ability in different breeds. Equine Vet J 2002; Suppl 34:319–324.
18. Anonymous. French horses medal at World Equestrian Games. www.sellefrancais.org, 29 October 2002.
19. Anonymous. FEI Veterinary Regulations. Fédération Equestre Internationale, Lausanne, Switzerland, 2002.
20. Clayton HM. Conditioning sport horses. Saskatoon, Canada: Sport Horse Publications; 1991.
21. Dyson S, Wright I, Kold S, et al. Clinical and radiographic features, treatment and outcome in 15 horses with fracture of the medial aspect of the patella. Equine Vet J 1992; 24:264–268.
22. Dyson S. Stifle trauma in the event horse. Equine Vet Educ 1994; 6:234–240.
23. Dyson S. Patellar injuries. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:440–447.
24. Valberg SJ. Muscular causes of exercise intolerance in horses. Vet Clin North Am Equine Pract 1996; 12:495–515.
25. MacLeay JM, Valberg SJ, Geyer CJ, et al. Heritability of recurrent exertional rhabdomyolysis in Thoroughbred racehorses. Am J Vet Res 1999; 60:250–256.
26. MacLeay JM, Valberg SJ, Pagan JD, et al. Effect of diet on Thoroughbred horses with recurrent exertional rhabdomyolysis performing a standardized exercise test. Equine Vet J 1999; Suppl 30:458–462.
27. Foreman JH. Metabolic causes of equine exercise intolerance. Vet Clin North Am Equine Pract 1996; 12:537–554.
28. Cox JH. An episodic weakness in four horses associated with intermittent serum hyperkalemia and the similarity of the disease to hyperkalemic periodic paralysis in man. Proc Am Assoc Equine Pract 1985; 31:383–391.
29. Spier SJ, Carlson GP, Harrold D, et al. Genetic study of hyperkalemic periodic paralysis in horses. J Am Vet Med Assoc 1993; 202:933–937.
30. Valentine BA, Van Saun RJ, Thompson KN, et al. Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. J Am Vet Med Assoc 2001; 219:1537–1544.
31. Harmon J. Tack and saddle fit. Vet Clin North Am Equine Pract 1999; 15:247–261.
32. Haussler KK. Osseous spinal pathology. Vet Clin North Am Equine Pract 1999; 15:103–112.
33. von Schweinitz DG. Thermographic diagnostics in equine back pain. Vet Clin North Am Equine Pract 1999; 15:161–177.
34. Weaver MP, Jeffcott LB, Nowak M. Radiography and scintigraphy. Vet Clin North Am Equine Pract 1999; 15:113–129.
35. Martin BB Jr, Klide AM. Use of acupuncture for the treatment of chronic back pain in horses: Stimulation of acupuncture points with saline solution injections. J Am Vet Med Assoc 1987; 190:1177–1180.
36. Klide AM, Martin BB Jr. Methods of stimulating acupuncture points for treatment of chronic back pain in horses. J Am Vet Med Assoc 1989; 195:1375–1379.
37. Martin BB Jr, Klide AM. Treatment of chronic back pain in horses. Stimulation of acupuncture points with a low powered infrared laser. Vet Surg 1987; 16:106–110.
38. Meagher J. Beating muscle injuries for horses. Hamilton, MA: Hamilton Horse Association; 1985.
39. Porter M. Equine sports therapy. Wildomar, CA: Veterinary Data; 1990.
40. Snader ML. Willoughby SL, Khalsa DK, et al. Healing your horse – alternative therapies. New York: Macmillan; 1993.
41. Denoix J-M, Pailloux J-P. Physical therapy and massage for the horse. North Pomfret, VT: Trafalger Square Publishing; 1996.
42. Haussler KK. Chiropractic evaluation and management. Vet Clin North Am Equine Pract 1999; 15:195–209.
43. Wolf L. The role of complementary techniques in managing musculoskeletal pain in performance horses. Vet Clin North Am Equine Pract 2002; 18:107–115.
44. Kohn CW. Guidelines for horse transport by road and air. New York: American Horse Shows Association; 1999.
45. Austin SM, Foreman JH, Hungerford LL. Case-control study of risk factors for development of pleuropneumonia in horses. J Am Vet Med Assoc 1995; 207:325–328.
46. Kollias-Baker C, Stanley D. Detection of albuterol administered to performance horses with Torpex® (aerosol albuterol sulfate) device. In: Torpex® (aerosol albuterol sulfate) technical research review. St Joseph, MO: Boehringer Ingelheim Vetmedica; 2002:11–13.
47. Dirikolu L, Mollett BA, Troppmann A, et al. Apparent ELISA detection times for albuterol after administration with the Torpex® equine inhaler device. Vet Ther 2002; 3:297–307.
48. Murray MJ, Eichorn ES. Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. Am J Vet Res 1996; 57:1599–1603.
49. Andrews FM, Ralston SL, Williamson LH, et al. Weight loss, water loss and cation balance during the endurance test of a 3-day-event. Equine Vet J 1995; Suppl 18:294–297.
50. Harris PA, Marlin DJ, Scott CM, et al. Electrolyte and total protein changes in nonheat acclimated horses performing treadmill exercise in cool (20 C/40% RH), hot, dry (30 C/40% RH) or hot, humid (30 C/80% RH) conditions. Equine Vet J 1995; Suppl 20:85–96.
51. Carlson GP. Hematology and body fluids. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications; 1987:393–425.
52. Briggs K. Tragedy at 1998 Rolex Kentucky CCI***. The Horse, June 1998, p 59.
53. Rasin B. Nothing dampens Vinoski's first four-star win at Rolex Kentucky. Chronicle of the Horse 2002; 65:8–17.
54. Vischer CM, Foreman JH, Constable PD, et al. Hemodynamic effects of thyroidectomy in sedentary horses. Am J Vet Res 1999; 60:14–21.
55. Foreman JH. Hematological and endocrine assessment of the performance horse. In: Robinson NE, ed. Current therapy in equine medicine 3. Philadelphia: WB Saunders; 1992:807–809.
56. Pittenger PJ. Reschooling the thoroughbred. Menasha, WI: Russell Meerdink; 1991.
57. Kohn CW, Hinchcliff KW. Physiological responses to the endurance test of a 3-day-event during hot and cool weather. Equine Vet J 1995; Suppl 20:31–36.
58. Geor RJ, McCutcheon LJ, Ecker GL, et al. Thermal and cardiorespiratory responses of horses to submaximal exercise under hot and humid conditions. Equine Vet J 1995; Suppl 20:125–132.
59. Harris PA, Marlin DJ, Mills PC, et al. Clinical observations made in nonheat acclimated horses performing treadmill exercise in cool (20 C/40% RH), hot, dry (30 C/40% RH) or

hot, humid (30 C/80% RH) conditions. Equine Vet J 1995; Suppl 20:78–84.
60. Kohn CW, Hinchcliff KW, McKeever KH. Effect of ambient temperature and humidity on pulmonary artery temperature of exercising horses. Equine Vet J 1999; Suppl 30:404–411.
61. Williamson L, White S, Maykuth P, et al. Comparison between post exercise cooling methods. Equine Vet J 1995; Suppl 18:337–340.
62. Kohn CW, Hinchcliff KW, McKeever K. Evaluation of washing with cold water to facilitate heat dissipation in horses exercised in hot, humid conditions. Am J Vet Res 1999; 60:299–305.
63. Bradbury G, Allen AK. Equi-mist fan/mist system evaluation. In: Clarke AF, Jeffcott LB, eds. On to Atlanta '96. Equine Research Centre, University of Guelph, Guelph, Ontario, Canada, 1995:75–78.
64. Butudom P, Schott HC, Davis MW, et al. Drinking salt water enhances rehydration in horses dehydrated by frusemide administration and endurance exercise. Equine Vet J 2002; Suppl 34:513–518.
65. Lawrence L, Jackson S, Kline K, et al. Observations on bodyweight and condition of horses in a 150-mile endurance ride. J Equine Vet Sci 1992; 12:320–324.
66. Schott HC II, McGlade KS, Molander HA, et al. Bodyweight, fluid, electrolyte, and hormonal changes in horses competing in 50- and 100-mile endurance rides. Am J Vet Res 1997; 58:303–309.
67. Sosa Leon LA, Davie AJ, Hodgson DR, et al. Effects of oral fluid on cardiorespiratory and metabolic responses to prolonged exercise. Equine Vet J 1995; Suppl 18:274–278.
68. Sosa Leon LA, Davie AJ, Hodgson DR, et al. The effects of tonicity, glucose concentration and temperature of an oral rehydration fluid solution on its absorption and elimination. Equine Vet J 1995; Suppl 20:140–146.
69. Sosa Leon LA, Hodgson DR, Evans DL, et al. Effects of hyperhydration on cardiorespiratory and metabolic responses to exercise in horses during a simulated 2nd day of the 3-day-event. Pferdeheilkunde 1996; 12:459–462.
70. Geor RJ, McCutcheon LJ. Hydration effects on physiological strain of horses during exercise-heat stress. J Appl Physiol 1998; 84:2042–2051.

CHAPTER 52

Veterinary aspects of endurance riding

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Overview of the sport

Endurance riding is an internationally recognized sport in which a horse and rider team covers a designated course within a set time. Although horses have been used for centuries to transport people over long distances, the sport of endurance racing originated in the USA relatively recently, and then spread rapidly to Australia and other parts of Oceania, Europe and the Middle East. The Western States (USA) 100 has run continuously since 1955 and involves a one-day event that has a 7500 foot elevation change over a challenging terrain. A well-known eastern US event, the Old Dominion, is a 100-mile event that has been run for 29 years. In the USA, the major endurance organization, the American Endurance Ride Conference (AERC), was started in 1972 and now sanctions over 700 rides annually. In 1990, an endurance event was held at the first World Equestrian Games in Stockholm. In 1992, the Fédération Equestre Internationale (FEI) recognized endurance riding. With this sanction, endurance racing became a truly international equine sport (Table 52.1). At the 2002 World Endurance Championship, a total of 36 countries participated. In 2002, the Pan American Endurance Championship had nearly 90 horses participating from nine countries. Some countries have established endurance programs dating back to the 1960s, while in other countries the sport is new. In most of these countries, the rules of endurance racing are very similar to the FEI rules, although the courses and climate can be quite different.

Endurance rides vary in distance from 20 to 480 km, although single day rides are usually between 40 and 160 km (25–100 miles). Single day events are the most common, although some rides last several days and cover several hundred kilometers. FEI-sanctioned rides must be over 80 km.[1] The course has multiple check points (known as 'vet gates') at which veterinarians inspect the horses and determine whether or not the horse may continue in the race.[2] The first horse and rider to cross the finish line are declared the winners, but only if the horse is judged to be sound upon completion. Emphasis is on completing the event safely (to finish is to win) and formal recognition is made of the top finisher (usually in the first 10 placings) that is in the best overall physical condition.[3]

The wellbeing of the horse is emphasized and the veterinarian plays a key role in this regard. The veterinarian has complete control concerning fitness to continue during an event. Riders also place a premium on welfare of the horse; they are generally very respectful of veterinary judgments, even in those situations in which the horse is removed ('pulled') from competition. The use of heart rate monitors for continuous assessment of the horse's heart rate is common.

Types of horses

Arabians and Arabian-crosses are the predominant breed used for endurance riding. This distinction is probably based on their muscle fiber composition[4] and a preferential ability to utilize lipid during submaximal exercise.[5] That said, mules, Tennessee walkers, and a mix of other breeds can be seen in any endurance event. The monetary value of horses participating runs a large gamut, ranging from horses trained in the stables of Sheiks to the 'backyard' horse.

Endurance horses are typically of a lean, medium build, 14-2 to 15-1 hands tall, with bodyweight ranging between 390 and 480 kg (850 to 1050 pounds). Deep chest, medium to short back, and correct legs are other desirable physical characteristics. The feet should be large, medium to short toed, strong walled and set to support the leg. The movement

Table 52.1 A list of different organizations sponsoring or sanctioning endurance rides in different countries. This is not meant to be a complete listing as there are myriad local and regional horse groups that participate in endurance and trail riding

Country	Organizations
Australia	Australian Endurance Ride Association; The Victorian Endurance Riders Assoc (VERA)
Austria	Verein Osterrichischer Distanzreiter
Belgium	Belgium Equestrian Endurance League
Brazil	Enduro Equestre
Canada	Atlantic Canada Trail Riding Association; Canadian Long Distance Riding Association; Endurance Riders Association of British Columbia, Endurance Riders of Alberta
Chile	Carreras y Caballos (Chile)
France	Comité Endurance Equestre de la Region de Versailles; Comité National des Raids Equestres d'Endurance; National Committee of France Endurance Riders
Germany	Verein Deutscher Distanzreiter, 40–80+ km rides
Guatemala	Grupo Endurance de Guatemala
Holland	Dutch Endurance Riders (DER); Nederlandse Vereniging van Lange Afstandsruiters
Italy	Associazione Nazionale per il Turismo Equestre e per l'Equitazione di Campagna; Gruppo Italiano Endurance
New Zealand	Canterbury Endurance and Trail Riding Club (25–160 km); Counties Distance Riding Club (Auckland); New Zealand Endurance and Competitive Trail Riding Association (first ride in 1970)
Slovenia	Slovenian Endurance Committee
South Africa	Endurance ride association of South Africa, in 2003, 82 races with distances of 80–480 km
Sweden	Distans Uppland
Switzerland	European Long Distance Riders Conference; Swiss Endurance Distanzreiter
UAE	UAE Equestrian and Racing Federation, established 1992
UK	Welsh Long Distance Riding Center The British Horse Society Endurance Riding Group Long Distance Riding Center (Gloucestershire); The Endurance Horse and Pony Society; Scottish Endurance Riding Club founded in 1982; Irish Long Distance Riding Association; British Equestrian Federation (Endurance GB)
USA	AERC, IAHA USA Equestrian Nation Rides 50–300 miles sanctioned by AERC and USA Federations; Ride and Tie Championship, now on its 33rd (2003) 30 mile event – Ride and Tie Association

of the horse's legs must be smooth and efficient. Any movement away from the axis of a leg during the swing phase of the stride, such as winging out, is a weakness. Long sloping pasterns that place the heels under the front of the cannon bone are also a weakness.

Control veterinarian

This individual takes responsibility for knowing the rules (regulations are provided by each sanctioning group, e.g. AERC or FEI) and controlling the flow of the ride. The control veterinarian determines and sets the criteria for heart and respiratory rates required for a horse to continue in a race (common criteria would be a heart rate of 60 beats per minute and a respiratory rate of 40 per minute). In hot and humid climates, particularly when the heat index is high, the time to reach target heart and respiratory rates may be lengthened to ensure adequate recovery. Throughout the ride, as weather conditions change, the control veterinarian can dictate changes in these control parameters. The control veterinarian also attempts to ensure uniformity in veterinary assessment throughout the race. There are likely to be several veterinarians seeing multiple horses, but not necessarily the same one throughout a race.

Treatment veterinarians

These individuals, acting under the supervision of the control veterinarian, participate in horse assessment pre-ride and during the ride itself. The role of the treatment veterinarian is to treat problems encountered at the ride. The intermingling of 50 to 250 horses at one venue increases the likelihood of infectious disease. As well, life-threatening metabolic conditions somewhat unique to horses engaged in endurance races are common. The treatment veterinarian must be skilled in the early recognition and treatment of these problems. Even a short delay in treatment until clinical signs are advanced can result in poor outcome. The treatment veterinarian must be prepared for the worst-case scenario that may occur in a remote area. Treatment rates at rides vary from 2% to 20% of the entries, and it is not unusual for 10% of the entries (at a high-profile ride) to require treatment for metabolic disease. One horse with a metabolic condition may require 50 or more liters of

intravenous (i.v.) fluid. Therefore, it is mandatory for the veterinarian to have a large supply of i.v. fluids.

Team veterinarian

The role of the team veterinarian is to help the horse and rider prepare for a competition (usually a championship) and assist them during the competition. This usually involves working with a team of people such as the farrier, physiotherapist, private veterinarian and the horse's support group.

Pre-ride inspection

Baseline data are collected prior to the start of the ride. A physical examination includes auscultation of the heart, lungs and abdomen, assessment of hydration state (skin pinch and capillary refill time), and examination for any pre-existing cuts, scrapes, bruises, tack sores, etc. The horse should then be trotted out (40 m) and back for assessment of gait and soundness. After the trot, a more complete lameness examination, including flexion tests and digital palpation (particularly to assess tendon/suspensory problems), may be indicated. Palpation of the back using gentle pressure is important for evaluation of soreness. Tone of the gluteal and semitendinosus muscles is also determined. Careful recording of these data on a ride card provides an important baseline for temporal monitoring of the horse's performance throughout the race.

Vet gates

Ride management, usually in consultation with the control veterinarian, determines the location and number of vet gates. Horses coming into these gates have their arrival time noted on the card and may not leave until a certain time has elapsed and/or they have reached the heart and respiratory rate criteria. A commonly used test is called the ridgeway trot or cardiac recovery index (CRI). After measurement of the pulse rate, the horse is trotted to a point 40 meters away and trotted back. The horse's pulse is recounted 60 seconds after the *start* of the trot. If the pulse rate recovers to the original pulse (± 4 beats), then the horse is considered metabolically stable. If the horse's pulse is more than 4 beats above the original value, the horse is examined more closely. If the recovery pulse is greater than 12 beats above the original value, an underlying metabolic problem should be considered. General physical and lameness examinations are also performed at many of these gates and the results are recorded on the ride card that accompanies the horse and rider.

Finish

A post-race physical and lameness examination is done to identify the 'best of condition' finisher (usually out of the top 10 finishers) but more importantly, to identify potential metabolic problems. Best Condition is the award given to the horse judged to be in the best condition after the completion of the ride – the soundness of the horse along with metabolic parameters and signs of wear and tear are scored. Some riders would rather win the best condition accolade than finish first.

Metabolic conditions

Metabolic conditions secondary to dehydration, electrolyte and acid–base abnormalities, heat accumulation and substrate depletion are common in endurance horses and can be life-threatening. Sweat fluid losses as high as 15–20 liters per hour may occur during the course of a ride. Therefore, some degree of dehydration is the norm rather than the exception.[6] Any endurance horse in metabolic distress should receive *at least* 15 to 20 liters of fluids, preferably via the i.v. route. Figure 52.1 provides one view of a field hospital where large amounts of fluid can be delivered on site.

Exhaustion

Exhaustion is due to the compound effects of dehydration, electrolyte imbalances, heat accumulation and substrate depletion.[7] The condition carries a favorable prognosis if recognized and treated early in the clinical course. On the other hand, a delay in treatment can lead to life-threatening complications such as laminitis and renal failure. Presenting history is variable but may include depression, stumbling or weak gait, lameness, depressed appetite, anorexia, dehydration and an unwillingness to drink, and a facial expression often described as 'glazed-over', 'blank' or 'grimaced'. Affected horses are often dehydrated with dry mucous membranes; membranes may demonstrate peripheral congestion

Fig. 52.1
The mobile animal super-rehydration hospital (MASH) at the Western States 100 endurance ride. The trailer contains cases of fluids. Three liter bags are hoisted up the side of the trailer to provide rapid gravity flow i.v. infusions. Photograph by SJW.

(margination of the gum line). Heart rate recovery is often delayed, seldom dropping below 64 beats/min in the CRI test. Gastrointestinal sounds may be diminished or absent, and there may be signs of colic. The stool may be covered in mucoid material. Signs of hyperthermia, myositis, and synchronous diaphragmatic flutter also may be present.

Blood analysis usually reveals findings consistent with dehydration and electrolyte depletion. The total protein concentration can be greater than 8 g/dL, packed cell volume (PCV) greater than 50%, blood glucose concentration decreased, creatine phosphokinase and aspartate aminotransferase activities elevated, and total carbon dioxide or bicarbonate concentrations decreased (alkalosis). Electrolyte abnormalities often include hypocalcemia, hyponatremia, hypochloremia, hypokalemia and hypomagnesemia.

The primary goals of therapy are to rehydrate and refuel the horse. In mild cases of exhaustion, a longer 'hold' period (e.g. additional 30–60 min) in the vet gate often facilitates recovery. This extended rest allows the horse to eat and drink, thereby replacing fluid and electrolyte deficits. Importantly, the rider must be instructed to significantly slow the pace of the ride. If the horse is removed from competition, further treatments can be administered. It is important to consider the duration of transportation between race venue and the home farm or stable. Long transportation periods will place additional stress on the exhausted horse. Clinical experience has shown that aggressive rehydration will help the horse recover quickly and make the trip home less stressful. If the horse has a functional gastrointestinal tract, it is helpful to rehydrate by administering 4 to 6 liters of isotonic water through a nasogastric tube. This can be repeated every 30 to 60 minutes as needed. In most cases the authors prefer to employ the i.v. route due to ease of fluid administration and comfort to the horse – 15 to 20 liters should be given initially, with the administration of further fluid if the horse does not urinate.

The prognosis for uncomplicated exhaustion is good. However, exhaustion that is complicated by colic, persistent hyperthermia or laminitis carries a more guarded prognosis. Prevention of exhaustion is reliant on the skill of the rider in managing race speed in relation to horse fitness, weather, competition conditions, and trail conditions. More aggressive electrolyte supplementation regimens also may be indicated in horses with a history of exhaustion in previous rides.

Hyperthermia

The metabolic consequences of sustained exercise include the accumulation of a substantial heat load.[8] A failure to balance this heat gain with heat loss leads to an excessive elevation in body temperature that decreases athletic performance and can be potentially fatal. When the gradients for convective, conductive and radiant heat loss are small or non-existent (typical of a sunny, hot and humid day), the *only* mechanism for heat loss is evaporation. When humidity is high, heat loss by this mechanism is also inefficient. Some horses develop an inability to sweat (anhidrosis) that exacerbates the occurrence of excessive hyperthermia.[9] Typically these horses are raised in cooler climates and the onset is precipitated by transport to and performance in hot and/or humid climates.

At veterinary checkpoints, riders will complain that their horse is tired. If the horse is trotted out for a lameness examination, it will show poor impulsion. These horses have delayed recovery rates, and may present with an elevated heart rate. Respiratory rates are elevated and may be rapid and shallow (panting). Rectal temperature is often greater than 40°C (104°F). Borborygmi are diminished (or may be absent) and there may be signs of dehydration. Blood parameters may be normal or indicative of hemoconcentration (increased plasma total protein and PCV).

The primary goal of treatment is to cool the horse rapidly. All tack should be removed and the horse moved to a shaded area. Aggressive cooling can be done with large quantities of water applied with a hose or sponge. Cool (or, in very hot conditions, ice cold) water is preferred as it creates the largest gradient for heat transfer between the skin and the applied water. Water should be applied over the entire animal, including neck and legs. Repeated cycles of water application and removal (using a scraper) are necessary for continued heat loss at the skin surface. Controversy exists on the use of cold water over the lumbar and gluteal muscles.[10] One of the authors (MAF) avoids cold water in this area with the experience that this practice can result in muscular cramping. Isopropyl alcohol may be added to the cooling wash. The use of ice water enemas has been advocated in severe situations. Misting fans and sprayers are very useful when available.

The effectiveness of cooling procedures is easily monitored by frequent measurement of rectal temperature. Once rectal temperature falls below 40°C (103.5°F), cooling efforts can be discontinued. As hyperthermic horses are dehydrated, hydration status should be assessed and appropriate fluid therapy provided.

The prognosis for recovery is good, but failure to resolve the hyperthermia may lead to exhaustion, colic, heat stroke and potentially death. There are two facets to the prevention of excessive hyperthermia. First, the rider must be willing to decrease racing speed when environmental conditions compromise heat loss. Second, close attention must be paid to the monitoring of body temperature and hydration state during rides.

Colic

Endurance horses often experience colic during or soon after a ride. Although the etiology of these colic episodes is not known, it is likely that dehydration and acid–base and electrolyte abnormalities predispose to disturbances in gastrointestinal function, including ileus. Clinical signs are variable, ranging from mild to severe abdominal pain. In the authors' experience, failure to recognize and treat mild colic in endurance horses can contribute to the development of more serious conditions (anterior enteritis, impactions, strangulation, or even death).

Initial clinical complaints may be mild and vague. For example, a rider may state that the horse is 'just not right'.

During rest periods or even on the trail, the rider may report that the horse is unwilling to eat, or that it appears colicky after eating. Painful episodes vary from mild to uncontrollable. Greatly diminished or absent borborygmi are a consistent finding. Mucous membranes are often dry (dehydration) and may be congested. The horse's energy level will vary from slightly to severely depressed. Palpation per rectum should be done with extreme care because the rectal mucosa may be very dry and friable. In horses with ileus, small intestinal distension may be detected. Laboratory findings are non-specific, but may include evidence of metabolic alkalosis (pH > 7.5), hypokalemia, hypocalcemia, hypochloremia and hemoconcentration.

The therapeutic aims are to reduce pain and correct fluid deficits and electrolyte imbalances. Butorphanol, detomedine and xylazine are the first choice drugs for management of pain. Low doses of flunixin meglumine can be used but only after correction of dehydration. Intravenous fluids should be given, with a minimum dose of 15 to 30 liters administered over a 60 to 90 min period. Fluid therapy should be continued until the horse urinates and gut sounds return. In the authors' experience, as much as 80 liters of fluid can be required for complete rehydration and restoration of normal gastrointestinal function. It is advisable to leave a nasogastric tube in the stomach during treatment because in some horses small intestinal distension and gastric reflux develops during the rehydration process. For this reason, close monitoring is required if the oral route is used for fluid administration. If oral fluids are given, they should be administered in small amounts and frequently, e.g. 4 to 5 liters every 30 to 60 minutes. Some veterinarians also favor the use of intestinal stimulants in horses with non-obstructive colic (see the 'Medications' section).

A key to preventing colic during and after endurance rides is the early recognition of dehydration. Adequate electrolyte administration during the ride, provision of palatable drinking water, and modulation of the intensity of the ride based on ambient conditions are essential. When diminished gut sounds are first recognized, the horse should be rested and given time to eat and drink. Thereafter, the horse may continue the ride at a slower speed.

Exertional rhabdomyolysis (tying up, Monday morning disease)

Exertional rhabdomyolysis (ER) appears in two syndromes in the endurance horse. The first and most common syndrome is seen early in the ride, usually before the 20-mile point. The second syndrome is observed later in the ride, usually after 50 miles. They both are treated similarly but may have different predisposing factors.

The early-onset ER may occur within just a few miles of the race start. Often the rider reports an abnormal behavior of the horse, such as cantering but reluctance to trot, extreme anxiety or just not moving out normally. Upon clinical examination, the horse may be reluctant to move or lame with a shortened stride. Swollen gluteal or lumbar muscles are often detected. On rare occasions, the horse may be recumbent and unwilling to rise. Sometimes the first sign is simply an elevated pulse in the vet gate.

Horses with the later onset ER seldom have swollen muscles and may not be lame. The overall clinical picture is one of exhaustion and a diagnosis of ER is often based on recognition of myoglobinuria and/or elevated muscle enzyme activities. Some affected horses will be persistently tachycardic (usually above 60 beats/min), and it is often possible to elicit muscle cramping or spasm when the lumbar or hindlimb muscles are carefully palpated.

Measurement of serum muscle enzyme activities (creatine kinase (CK) and aspartate aminotransferase (AST)) is key to the diagnosis. In this regard, the advent of portable analyzers has been useful in facilitating rapid diagnosis.[11] Serum electrolyte values are usually within normal limits.

Prompt and aggressive treatment is required in horses with ER. In particular, horses with evidence of myoglobinuria require i.v. fluid therapy to avoid development of pigment nephropathy. Fluid delivery rates as high as 15–20 liters per hour are recommended until the horse urinates. The rate of administration should then be decreased to 5 to 10 liters per hour and maintained at this rate until the urine is clear. Pain may be controlled by use of butorphanol (0.01–0.02 mg/kg), detomidine (5–10 μg/kg) or xylazine (0.2–0.5 mg/kg). Flunixin meglumine must be used with caution as clinical experience has indicated that even low doses (0.5 mg/kg) have been associated with development of renal failure in dehydrated endurance horses. Acepromazine (0.02 mg/kg) for vasodilation can be used in conjunction with i.v. fluids. As dysregulation of calcium flux in skeletal muscle is one proposed mechanism for development of ER,[12] the use of dantrolene sodium (6–10 mg/kg via nasogastric tube) has been advocated in the treatment of clinical episodes. Massage and heat treatment of the affected muscles can be effective. Hot packs can be improvised by heating water, soaking a towel in the hot water and then enclosing the towel within a plastic bag. This approach will keep the horse's hair dry, thereby preventing chilling when the hot pack is removed. The horse should be blanketed during treatment. The protocol is to apply heat and massage for 30 minutes followed by 30 minutes of rest. Hot packing and massage are continued until the muscle softens. Electrical stimulation of affected muscles may also be effective for attainment of muscle relaxation. Acupuncture is another treatment modality favored by some clinicians. Transportation of the horse can exacerbate the condition and should be delayed until the horse is stabilized.

With appropriate and aggressive treatment, the prognosis for recovery is good. It is possible, but not recommended, to have a horse compete successfully within a few weeks of a very serious ER episode.

There are a number of theories relating to the pathophysiology of ER.[13,14] However, no specific etiology has been identified for ER in endurance horses, although, anecdotally, long-distance transportation has been identified as a predisposing factor. In addition, horses that develop ER during rides often have had a 1–2 week period of lay-up just prior to a competition. Preventive strategies in horses with a history of

repeated episodes of ER include feeding higher-fat, lower-starch diets, the elimination of grass pasture from the diet, and the maintenance of a regular training schedule in the weeks preceding the ride.[14,15]

Synchronous diaphragmatic flutter (SDF, thumps)

Development of SDF is relatively common in endurance horses[16] and is indicative of underlying fluid, electrolyte and acid–base disturbances (see Chapter 40). The incidence of SDF increases in hot and humid conditions, when the horse is ridden at speeds beyond its current level of conditioning, or when the first 20 miles of the ride are run at a fast pace. All of these factors promote large sweat fluid losses with attendant dehydration, acid–base and electrolyte disturbances. Riders often do not detect the SDF and require counseling regarding the underlying cause and prevention of the problem. Clinical signs of SDF can develop at various distances along the ride and are often noticed while evaluating heart rate.

The striking clinical feature is contraction of the diaphragm and flank that coincides with cardiac contraction. As a result, respiratory and heart rates are similar. Even after a mandatory hold when heart rate has returned to the release criterion (e.g. 60 beats/min), respiratory rate remains elevated. In severe cases the entire body appears to jump with the diaphragmatic contraction. Heart rate may be elevated and gut sounds are usually diminished or absent. Often the horse appears dehydrated and tired.

There are no other conditions that mimic SDF. However, the clinician must determine whether other conditions exist, e.g. dehydration, overheating, ER. Dehydration is usually the most significant additional factor. Results of a serum biochemical analysis can reveal some or all of the following: alkalosis, hypokalemia, hypocalcemia, hypochloremia, and hyperproteinemia.[17] Response to treatment with calcium is considered proof of the diagnosis.

The cornerstone of treatment is the administration of calcium-containing solutions. The horse should be withdrawn from the ride. Even in the absence of serum biochemical testing, it is reasonable to assume that horses with clinical signs of SDF are dehydrated, hypocalcemic and alkalemic. One of the authors (MAF) initially administers 125 ml of 23% calcium borogluconate that is diluted in 1 liter of saline or other polyionic fluid. The heart should be asculted during calcium administration; the rate of fluid administration should be slowed or discontinued if tachycardia or arrhythmias develop. Further calcium should be given until resolution of thumping. Large volume fluid replacement is usually indicated in horses with SDF; additional calcium may be added to these fluids and administered over the next few hours. If i.v. fluids and calcium are not available, the horse should be allowed access to forage, preferably leafy alfalfa, and encouraged to drink. Oral electrolytes with calcium should be provided when possible. An alternative approach to therapy is to administer 500 mL of calcium borogluconate by mouth.

The prognosis for SDF recovery alone is excellent when appropriate treatment is used. The underlying dehydration must be corrected. Prevention strategies are aimed at minimizing electrolyte imbalances during rides, specifically decreases in ionized calcium. Therefore, appropriate supplementation of oral electrolytes should be practiced during the ride (see 'Oral electrolytes' section). At times it is necessary to adjust the composition of the electrolytes to meet the needs of individual horses. The effectiveness of the supplementation strategy can be assessed by analysis of blood samples collected under competition conditions. It is recommended to reduce alfalfa intake prior to an event. Grass hay is preferred but oat hay is suitable when grass hay is not available.

Laminitis

Laminitis is a possible sequel of any metabolic problem, but may not be clinically apparent for several days after resolution of the metabolic crisis. Consequently, riders should be advised to observe the horse closely for several days after treatment of metabolic problems. Aggressive treatment of the primary problem, including correction of fluid deficits, is the most important preventive measure. It is beyond the scope of this chapter to address the treatment of laminitis.

Lameness

Lameness is the most common reason for elimination from competition. This section will briefly describe the lameness problems most commonly encountered in endurance horses. More in-depth description of these conditions can be found elsewhere in this text.

Suspensory desmitis

This condition is the most common cause of lameness in endurance horses. If not diagnosed early, it can lead to a long layoff or to termination of a competitive career. Although common, suspensory desmitis is often difficult to diagnose. For example, affected horses can appear sound after a warm-up. Important history includes recent competition in soft, sandy or muddy terrain.

Palpation of the leg is important. The ligament may be of normal size, shape, and texture; there seldom is visible swelling of the ligament. However, it should be noted that many sound endurance horses have enlarged suspensory ligaments that are not inflamed, although there may be some degree of sensitivity to palpation. In horses with clinical desmitis, it is usually possible to locate a point of sensitivity upon careful palpation. Pain level can be slight to extreme. Confirmation of suspensory desmitis requires a diagnostic workup that does not lend itself to the field. Nerve blocks may be diagnostic but are not always conclusive. Ultrasound and radiographs are the most commonly used tools. However, thermography is sometimes helpful.

Therapy is aimed at relieving pain, eliminating predisposing factors and rehabilitation. Anti-inflammatory drugs, rest and corrective shoeing are the main components of therapy. Phenylbutazone (2 to 4 mg/kg once daily) and methylsulfomethamine (MSM; 15 ml per 450 kg) are commonly effective in the relief of pain. In acute cases (first 12 hours), ice therapy is very useful (see 'Tendinitis' section, below).

Leg and foot conformation of affected horses should be evaluated to determine the need for corrective shoeing. Heel support is essential and can be achieved by several shoeing methods, including egg bar shoes, extended heels and the wide web plastic shoes. When viewed from the side, the heel of the shoe should be directly under some portion of the cannon bone. The use of shoes that extend behind the heel must be weighed against the tendency of the horse to pull off shoes that protrude behind the heel. The length of the rest period depends on the severity of the injury. Mild cases need only a few weeks of rest, whereas a 12- to 18-month lay-up may be required for a horse with substantial fiber tearing. The results of an ultrasound examination will guide recommendations for the duration of the rest period. Furthermore, regular ultrasound examinations are useful to monitor recovery. The horse can be slowly returned to regular exercise when pain has subsided.

The prognosis for mild cases is usually excellent. On the other hand, more severe cases are prone to recurrence and can result in termination of the horse's competitive career. Prevention is aimed at minimizing conformational predisposition. It is important to work closely with a knowledgeable farrier. Long toes and low heels can predispose to suspensory injury and should be avoided. Finally one must carefully evaluate the underfoot conditions used for training in relation to those present at rides. If the horse has only been conditioned in firm footing, a competitive ride in sandy conditions will unduly stress the suspensory ligaments. Accordingly, if the horse is going to compete in deep sand, a conditioning program that includes training in similar terrain should be designed.

Tendinitis (bowed tendon)

As with distal ligaments, tendons are at high risk for injury in endurance horses. There also appears to be a higher prevalence of hindlimb tendinitis in endurance horses compared with other disciplines. Most endurance horses can recover from tendinitis and depending upon the severity, can resume mild to moderate competition. However, such injuries can be career limiting in the elite, 100-mile horse.

Muscle pain (myositis, muscle cramps, stiff)

Horses with localized muscle pain may be acutely lame or present with subtler gait abnormalities (e.g. stiff; 'not moving right'). The gluteal and lumbar muscles are most often affected, followed by the gracilis muscle. Upon physical examination, hard and/or painful areas can often be found, but it should be recognized that in many horses it is difficult to identify a source of pain. If laboratory testing is available, muscle enzyme activities and serum electrolyte concentrations should be evaluated. Myositis can elevate CK and AST dramatically, aiding in the differential diagnosis. Low calcium and potassium may contribute to muscle problems, as might low selenium.

As with true exertional rhabdomyolysis, therapy for myositis includes the use of anti-inflammatory drugs and i.v. or oral fluids. If these are muscle cramps and the rider intends to remain in the ride, no medications may be used. Acupressure, massage, heat and stretching may be tried in these circumstances. After competition, butorphanol and non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for analgesia. Electrical stimulation and acupuncture may also aid in recovery.

The prognosis for simple muscle cramps is good. Muscle cramping is often related to inadequate conditioning and holding an abnormal posture while working. Therefore, the level of conditioning should be tailored to meet the demands of the trail. Hill work often helps to decrease cramping. The identification and treatment of underlying lameness problems (e.g. sore back) may decrease the tendency for compensatory posturing.

Sore feet (stone bruise, corns, sore heels)

This lameness is usually recognized during a ride and may be intermittent, acute, chronic, related to shoeing, related to trail conditions or have no identifiable pattern. Standard diagnostic and therapeutic procedures should be applied, but particular attention should be paid to the hoof conformation and the need for corrective shoeing. Frequently, the heels of the shoe are too short and narrow. The heels should not be rolled in or crushed, and the shoe must be wide enough to support the heel even when the shoes have been in place for 5 or 6 weeks. Unbalanced feet and thin or soft soles also predispose to bruising, the former by promoting uneven loading pressures on the sole. Some variation of the egg bar shoe, wide web shoes or a combination of these designs can be used for horses with stone bruises or sore heels. Pads may be used, but it is preferred to have a correct shoe without pads. For horses with soft or thin soles, it is advisable to schedule shoeing appointments at least one week prior to a ride. Many riders will use sole 'toughener's' that consist of a mixture of tincture of iodine, acetone, alcohol and formaldehyde. If the horse lives in a moist environment and will be riding on a rocky trail, footpads should be applied. If the course is sandy, holes should be cut in the pads to prevent the trapping of sand under the pad.

Degenerative joint disease (DJD, arthritis, dry joint)

The signs of DJD include a vague lameness that progresses from lameness post-ride, to intermittent lameness during rides, and finally to a consistent lameness. Progression may

take more than a year. DJD is very common in endurance horses, perhaps because these animals are subject to very high concussive loads. The metacarpal-phalangeal joint is the most often affected, but may include the distal interphalangeal joint, and to a lesser extent, the distal tarsal-metatarsal joint. The prognosis for athletic performance is usually guarded to poor.

Therapeutic aims are to reduce inflammation, increase joint fluid quality and preserve the remaining joint. Training and competition workloads must be curtailed. Using hill and interval training techniques will allow for a decrease in the number of miles needed to condition a horse. Intra-articular steroids have limited use in endurance due to the 'no-drug' philosophy and inexact withdrawal times of the medications. However, glycosoaminoglycans and hyaluronic acid are commonly used in an attempt to improve the quality of joint fluid. Oral supplementation with glucosamine, chondroitin sulfate, and MSM is also widely practiced, although there are limited data from controlled studies to support the effectiveness of these supplements.

Interference

Interference injuries are common in endurance horses. The most common site is on the caudo-medial side of the metatarsal-phalangeal joints. Interference seems to occur when the horse becomes tired or when it is on a technical portion of the trail. Poor shoeing and conformation also contribute to this problem. Acute interference is best treated with ice, NSAIDs, and rest. Prevention is attempted through careful evaluation of hoof balance and shoeing. Boots can be applied to the leg but are not wholly protective in severe cases.

Trauma

Trauma is common in endurance riding. The terrain of the course is the most significant factor in determining the type and extent of injury. Horses are injured by events ranging from running into sticks to falling off cliffs. The veterinarian must be prepared to treat everything from a small cut to fractures and should be prepared to treat a horse in a remote area, many miles from a road.

Shoeing

Proper shoeing is essential to the endurance horse. Even a small error in shoeing will result in lameness as the hoof strikes the ground thousands of times. The most common error is the use of under-sized shoes. This results in weak support of the heels, and therefore the entire bony column of the leg. The small shoe also allows the heels of the hoof to expand over the shoe as the hoof grows, resulting in pressure on the sole rather than the wall and the development of bruising, pain and crushed heels. Hoof imbalance is also quite common. Correction of shoeing problems requires clear communication between the veterinarian, the owner and the farrier. A very useful tool is video gait analysis on a high-speed treadmill. This removes subjectivity and allows one to experiment with a variety of shoeing techniques in a short period of time.

Lameness of unknown source

During the ride, the principal role of the control veterinarian is to prevent injury (or further injury) to the horse. The first role, then, is to decide whether the horse is sound or lame, but it is beyond the expected duties to diagnose the source of pain. Rather, the team, advising or treatment veterinarian should investigate the cause of lameness. On many occasions the source of lameness will not be identified. If the horse recovers fully within two or three days it may not be necessary to establish a diagnosis, unless this is a recurring situation. In these situations, a very useful diagnostic tool is nuclear scintigraphy. Another approach for dealing with these vague lameness problems is chiropractic evaluation and treatment. While many veterinarians do not recognize the value of acupuncture and chiropractics, these modalities are used extensively in endurance horses.

Miscellaneous problems

Gastric ulcers

Clinical experience has indicated that gastric ulcer disease is common in endurance horses. Presenting clinical signs are variable but include poor appetite, weight loss, recurrent bouts of mild cold, behavioral changes after the administration of oral electrolytes, or simply a prolonged post-exercise recovery time. Physical examination may reveal little other than rough hair coat and thin body condition. A definitive diagnosis is made by endoscopic examination of the stomach. Standard anti-ulcer treatment (e.g. omeprazole) is usually effective and the prognosis is good.

Tack injuries

The endurance horse has more opportunity for tack injuries than most horses simply due to the time the tack is on the animal. Injury commonly occurs at the girth, over the back, at the corners of the mouth, rostral jaw and on the medial aspect of the metacarpal- or metatarsal-phalangeal joints. During a ride, the application of ice to these lesions is beneficial. If not in competition, NSAIDs along with topical cortisone are helpful. Insuring properly fitted tack is the key to treatment and prevention. Some materials do not work for certain horses and the rider must keep trying additional designs and/or materials. Sheepskin and neoprene products seem to work well. These materials still have to be kept smooth, clean and free of plant material.

The boots worn on the legs of horses can cause as many problems as they are supposed to prevent. 'Splint boots' and 'interference boots' must fit properly and not slide while the horse is working. In certain conditions the boots will trap sand and cause abrasion. The heavy boots that enclose most of the leg can trap heat and actually precipitate dermatitis. It is the authors' opinion that 'sports medicine boots' are inappropriate for endurance horses. Other types of protective boots should only be worn during the part of the competition where injury is likely, such as the last part of the ride or a particularly rocky section of the trail. There is no indication that boots reduce concussion.[18]

Back pain

Back pain is very common in endurance horses and is probably responsible for many cases of poor performance and 'sour' attitude. However, back pain tends to be underdiagnosed and poorly treated. Back pain can present as lameness, a reluctance to work, bucking/rearing, or more subtle changes. A thorough physical examination of the back begins with a soft touch using the palm of the hand and gentle stroking from the withers to the pelvis. Next, the same area is re-examined using fingertips and moderate pressure to identify individual muscles. It is important not to apply heavy pressure, as many normal horses will find this painful. Areas of edema and open sores can be detected using this technique. Treatment of acute back pain should be aggressive. Swollen or raw lesions should be iced. A topical solution of dilute DMSO containing dexamethasone (0.2 mg/mL) should be applied twice daily. Flunixin meglumine is the NSAID of choice. To continue training the rider may need to modify a saddle pad to prevent any pressure on the affected area (such as cutting out a piece of the pad over the affected area). The prognosis is generally good, but some horses can have recurrent problems and skill in acupuncture, chiropractic treatment and saddle fitting is required to manage these cases effectively.

Transportation-related problems

Endurance competitions attract riders from long distances. It is not unusual for horses to be transported hundreds of miles for a 'local ride'. Championships will draw horses from thousands of miles. It has become apparent that the athlete who travels long distances is at a disadvantage and is more predisposed to metabolic problems. The typical history involves a horse that competes without problems close to home but experiences metabolic problems when competing at a venue some distance from home base. This 'problem distance' is unique to each horse but approximately 500 miles is common. The most common problem in horses transported long distances to endurance rides is exertional rhabdomyolysis, followed by colic.

In many cases, no abnormalities are detected at the pre-ride examination. Some horses will be mildly dehydrated. If the transportation was undertaken in very high temperatures, dehydration can be more severe. Some horses will develop a cough if conditions are dusty. There is also risk of shipping fever (pleuropneumonia); horses with signs of depression should be evaluated for pneumonia or infectious respiratory disease. Results of serum biochemistry tests are usually within normal limits in transported horses. Any elevation in serum CK activity should be considered significant, and the horse considered at high risk for development of myositis.[19]

Experienced practitioners often think of a transported horse as a horse that will tie up unless treated correctly. This treatment focuses on rehydration and controlled exercise aimed at restoration of normal muscle function. Rehydration is accomplished through the administration of electrolyte solutions (see Chapter 64) via nasogastric tube two to three times daily until hydration is satisfactory. If CK activity is increased, a controlled exercise protocol should also be initiated. The exercise protocol begins with hand walking for 40 to 60 minutes two to three times a day for 3 days. On the fourth day, begin riding the horse twice daily. Start with only a walk and do not 'collect' the horse during these workouts. After the horse is adequately warmed up (30 minutes), begin adding a few trot steps. Trot for 10 seconds, walk for 3 minutes, trot for 20 seconds, walk for 3 minutes, trot for 30 seconds, walk for 3 minutes. Continue increasing the trot phase by small increments until the horse is trotting for 2 minutes. Walk to cool out and then stretch the horse. Thoroughly educate the rider about the very early signs of tying up. Exercise should be stopped immediately if the horse has any reluctance to trot or walk with a full stride. The horse can probably return to a normal routine when it has reached 20 minutes of continuous trotting. During this phase the horse must be carefully monitored. Measurement of CK activity on a daily basis is very important. Daily examinations and palpation of all back and leg muscles should also be performed. Muscle massage is also very useful.

Prognosis is good to excellent. Recurrence is likely in horses that have experienced metabolic problems subsequent to long-distance transportation unless a successful management plan is designed. Some horses simply do not seem capable of dealing with long-distance transport.

The cause of these conditions is speculative, although dehydration and restriction of movement during transport are suspected to be contributing factors. Most endurance horses are not kept in stalls, but rather in large paddocks where there is the opportunity for ample exercise. It is possible that when these horses are forced to stand in a small space such as a horse trailer or box in an airplane, their muscles are somehow compromised and prone to tying up.

Prevention requires planning and time. If the competitor is serious about giving the horse the best chance for optimal performance, careful planning of transportation is required. If the horse is being transported privately in a truck or trailer, the duration of transport should be not more than 10 hours per day and rest stops should be taken every 4 hours. At rest

stops, the horse must be taken out of the trailer and hand walked for 30 minutes. If possible, the horse should be allowed to graze. At one of the rest stops, it is recommended to ride the horse for 30 to 60 minutes. The horse should be fed only hay, with no grain or concentrate. The maintenance of hydration is critical. This is accomplished through the administration of water (6 to 8 liters) via nasogastric tube two to three times daily during transportation. If a veterinarian is not available for this treatment, an alternative is to dose with oral electrolytes twice daily and ensure free access to fresh drinking water (see 'Oral electrolytes' section).

If the horse is transported in a commercial vehicle, there must be adequate time to rest after the trip. Unless there is a unique circumstance, the horse must not be ridden until it has gone through the aforementioned exercise regimen. This usually requires a minimum of a week before normal exercise can be resumed. A long and strenuous trip requires two weeks.

It is now common practice to administer anti-ulcer medications prophylactically to horses traveling long distances. Omeprazole is the medication of choice.

Nutrition

The complete nutritional needs of the endurance horse are inadequately studied[20] and are beyond the scope of this chapter. A few basic ideas are presented here; further information about the nutritional management of equine athletes is presented elsewhere in this text.

Forage-based ration

Forage should be the foundation of the endurance horse's ration. If the horse has 'happy guts' it will perform much better. The ideal forage is high-quality grass hay. When grass hay is not available, oat hay is acceptable. The last and poorest choice is legume or alfalfa hay. Horses fed primarily alfalfa hay are more prone to metabolic problems, especially synchronous diaphragmatic flutter.

Concentrates

Endurance horses require less grain than other equine athletes. Many horses compete successfully when consuming less than 3 kg (6 lb) of concentrate daily. Diets high in corn seem to lead to metabolic problems. Vegetable oil and rice bran are used for the horse that cannot maintain weight.

Supplements

A wide variety of supplements are available. The value of many of these supplements is questionable given the lack of data regarding safety and efficacy. Many horses are on multiple supplements and the complete ration should be evaluated for excesses and imbalances, contraindications and possible illegal substances. Some metabolic enhancers contain caffeine.

Feeding during rides

The endurance horse must eat during a competition. The ideal caloric intake during a ride is controversial, but if the horse's intestinal tract is not functioning normally, the horse will not be able to complete. It is acceptable to let the horse eat whatever it wants. 'Smorgasbord' is a good description of offerings to the horse at a ride. Hay, the feedstuff usually identified as the favorite, must always be present. Some riders soak the hay in water. Grain and beet pulp can be offered separately or together as a slurry or mash. Apples, carrots and other treats may also be offered. Electrolytes are not usually mixed in with the food; instead they are administered after the horse has eaten. Vegetable oils are believed to be of little use during the ride.

Training

General considerations

Training of the endurance horse is an exercise in extreme patience. It takes approximately 4 years to develop a fit, 160 km competitor. The horse will always feel like it can do more than it should. It is up to the rider to prevent injury of the horse. A thorough explanation of training is beyond the scope of this chapter.

Regular health maintenance

Routine preventive health care of the endurance horse is paramount. It is best to schedule dental work in the resting season. In general, vaccination programs should be tailored to the region but horses traveling internationally have special vaccination requirements, the specifics of which will depend on the destination country. It is important to bear in mind that exposure to contagious pathogens is the rule rather than the exception as all horses drink from common troughs during competitions. Standard parasite prophylaxis should also be practiced, including routine fecal egg examinations.

Medications

Oral electrolytes

Oral electrolyte supplementation is used extensively.[21–25] The basic premise is that the horse will lose far more electrolytes via sweating during a competition than can be reasonably

replaced by voluntary consumption. There is limited research on the benefits of electrolyte supplementation in endurance horses during competitions but clinical experience strongly supports their use. Many supplements are available and the clinician must evaluate them carefully. The electrolyte mixture must replace what is lost in sweat and it must be absorbable (see Chapter 40). The dosing of electrolytes is more art than science. Weather and competitive factors are the largest influences on the amount of electrolyte needed. In general, the higher the heat and humidity and the harder the horse has to work, in terms of both speed and terrain (sand or mud footing; hilly course), the more electrolytes the horse needs. The general guidelines to use in planning an electrolyte supplementation protocol are: (1) electrolytes have optimal benefit prior to dehydration and electrolyte depletion; (2) the composition of supplements should be matched to losses; and (3) a functional intestinal tract is an absolute requirement for absorption and the administration of oral electrolytes is contraindicated in horses with ileus. Oral electrolytes are poorly effective once the horse is clinically dehydrated. A commonly used protocol is to give a dose of electrolytes the night before the ride, a second dose the morning of the ride prior to the start, and then a dose at every veterinary check. With experience, this regimen is either increased or decreased.

Analgesics

Pain relief is important in treating problems. Butorphanol is commonly used for many applications, especially ER and colic. Detomodine and xylazine are used for colic.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) are a very popular and effective class of medication. However, care must be taken when administering these drugs to endurance horses during competitions because of the potential for nephrotoxicity. Flunixin meglumine is the most popular NSAID and is used at 0.4 to 1.0 mg/kg for abdominal pain. Clinical experience has indicated that even the low dose can be nephrotoxic in some severely dehydrated horses. Phenylbutazone is commonly used for musculoskeletal pain. A dose of 2 mg/kg is given initially and only after the horse is known to be eating and drinking well. The dose may be increased to 4 mg/kg after return to normal hydration. Ketoprofen is used for abdominal and muscular pain at a dosage of 0.5–1 mg/kg. If any NSAIDs are used, adequate hydration must be assured.

Corticosteroids

Dexamethasone is rarely used in endurance horses. Experience has suggested an association between the use of dexamethasone and the development of laminitis in exhausted and dehydrated horses. Prednisolone sodium succinate (Soludeltacortef) has been used safely. Triamcinolone and methylprednisolone acetate (Depo-Medrol) are used in treating joint pathologies. The clinician must always consider withdrawal times as the rules of endurance riding prohibit the presence of any drug at the time of competition.

Intravenous fluids

Intravenous fluids are the most important medication for endurance horses. Rehydration with i.v. fluids is frequently the only treatment required for many medical problems. During competition, as much as 10 to 15 liters of fluid is lost per hour of exercise. In dehydrated horses, fluids should be administered until the horse urinates. This usually occurs after 15 to 20 liters of fluid has been administered. Once the horse urinates, the horse's clinical signs should dictate the rate and quantity of fluid administration. If all parameters are acceptable, the authors recommend the administration of 50% more fluid than it took to produce urination. Otherwise, continue fluids until clinical signs are resolved. Rate of flow is usually limited by the catheter size or fluid administration set. Many horses need infusion rates of 20 liters per hour. In our experience, over-hydration does not occur, rather the tendency is to be too conservative with fluid treatment.

To achieve an adequate fluid rate, a large bore catheter is needed (10- or 12-gauge catheters are recommended). If 14-gauge catheters are used, then it may be necessary to insert catheters into both jugular veins. Sutures or use of skin glue should anchor catheters. Thrombosis is a potential complication. Fluid delivery systems are very useful. One should take a pole to serve as an i.v. stand. Several models of extendable poles are available commercially, but one can always be inventive when in the field.

It is generally assumed that the dehydrated endurance horse is hypokalemic, hypochloremic, hyponatremic, hypocalcemic, hypomagnesemic and alkalotic. Accordingly, the i.v. fluid of choice is Ringer's solution. The next choice is normal saline (0.9%) supplemented with potassium (20 meq/L) and calcium. Multisol and Normasol are often used. Although these fluids contain alkalinizing agents (acetate and gluconate), they are still very useful. The last choice is lactated Ringer's solution. Again, although this fluid is alkalinizing it is suitable in situations where no other fluid types are available and i.v. fluid therapy is required.

Intravenous fluid additives

The working endurance horse develops abnormalities not adequately corrected by commercial preparations. Commonly used additives are listed below.

- Potassium is usually added as KCl solution. Normally 20 meq/L is added to appropriate i.v. fluids.
- Dextrose: Blood glucose can be supported by giving 50 to 100 g of dextrose per hour. A 5% dextrose solution is made by adding 100 mL of 50% dextrose per liter of fluid.
- Calcium: It is usually supplemented as a diluted bovine milk fever solution. The authors add 125 ml of

NorCalciphos to a bag of fluid and administer this solution to effect. Heart rate and respiration are monitored during treatment.

- Sodium bicarbonate. This is contraindicated in endurance horses since they are normally alkalotic when they are in metabolic distress.

Intestinal stimulants

Ileus is a common problem during competition rides. Intravenous fluids should be the first medication used in an attempt to restore intestinal motility. If i.v. fluids are not effective and the clinician has ruled out intestinal displacement or severe impaction, further medications may be used. One of the authors has used: prostaglandin $F_{2\alpha}$ (Lutalyse) at 10 mg i.m. for small and large intestinal ileus, and erythromycin lactobinate (200 mg/mL) at 100 mg i.v. for treatment of small intestinal ileus.

Use of oral laxatives is contraindicated until dehydration has been corrected. Saline cathartics (Magnalax) and dioctyl sodium succinate (DSS) are useful to break up impactions. Mineral oil is very widely used but has minimal effect in softening impactions.

Diuretics and miscellaneous medications

Intravenous fluids are the most effective diuretic and should be used before any other diuretic is considered. Furosemide (frusemide) depletes potassium and adequate hydration must be assured prior to its use.

Dopamine is most often used to treat myositis, but its use is controversial. Dopamine is used only after 20 L of i.v. fluids have been administered and no urine has been produced. Intravenous fluids must be continued while dopamine is administered. Dopamine should be given through a separate i.v. catheter to allow for a slow drip. The dose is 2 to 5 μg/kg per minute. One of the authors adds 120 mg of dopamine to 1 liter of saline and infuses 2 to 4 mL per minute to effect. Once urination occurs, the infusion is discontinued.

DMSO may be given either i.v. or orally. The i.v. dose is 100 to 250 mL as a 10% solution. Oral DMSO is given through a nasogastric tube. A maximum of 1 pint of DMSO can be given as a 10% to 20% solution.

Dantrolene is used in the treatment of acute myositis. It can be given orally and i.v. The oral dose is 3 to 5 g per horse. No dose is found in the literature for i.v. usage but one of the authors (MAF) feels there is benefit from as little as 500 mg.

Acepromazine is a potent vasodilator and useful in acute myositis. The horse must be adequately hydrated before acepromazine is given. The dose is 10 mg every 6 to 12 hours.

Methocarbamol is occasionally used for myositis. Its effectiveness is questionable, although its sedative action may offer some benefit.

References

1. Anon. Rules for endurance riding. 5th edn. Bern, Switzerland: Equestrc Internationale FEI; 2000.
2. Robert C, Benamou-Smith A, Leclerc JL. Use of the recovery check in long-distance endurance rides. Equine Vet J 2002; Suppl 34:106–111.
3. Ridgeway KJ. Inride veterinary examination, postride examination and judging of best condition. Proc Am Assoc Equine Pract 1991; 37:815–826.
4. Lopez-Rivero JL, Aguera E, Monterde JG, et al. Comparative of muscle fiber type composition in the middle gluteal muscle of Andulusian, Thoroughbred and Arabian horses. J Equine Vet Sci 1989; 9:337–340.
5. Prince A, Geor R, Harris P, et al. Comparison of the metabolic responses of trained Arabians and Thoroughbreds during high- and low-intensity exercise. Equine Vet J 2002; Suppl 34:95–99.
6. Rose RJ, Ilkiw JE, Martin IC. Blood–gas, acid–base and haematological values in horses during an endurance ride. Equine Vet J 1979; 11:56–59.
7. Foreman JH. The exhausted horse syndrome. Vet Clin North Am Equine Pract 1998; 14:205–219.
8. Jones JH, Carlson GP. Estimation of metabolic energy cost and heat production during a 3-day event. Equine Vet J 1995; Suppl 20:23–30.
9. Marlin DJ, Schroter RC, Scott CM, et al. Sweating and skin temperature responses of normal and anhidrotic horses to intravenous adrenaline. Equine Vet J 1999; Suppl 30:362–369.
10. Kohn CW, Hinchcliff KW, McKeever KH. Evaluation of washing with cold water to facilitate heat dissipation in horses exercised in hot, humid conditions. Am J Vet Res 1999; 60:299–305.
11. Silverman SC, Birks EK. Evaluation of the i-STAT hand-held chemical analyser during treadmill and endurance exercise. Equine Vet J 2002; Suppl. 34:551–554.
12. Lopez JR, Linares N, Cordovez G, Terzic A. Elevated myoplasmic calcium in exercise-induced equine rhabdomyolysis. Pflugers Arch 1995; 430:293–295.
13. Valberg SJ, Mickelson JR, Gallant EM, et al. Exertional rhabodomyolysis in quarter horses and thoroughbreds: one syndrome, multiple aetiologies. Equine Vet J 1999; Suppl 30:533–538.
14. McKenzie EC, Valberg SJ, Pagan JD. Nutritional management of external rhabodomyolysis. In: Robinson E, ed. Current therapy in equine medicine. Philadelphia: WB Saunders; 2003:727–734.
15. Quiroz-Rothe E, Novales M, Aguilera-Tejero E, Rivero JL. Polysaccharide storage myopathy in the M. longissimus lumborum of showjumpers and dressage horses with back pain. Equine Vet J 2002; 34:171–176.
16. Fowler ME. Veterinary problems during endurance trail rides. Proc Am Assoc Equine Pract 1979; 469–478.
17. Schott HC 2nd, McGlade KS, Molander HA, et al. Bodyweight, fluid, electrolyte, and hormonal changes in horses competing in 50- and 100-mile endurance rides. Am J Vet Res 1997; 58:303–309.
18. Luhman L, Wickler SJ, Hoyt DF, Kobluk CN. Shock attention in the forelimb of the horse. J Equine Vet Sci 2000; 20:503–510.
19. Hayakawa Y, Komae H, Ide H, et al. An occurrence of equine transport pneumonia caused by mixed infection with *Pasteurella caballi*, *Streptococcus suis*, *Streptococcus zooepidemicus*. J Vet Med Sci 1993; 55:455–456.

20. Bray RE, Wickler SJ. Nutrition portfolio of the endurance horse. In: Thompson KN, ed. The veterinarian's practical reference to equine nutrition. American Association of Equine Practioners; 1997.
21. Butudom P, Schott HC 2nd, Davis MW, et al. Drinking salt water enhances rehydration in horses dehydrated by frusemide administration and endurance exercise. Equine Vet J 2002; Suppl 34:513–518.
22. Flaminio MJ, Rush BR. Fluid and electrolyte balance in endurance horses. Vet Clin North Am Equine Pract 1998; 14:147–158.
23. McCutcheon LJ, Geor RJ. Sweating, fluid and ion losses and replacement. Vet Clin North Am Equine Pract 1998; 14:75–95.
24. Nyman S, Jansson A, Dahlborn K, Lindholm A. Strategies for voluntary rehydration in horses during endurance exercise. Equine Vet J 1996; Suppl 22:99–106.
25. Dusterdieck KF, Schott HC 2nd, Eberhart SW, et al. Electrolyte and glycerol supplementation improve water intake by horses performing a simulted 60 km endurance ride. Equine Vet J 1999; Suppl 30:418–424.

CHAPTER 53

Veterinary aspects of training and competing polo ponies

Rebecca E. Posner

Polo ponies represent a unique subset of the sporting horse population. The nature of the game of polo and the standard management and training procedures associated with it predispose this group of horses to a variety of disease conditions.

History

The sport of polo can be traced back to the Persian court of King Darius, who reigned during the fourth century BC. From there polo spread eastward to China, Japan, Mongolia, and Tibet. The name 'polo' actually comes from the Tibetan word 'pulu', meaning root, from which the wooden ball was made. The sport was first played in the UK in 1860 by returning British army officers who had seen it played in India. In 1875 the English Polo Association was established. The British went on to introduce the sport to the East Coast of the USA in 1876. The United States Polo Association was formed in 1890.[1] Today there are over 2000 playing members in the British Polo Association, officially called the Hurlingham Polo Association.[2] There are more than 3000 playing members in the United States Polo Association. Polo is now played around the world in over 30 countries[1] including countries from South America, where Argentina has produced some of the most accomplished players. In the USA polo is a recognized National Collegiate Athletic Association sport, with both men's and women's teams from universities such as Cornell, University of Connecticut, University of Virginia, and University of Colorado competing, with each season culminating in National Finals.

The game

Polo is played either 'indoors' or 'outdoors', with many horses playing indoor polo in the winter months and outdoor polo during the summer months. Outdoor polo is played on a 10-acre grass pitch measuring 300 yards in length and 160 yards in width. There are four members on each team, and a game consists of six chukkas each lasting 7 minutes. Indoor polo is played in a high-walled, dirt-floor arena, measuring 300 feet in length and 150 feet in width. An indoor polo team comprises only three members per team and a game consists of only four chukkas. Each polo pony commonly plays only one or possibly two alternating chukkas in a given game. An average outdoor player must therefore have a minimum of three, but more commonly six or seven ponies to play in a game (A Flint, personal communication, 2000).

Because of the smaller playing area, indoor polo tends to demand more turning, bumping, and physical contact than its outdoor equivalent. Outdoor ponies, due to the size of the field they must cover, often have greater flat speed and endurance. The different demands of outdoor and indoor polo not only often cause different types of horses to be used but also determine the types of injuries that may occur (TN Christian, personal communication, 2000).

General strategy and positions

The object of both the indoor and outdoor polo game is to be the team that scores the most goals at the end of the game. The ball is hit forward, backward and diagonally off both sides of the polo pony. There are eight basic shots that the player hits with a mallet which ranges from 48 to 52 inches in length depending on the size of his or her mount. The rules of polo are lengthy and can be confusing even for seasoned

players, but the majority are aimed at ensuring the safety of horse and rider. Many of the rules are based around the 'line of the ball' to ensure a right- of-way system. When a polo ball is hit there is an imaginary line that extends in front and to the back of that ball dictated by the ball's trajectory. If a player crosses that line, and in so doing, impedes the action of an opposing player, the player is deemed guilty, by an umpire, of crossing 'the line' and a foul is then given.[1]

The most basic strategy of polo is to keep one player in front of the ball (offensive), one or two players in the action in the center of play, and one player behind the ball (defensive). The players play positions in a game, numbered 1 to 4 in an outdoor game and 1 to 3 in an indoor/arena game. The number 1 player indoors, and the 1 and 2 outdoors, are the most offensive and 'optimistic'. These players try to keep themselves ahead of the ball, ready to take a forward pass and score. The number 2 indoors and the number 3 outdoors is often the most skilled, and aggressive of the team. These players are also often the best mounted. This is the pivot position in which the player should have his nose in every play and be the one who must 'make things happen'. The number 3 indoors and the number 4 outdoors is the most defensive, 'pessimistic' player or 'the back'. They are responsible for initiating defensive maneuvers, closing the back door, and preventing the opposing number 1 from scoring (DE Eldredge, personal communication, 2000).

Rating

A handicap system is used in the sport of polo to try to ensure evenly matched games. Beginning players have low ratings or 'goals'. Starting at –2 goals, ratings increase to the ultimate rating of 10 goals. Professional polo players are usually rated 7 to 10 goals and are often paid by patrons who are lower rated. The remaining members of the team may be made up of medium rated players who are usually other patrons, lower-rated professionals, or young up-and-coming players. The mount of a 'high goaler' is expected to run faster, turn quicker, and be involved in more plays than its lower goal counterpart. Whilst the lower goal mount's job may seem easier its rider is often not as experienced. This mount may be asked to turn before being properly set up, or for a burst of speed at the end of a long chukka. Thus the polo ponies' job, and the injuries they are exposed to may also vary depending on the rating of the player (A Snow, personal communication, 2000).

Demographics

The United States Polo Association defines a polo pony as 'A horse or pony of any breed or size'.[1] The job of the polo pony does, however, tend to dictate the size, breed or 'type' of horse. The polo mount must be fast enough to outrun competitors, sturdy enough to bump another horse off a play and survive the rigors of a 7-minute chukka. They must also be able to accelerate quickly, then stop, turn on their haunches, and accelerate again. Finally, it must be sufficiently stable during galloping to allow the rider to hit a ball accurately. Depending on the particular flow of the game a chukka may be mostly galloping, or it may be filled with many stops in the action. Even low-goal (non-elite) polo has been shown to put moderate to high stress on the cardiovascular system.[3] Compared with racing Standardbreds or Thoroughbreds polo ponies have high blood lactate concentrations.[4] Because of these requirements, many polo ponies are Thoroughbred or Thoroughbred crosses. The Argentine Thoroughbred is stockier and somewhat shorter than its British and American counterparts and is particularly suited to the game. Many of these horses are transported worldwide and make up the majority of mounts in a high-goal game. American and British Thoroughbreds that may have been destined for the track are often successful on the polo field. In the USA the larger and longer American Thoroughbred may be crossed with the Quarter Horse to improve its turning and sprinting ability. Although originally there was a height limit for polo ponies of 12 hands this was abolished in 1919 and now 'polo ponies' are usually horses averaging 15.1 to 15.3 hands in height. Mares and geldings both play polo, whereas stallions are excluded due to their temperament and the close-quartered nature of the game (Fig. 53.1). Mares tend to be over-represented in the sport of polo and are thought to

Fig. 53.1
Polo game at the British Universities Championships demonstrating the close contact characteristic of the game.

be 'tougher' and have 'more heart' than their male counterparts (J Horsewell, personal communication, 2000).

Polo ponies are usually broken between the ages of 2 and 3, and then first played in slow or 'green' chukkas at the age of 4. Polo, like any equine discipline, takes time, experience, and training to develop a good mount, and the polo pony will be in its prime between the ages of 6 and 8. Often a 'high goal' pony will be 'retired' to a lower goal young player or a patron, and it is certainly common to have ponies playing well into their teenage years. These seasoned campaigners can be a challenge to the polo veterinarian as they more often have chronic or arthritic conditions that require management to prolong their playing career.

Polo is a game of physical contact, quick stops, turns, and rapid acceleration. Players of different experience and skill levels play it. The majority of injuries and unsoundnesses are related to these factors.

Traumatic injuries

While every precaution is taken to ensure the safety of the polo pony, traumatic injuries during the game do occur. The pony may be hit in the legs, body or head by a mallet or a speeding ball. Overreach injuries to the heel bulbs are also common in the galloping polo mount. Often cold therapy (icing, hosing), administration of non-steroidal anti-inflammatory drugs (NSAIDs) and rest are all that is required but more serious injuries such as fractures can occasionally occur. Proper leg protection is essential in polo and is required for play by both American and British polo associations.[1,2] Protection can be in the standard form of 'polo wraps', but neoprene and other synthetic leg protection are now also commonly used. These are thought to offer greater protection and support. Bell boots offer not only protection at the heel bulbs from an overreach, but also for the rest of the sensitive coronary band which may be inadvertently stepped on by another player's mount.

Due to the close contact inherent in the sport, a certain amount of muscle soreness and bruising occurs. These injuries can usually be treated with NSAIDs, massage and rest. Proper conditioning will limit the severity of these injuries.

Conditions of tendons and ligaments

Tendon and ligament injuries are common in polo ponies. Their treatment and management may depend on the value of the horse, the point in the season that the injury occurs, and the availability of alternative mounts for the player. For example, a player may be more inclined to rest a tendon for 6 months if it is late in the season and he has enough other ponies to mount him in the remainder of his games.

Proximal sesamoidian ligament injury is the most common injury amongst hard-playing ponies. The constant wear and tear caused by quick turns and stops affects the superficial, middle and lateral collateral sesamoidian ligaments. The damaged ligament is replaced by fibrous tissue and eventually the pony develops thickened fetlocks. This is a chronic injury and many affected horses are nursed through the polo season by icings after chukkas, good wrapping and the judicious use of anti-inflammatories. Eventually, these horses may have to be 'retired' down to lower goal polo.[5]

Suspensory ligament injury occurs regularly in the polo pony. The area usually affected is the distal body and the sesamoidian branches. Although acute injuries do occur, it is more likely that the polo pony will be suffering from a chronic desmitis. Veterinarians are often asked to see these injuries in the early season when fitness level may not be up to standard, and again late in the season as a result of constant pounding on hard ground.[5,6]

The proximal superficial digital flexor tendon is the commonest site of tendon injury in polo ponies and many horses will successfully play with a chronic 'bow'. Some retired Thoroughbred ponies, bought off the track, may have been retired due to an injury in this area. They may well, therefore, have a weakness at this point. Injuries to the palmar aspect of the proximal metacarpal also include problems with the inferior check ligament, specifically at its insertion to the deep digital flexor tendon. Sliding stops and spins add to the strain created in this region of the cannon bone.[5]

Treatment for any of these acutely occurring injuries demands rest, administration of NSAIDs and cold therapy. Repeated diagnostic ultrasounds are of utmost importance both to determine the size of the lesion and to track the healing process, thus determining when the pony is ready to play again.[6]

Many of the injuries seen in polo ponies are chronic lesions caused by the constant rigors of the game. These injuries tend to be managed rather than treated or cured, and can be challenging to the polo veterinarian. Chronic injuries are managed with NSAIDs, chondroprotectives such as hyaluronic acid and polysulfated glycosaminoglycans, along with judicious use of the horse.[6] Good nursing care by experienced grooms including icing, sweating and wrapping is invaluable, and allows many of these horses to continue playing season after season.

The most commonly used NSAID in the playing polo pony is phenylbutazone. There is no rule to limit the amount of phenylbutazone a polo pony can be given before or even during a game, but there is a general belief among polo players that one cannot play good polo on a horse that has received a large amount of phenylbutazone. Such a horse is said to 'lose' its mouth, becoming less sensitive to the bit, and therefore much less likely to perform the necessary quick turns and stops. This causes the use of phenylbutazone to be self-limiting and therefore the need for tight regulation on its use as in other equestrian sports is not required at this time (TN Christian, personal communication 2000).

Arthritic conditions

Navicular syndrome or caudal heel syndrome can affect all breeds and ages of ponies, but is often seen in older polo ponies, particularly those that are part Quarter Horse. Short stops on hard ground can cause this region of the foot to become chronically sore, especially in those horses who stop 'improperly' on their front ends, rather than stopping and turning with the majority of their weight on their hind ends. Improper shoeing and trimming, leading to a long toe and low heel, may predispose or exacerbate this condition.

Conservative therapy often allows many of these horses to continue their career for many years. This includes proper shoeing utilizing wide webbed or bar shoes, glucosamine supplementation, oral isoxsuprine and hyaluronic acid and steroid injections to the coffin joint.[7]

Quick turns and stops, on hard ground with little give, predispose polo ponies to hock arthritis. Usually the intertarsal and tarsometatarsal joints are affected. Often the first sign of this in polo ponies is the reluctance to pick up a given lead. These horses will be significantly positive on flexion tests. Glucosamine supplementation, NSAIDs and joint injections with a combination of hyaluronic acid and corticosteroid all often aid in managing these ponies.[7]

Exertional rhabdomyolysis

Polo ponies may be predisposed to conditions caused by overexertion. The physical demands, combined with playing in weather extremes puts the polo pony under considerable stress. This is compounded by long distance traveling to different games each weekend and the nervous and excitable temperament, which is common in the polo pony. Proper conditioning is vital, though early season games and lay-ups from injury may cause a pony to be inadvertently played harder than appropriate for its fitness level. It is easy, however, and essential to some degree, for players to forget about the horse they are riding and concentrate on the game at hand. This can result in a horse playing harder than the pony's fitness level should dictate.

Exertional rhabdomyolysis (ER), often called 'tying up', is common in polo ponies. It is reported to occur more frequently in this group of horses than in any other competition horses. The incidence rate is approximately 7% per year.[8] Unlike reports from studies in Thoroughbreds, management factors, age and sex appear to play little role as risk factors. However, predisposing factors in polo ponies have been shown to include excitable temperaments, playing early in the season or exercising harder than they are accustomed. In addition a hard chukka or one early in the season are also common risk factors for an episode of ER.[8] Polo ponies have not been reported to suffer from glycogen storage myopathies[9] and are presumed to suffer from ER due to overexertion.[8] Initial treatment relies on pain relief, and fluid replacement if needed.[10] Serum activities of creatinine kinase and aspartate aminotransferase should be measured at the initial onset, and measured again before returning to work.[11–13] ER is a significant cause of wastage in polo ponies.[8] In Thoroughbreds a heritable recurrent form of ER has been shown to exist. Therefore prevention is an area of management that needs to be addressed. This involves eliminating any known underlying cause.

Routine care

It is important not to overlook the value of routine veterinary care of the polo pony. Playing polo horses travel frequently from game to game, mix with many other horses, and are under considerable stress. A program of regular vaccinations and deworming are therefore of the utmost importance.

Regular dental care is also essential in the polo pony. Sharp hooks and points can interfere with the bit and make the horse generally uncomfortable in his mouth. A good mouth is one of the most important attributes in a polo pony; therefore dental checks at 6- to 12-month intervals are recommended.

Conclusion

The polo veterinarian faces unique challenges due to the rigors that polo ponies are exposed to, combined with the expected longevity of their careers. Chronic conditions must be managed and acute conditions must be acted upon promptly. There is a large and growing interest in the sport of polo throughout the world and it is becoming increasingly necessary for the equine veterinarian to become familiar with unsoundnesses or conditions that affect this large body of competition horses.

References

1. United States Polo Association Rules of Play 2002. http://www.uspoloorg/. Accessed November, 2002.
2. HPA Rules 2002. http://www.hpa-polo.co.uk/guidesASP. Accessed November, 2002.
3. Marlin DJ, Allen JC. Cardiovascular demands of competition on low goal (non-elite) polo ponies. Equine Vet J 1999; 31(5):378–382.
4. Saibene F, Cortilli G, Gavazzi P, et al. Maximal anaerobic (lactic) capacity and power of the horse. Equine Vet J 1985; 17(2):130–132.
5. Marcella KL. Polo pony injuries. Proc Am Assoc Equine Pract 1990; 36:647–660.
6. McIlwraith CW. Diseases of joints, tendons, ligaments, and related structures. In: Stashak TS, ed. Adams' lameness in horses, 5th edn. Baltimore, MD: Lippincott Williams and Wilkins, 2002:459–640.

7. Schramme MCA. Diseases of the foot and lower limbs. In: Mair T, Love S, Schumacher J, Watson E, eds. Equine medicine, surgery and reproduction. London: WB Saunders; 1998: 348–350.
8. McGowan CM, Posner RE, Christley RM. Incidence of exertional rhabdomyolysis in polo horses in the USA and the United Kingdom in 1999/2000 season. Vet Rec 2002; 150(17):535–537.
9. Valberg SJ, Cardinet GH III, Carlson GP. Polysaccharide storage myopathy associated with exertional rhabdomyolysis in the horse. Neuromusc Disord 1992; 2:351–359.
10. Farrow et al. Treatment for azoturia and tying-up – a panel report. Mod Vet Prac 1976: 57:223–233.
11. Harris PA. Equine rhabdomyolysis syndrome. In Practice 1989; 11:3–8.
12. Harris PA. The equine rhabdomyolysis syndrome in the United Kingdom: epidemiological and clinical descriptive information. Br Vet J 1991; 147:373–384.
13. Yamaoka S, Ikeda S, Watanabe H. Clinical and enzymological findings of tying up syndrome in Thoroughbred racehorses in Japan. Exp Rep Equine Health Lab 1978; 15:62–78.

CHAPTER 54

Veterinary aspects of training Western performance horses

Brad R. Jackman

Introduction

The disciplines of the Western performance horse are varied and include rodeo and barrel racing, breed shows, cutting and reining, and Western pleasure. The majority of these horses are American Quarter Horses but there are also Paint and Appaloosa horses involved in these competitions. Despite the variety of breeds and athletic competitions, there are several common maladies that generally affect this population of horses.

Universally, there is tremendous growth of Western performance competitions in both number of competitions and the purse money at these events. Subsequently, selective breeding programs have been utilized to produce a competitive athlete and training programs begin earlier and are more intensified to enhance the odds of success in the competitive arena. These approaches have increased the value of these horses but have also increased the incidence and severity of disease problems with which the veterinarian must be familiar.

Demographics

The rising popularity of Western performance horses has led to a growth of competitions and demand for these horses within the USA and Canada as well as Europe, New Zealand and Australia. Rodeos have historically been in the USA, Canada and Australia and continue to be confined to these areas. However, the number of breed shows for Quarter Horses and Paint horses in addition to cutting and reining competitions has dramatically increased in the last 10 years in Europe and Australia (Table 54.1). The growth in European countries has mostly been in Germany, Italy and France.

Table 54.1 American Quarter Horse registry statistics for 2001

Location	2001 Horse population	2001 New horse registrations	% Growth
USA	2 749 784	132 619	4.8
Canada	214 134	13 181	6.2
International	81 133	5120	6.3

Common disease problems

Despite the variety of athletic events in which these horses compete, there are some similar traits in conformation, training and use that lead to universal problems. As with all horses, there are a myriad of problems and diseases that may develop. However, the purpose of this discussion is to become familiar with the most common problems inherent with these particular athletes.

Hyperkalemic periodic paralysis (HYPP)

Occasionally seen in rodeo and barrel racing horses, HYPP is primarily a condition of Quarter Horses and Paint horses used in the breed shows. This is a genetic condition that originated from a single Quarter Horse stallion. When the genetic trait was discovered and a diagnostic test developed, it was thought that this would lead to elimination of this disease by selective breeding. On the contrary, halter and Western pleasure judges often prefer the body type and muscling of horses with this gene and HYPP has become a selected trait for

horses in Western show disciplines. The genetic test can determine if the horse is homozygous positive (HH), heterozygous (NH) or homozygous negative (NN). The HH horses tend to have a higher incidence and severity of clinical signs of HYPP and are not the preferred breeding for most owners. Breeders often select for the heterozygous animals, as they tend to maintain the body type desired with a decreased incidence of HYPP episodes. Horses with any breeding predisposed to the condition should be tested to determine if they carry the gene for HYPP.

Hyperkalemic periodic paralysis is a disorder that affects the normal ion movement across cellular membranes and thus muscular function. The clinical signs can vary from episodic minimal muscular fasciculations to acute death from cardiac dysfunction or laryngeal spasm. Clinical episodes are often more pronounced in young horses; episodes may decrease in incidence and severity as the horse ages. The most common signs observed are muscle fasciculations in the shoulder and flank regions and prolapse of the third eyelid. Episodes usually last 15 to 60 minutes and may or may not increase in severity during an episode or with subsequent episodes.

Therapy for HYPP is divided into treatment of current episodes and prevention from further episodes. During episodes, there is an increase of potassium released from cells and treatment is directed at driving potassium intracellularly. Medications used to promote this movement of potassium include intravenous dextrose, sodium bicarbonate, calcium gluconate, and insulin. Prevention of HYPP clinical signs is directed at decreasing dietary potassium intake (i.e. reduction or elimination of alfalfa and brome hay) and daily administration of diuretics that increase the renal excretion of potassium (i.e. acetazolamide).

The prognosis for heterozygous (NH) HYPP horses is generally favorable with the majority of horses manageable throughout their performance careers. The HH horses and horses that exhibit more severe clinical signs are more difficult to manage and have a poorer prognosis.

Musculoskeletal diseases

Lameness is by far the most common reason for Western performance horses to suffer a reduction in performance, or an end to their athletic career. Cutting and reining horses are primarily Quarter Horses and Paint horses. These horses are bred with an emphasis on small stature (14 to 15 hands), agility, and the mental capacity to perform under pressure. During their individual events, these horses have to be under complete control while performing quick stops and high torque turns (Fig. 54.1). Additionally, most of these horses begin training as late yearlings and early 2-year-olds with the goal of competing in futurity competitions in the fall and winter as 3-year-olds. The small stature, agility and athletic use of these horses predispose to certain stresses and injuries.

Rodeo and barrel racing horses generally have longer careers and therefore start training at a slightly older age.

Fig. 54.1
Cutting and reining horses have to perform quick stops and high torque turns.

There is a wide variation in size and conformation for these horses, but the repetitive high-speed turns and hard stops over time make these horses prone to injuries and chronic wear and tear maladies.

The horses used for breed show halter conformation classes have a very different body type than most of the other horses used in Western performance events. Judges are selecting for large heavily muscled horses that have relatively refined lower limb bone structure. These horses are shown in halter classes initially as weanlings and rarely past 3 years of age. Because of the need for rapid growth and size, these foals are often exposed to excessive or imbalanced nutritional programs and are predisposed to metabolic bone disease abnormalities. These horses also tend to have small feet that, when combined with a large, heavy frame, predispose to distal limb problems.

Western pleasure horses also have a wider variation in size and conformation than halter horses. Western pleasure horses usually begin training as late yearlings or early 2-year-olds. Currently, the preference for owners and trainers is a large horse but without the heavy body style of the halter horse. Conformationally, these horses must be able to move 'flat kneed' and level, which requires hock flexion and hindlimb advancement at a slow jog to enable the hind end to support the front end. The slower gaits also cause significant front feet concussion.

A thorough and systematic lameness examination is necessary to localize the source of lameness. Examination of the horse in a proper setting with both hard and soft footing is helpful to a consistent examination. Occasionally, examining the horse when ridden is beneficial. Perineural and intra-articular anesthetic blocks are necessary to accurately locate the origin of the lameness. Once localized, further diagnostics are performed to identify the etiology and severity of the disease process. Proper radiographs utilizing good technique and the appropriate views are required. If soft tissue

injury is suspected, then an ultrasound examination should be performed and the contralateral limb should also be examined for comparison. Other diagnostic modalities that may be useful include nuclear scintigraphy, computerized tomography (CT) and magnetic resonance imaging (MRI).

Forelimb lameness

Western performance horses can have many different causes of forelimb lameness but several are more common. Forelimb lameness can be grouped into two different types – concussive and fatigue. To be competitive in today's horse industry, breeding programs have selected for agile athletes with the body style desired, but many of the horses are also being bred with small feet. When this is combined with beginning work at an early age, foot problems often develop. Fatigue plays a role especially in the cutting and reining horses. These horses have to be calm and completely in control when performing and are often exercised for extended periods of time prior to competing to achieve this effect. Thus, these horses are often tired while competing, which predisposes to fatigue injury.

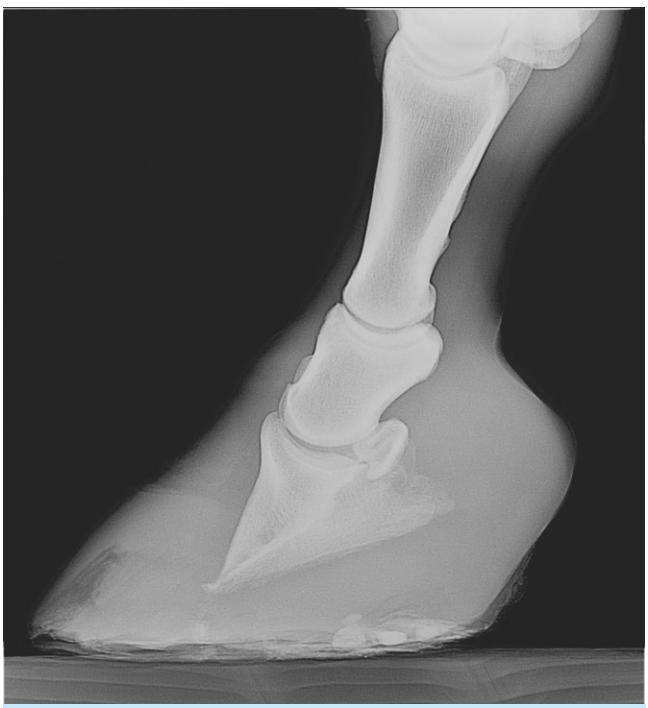

Fig. 54.2
Lateral radiograph of a laminitic horse.

Laminitis

Inflammation of the lamina within the front feet is more common in the halter horses than in the other Western disciplines. As mentioned earlier, the judges select for horses that are extremely large and heavily muscled but with relatively small distal limb bone structure and feet. Therefore, there is a tremendous amount of concussive pressure on the front feet reflected through the lamina. Additionally, these horses are also frequently being fed a high concentrate ration to maintain their size. The severity of laminitis is variable and both rotation and distal displacement (sinking) of the third phalanx can occur.

Diagnosis is usually relatively easy as there is often the characteristic laminitic gait, increased digital pulses, reluctance to move and/or pick up the feet, and pain over the toe of the foot with hoof tester examination. Palpation of the proximal dorsal coronary band should always be performed to assess for an indentation characteristic of distal displacement of the third phalanx. Radiographs are taken to assess the degree of rotation, presence of gas lines, thickness of the sole, or osseous abnormalities of the third phalanx (Fig. 54.2).

Treatment of laminitis should be aggressive and consists of anti-inflammatory medications, medications to help promote blood flow to the foot, and support of the foot. Anti-inflammatory medications include phenylbutazone, flunixin meglumine and intravenous DMSO. Medications proposed to enhance blood flow to the foot include acepromazine, isoxsuprine hydrochloride and aspirin. Other medications have also been suggested but clinical evidence is lacking. If the horse developed laminitis while shod, the shoes should be removed. The foot is trimmed if the toe is long and support of the foot is usually initiated with thick Styrofoam padding. The horse should not be reshod until there is stabilization in the clinical signs and the horse is responding to therapy.

Many of the halter horses have excessive body condition when laminitis develops. Therefore, it is recommended that the horse lose weight to decrease force through the front feet and consume a diet with low soluble carbohydrate (i.e. starch and sugar) content. The owner or trainer often refutes these recommendations and compliance can be difficult.

The prognosis is dependent on response to therapy. The less severe the rotation and the faster and more complete the therapeutic response, the better the prognosis. Distal displacement of the third phalanx has a worse prognosis than rotation in most situations. Recurrent laminitis is not uncommon in show horses, perhaps because of the perceived need to feed high grain diets to maintain show condition.

Palmar heel pain/navicular syndrome

The most common source of lameness in the forelimb of Western performance horses is the heel region. The smaller feet of these horses as well as the early training and sustained use of the horses produces excessive concussion in the foot. Clinically these horses exhibit lameness in one or both of their forelimbs. Pain across the central one-third of the frog may be present on hoof tester examination and these horses

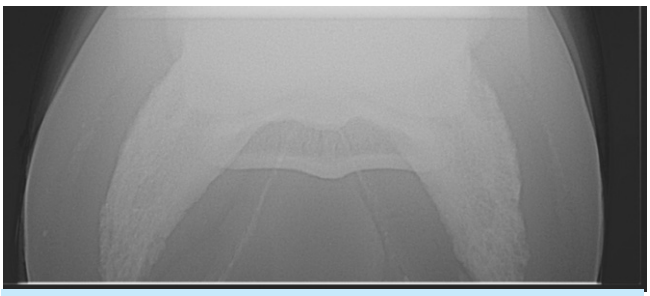

Fig. 54.3
Flexor skyline radiographic view of the navicular bone.

will have a tendency to land toe first instead of heel first. The lameness is alleviated with analgesia of the palmar digital nerves. Analgesia of the distal interphalangeal joint is often useful in further localizing the lameness. However, recently it has been suggested that the specificity of this block is questionable and can desensitize the sole when large volumes of anesthetic are used.[1]

Once the lameness has been localized, foot radiographs are made. It is imperative to take a complete series of good detail radiographs. Outside of the USA it is still common for a foot radiograph series to lack a flexor skyline view that may be the most important view to assess the navicular bone (Fig. 54.3). The radiographs are carefully examined for abnormalities as well as imbalance and angular deformities of the foot. Erosion of the flexor cortex, cystic-type lesions and medullary sclerosis of the navicular bone are more severe lesions and may warrant a lesser prognosis. If significant radiographic abnormalities exist, then a diagnosis of navicular syndrome is made.

Consistent and proper shoeing is the cornerstone of treatment of horses with palmar heel pain. The foot must be balanced and at an appropriate angle for the individual horse. An effort to hasten the break over of the foot should be made by rolling the toe or setting the shoe behind the toe of the hoof. Adequate heel support is also necessary. The shoeing interval should be a maximum of 5 to 6 weeks to maintain good hoof conformation. Additional therapy consists of anti-inflammatory medication and drugs that are purported to promote blood flow to the foot (e.g. isoxsuprine hydrochloride, aspirin). If more severe lameness is present or there is evidence of coffin joint inflammation, intra-articular injection of the coffin joint with hyaluronic acid and a corticosteroid may be beneficial. Despite aggressive shoeing and medical therapy, some horses remain lame. These more refractory cases usually require a palmar digital neurectomy to maintain athletic function.

Suspensory ligament desmitis

Damage and inflammation of the suspensory ligament is a common source of forelimb and to a lesser degree, hindlimb lameness of Western performance horses. The incidence of hindlimb suspensory desmitis has increased in recent years and is probably related to the greater athletic prowess of these horses together with the intensified level of competition. The severity of the inflammation can vary from slight pain on palpation to acute and, at times, severe lameness. Many of these horses have to exhibit a quiet and calm demeanor while performing, and therefore have to be worked until slightly fatigued prior to performing at their most demanding level. Aside from fatigue, other predisposing factors are improper shoeing (long toes, uneven feet, improper angles, lack of heel support), hindlimb soreness and poor ground conditions.

Injuries to the suspensory ligament most commonly occur at its proximal origin but may also involve the distal branches. The lameness observed is usually one to two grades more severe at a trot when the affected limb is on the outside of a circle (i.e. clockwise with a left forelimb lameness). Pain is usually elicited with palpation if the injury is present in the distal suspensory ligament but may be absent with proximal origin lesions. The location of the lameness is established with sequential local anesthetic injections. The proximal suspensory can be desensitized by local infiltration of anesthetic around the suspensory ligament or by perineural anesthetic injection around the lateral palmar nerve at the level of the middle carpal joint just distal to the accessory carpal bone.

After localization of the lameness, the affected region is radiographed to determine if osseous lesions of the fetlock or proximal metacarpus are present. An ultrasonographic examination of the suspensory ligament is performed to assess the integrity of the ligament and tendinous structures. If local infiltration of anesthetic was used to localize the lameness, then the ultrasound examination is often delayed for a day to minimize the possibility of distortion in the area. Fiber pattern, ligament size and percentage of damaged tissue should be assessed with the ultrasound examination. Additionally, the contralateral limb should be ultrasounded for comparison as individual variation can exist in the size and character of the proximal suspensory ligament. The severity of lameness does not always coincide with the degree of damage present ultrasonographically.

The treatment for suspensory ligament desmitis is rest, corrective shoeing, systemic non-steroidal anti-inflammatory medications and occasionally local injection of the proximal suspensory lesion. The duration of rest is determined by the severity of ultrasonographic abnormalities, degree of lameness and subsequent ultrasound examinations to monitor healing. In most cases, an initial 60 days of stall rest is recommended with a small amount of prescribed hand walking beginning 2 weeks after examination. The amount of walking exercise should be slowly increased. After 60 days, the horse should be re-examined, including ultrasonography of the affected ligament. Further rest and exercise regimens are recommended at that time depending on the response to therapy. Corrective shoeing involves maintaining the toes short and the foot at an appropriate

angle; usually an egg bar shoe is used to facilitate fetlock support. In horses where the lameness is minimal and there is a lack of ultrasonographic abnormalities, local injection of the proximal suspensory may be performed. Most often a corticosteroid is used in conjunction with polysulfated glycosaminoglycan (Adequan i.m., Luitpold Pharmaceutical Inc., Animal Health Division, Shirley, NY 11967). Occasionally, Sarapin (High Chemical Co., Levittown, PA 19056) is added as well. In cases where the lameness and lesion are severe or showing a slow or poor response to conventional therapy, ancillary therapies may be instituted. These horses may undergo injection of the affected proximal suspensory ligament with bone marrow aspirated from the sternum[2] or extracorporeal shock wave therapy.[3]

Cutting and reining horses frequently have a slight amount of proximal suspensory pain on palpation in association with a slightly shortened stride, but no obvious lameness. These athletes frequently have inflammation of the distal hock joints as the primary problem which causes the horse to place more stress on the forelimbs. Typically, the suspensory pain does not require direct treatmentand the pain is alleviated with resolution of the hock soreness.

The prognosis of Western performance horses with forelimb proximal suspensory desmitis is generally favorable. More severe lesions may be more prone to recurrent injury and efforts to reduce the incidence of reinjury are paramount. Proper conditioning is necessary to reduce the risk of fatigue. Appropriate shoeing is necessary to avoid long toes and improper angles; horses may be maintained in egg bar shoes for their entire athletic careers. Potentially, the most important preventive measure is to maintain these athletes as pain free as possible such that they are able to work off their hind ends and prevent excessive strain on the front limbs.

Fig. 54.4
High-speed stopping and turning can predispose to injury of the hindlimbs.

Hindlimb lameness

Despite the athletic riding discipline, all Western performance horses place a great deal of strain on their hindlimbs. These horses generally perform tasks that require them to have the conformation and willingness to move with their hindlimbs underneath themselves (Fig. 54.4). Moreover, they have to undergo extensive training at a young age to become proficient and consistent in these maneuvers. This repetitive stress predisposes the Western performance horse to injury of their hindlimbs, especially their hocks and stifles.

When evaluating the horse for hindlimb lameness it is important to perform a thorough and systematic examination and palpation of the horse. Specific areas to examine closely are the forelimb suspensory ligaments, the back and lumbar musculature, and any effusion or swelling in the hindlimbs.

Suspensory ligament desmitis

As mentioned earlier, inflammation and lameness of the proximal suspensory ligament in the hindlimbs is being diagnosed more frequently. The diagnosis and therapy are similar to the forelimbs. However, the prognosis is more guarded as the response to therapy can be unpredictable. In more severe cases, it may take 12 to 18 months for adequate healing to occur.

Inflammation/arthritis of the distal tarsal joints (distal tarsitis)

Lameness associated with the distal intertarsal and tarsometatarsal joints (distal tarsal joints) is the most common reason for a reduction in performance in the Western performance horse. Anatomically, the distal intertarsal and tarsometatarsal joints communicate in only 7–38% of horses; the distal tarsal joints very rarely communicate with the proximal intertarsal or tibiotarsal joints.[4–6] The distal tarsal joints are low motion joints that sustain repetitive torque force in these horses. Therefore, it is not generally a question if these joints will become inflamed but when they will become affected. The degree of soreness related to these joints can vary from severe, acute lameness to only a reduction in performance without notable lameness. Often the trainer will be suspicious of distal tarsal inflammation due to reduced performance of the horse prior to obvious lameness being noticed. Common complaints from cutting trainers about horses with inflamed distal tarsal joints are that the horse will not hold the ground or a cow, the horse is late making a turn on a cow, or the horse is backing off the cow and unwilling to get low in the ground. Reining trainers will complain of horses that are not stopping as well, seemingly uncomfortable on tight turns, or having difficulty with lead changes. Western

pleasure trainers will notice a reluctance of the horse to carry its head appropriately, unwillingness to pick up or maintain the appropriate lead, or just a slight shortening of stride length that affects the horse's gait.

Horses with distal tarsitis often palpate with soreness in their back and gluteal regions, especially in the lumbar area. Effusion within these joints is not palpable due to the narrow width of these joints. However, horses with extensive remodeling of these joints may have palpable thickening in the distal medial aspect of the tarsi. As this condition is related to occupational repetitive stress, it is often bilateral with one hock more affected than the other. Occasionally, the lameness is related to an acute injury and the lameness is generally unilateral and more severe. Typical inflammation of the distal tarsal joints has a characteristic gait where the stride is slightly shortened and the arc of flight of the hind leg is medially under the body with a quick lateral outward movement of the foot prior to placing the foot on the ground. An upper hindlimb flexion test exacerbates the shortening of stride and abnormal gait.

A presumptive diagnosis of inflammation of the distal tarsal joints is often made based on clinical findings. If there is any question about the source of lameness, a thorough lameness evaluation should be performed. Intra-articular anesthesia will localize the source of the pain; however, care must be taken not to infuse a large volume of anesthetic into the tarsometatarsal joint as this may also alleviate pain associated with injury of the proximal suspensory ligament. Sometimes it may be beneficial only to perform distal intertarsal joint analgesia initially, in an effort to differentiate distal tarsitis from suspensory desmitis.

Radiographs are taken of the hock to determine the presence or extent of arthritic changes. A complete study consisting of four radiographic views is necessary as abnormalities are often subtle. Radiographic abnormalities are frequently lacking in young horses with distal tarsitis. The radiographic changes frequently observed include narrowing of the joints, proliferation and/or lysis at the joint surfaces, and occasionally ankylosis of one or more joints. Infrequently, yearlings and 2-year-olds will exhibit significant lameness and have extensive lysis and proliferation associated with the distal joints. This condition has been termed juvenile arthritis and is most likely a form of osteochondrosis with delayed ossification of the tarsal cuboidal bones.

The treatment of distal tarsitis is often dependent on the future training and competition requirements of the individual horse. If the horse is young, lacks radiographic abnormalities and can have a respite from its training regimen, the horse is often prescribed rest and anti-inflammatory medication. However, most of the time a rest period is not preferred by the owner/trainer and a more aggressive treatment plan is instituted. Inflammation within the distal hock joints can generally be effectively managed throughout a horse's athletic career by intra-articular injection of hyaluronic acid and corticosteroids. Both the distal intertarsal and tarsometatarsal joints should be injected, as communication is unreliable. Additionally, these horses will also frequently benefit from concurrent use of intravenous hyaluronate sodium (Legend, Bayer Corp., Agriculture Division, Animal Health, Shawnee Mission, KS 66201) and/or intramuscular polysulfated glycosaminoglycan (Adequan i.m., Luitpold Pharmaceutical Inc., Animal Health Division, Shirley, NY 11967).

Many Western performance horses can sustain a productive athletic career despite the existence of chronic tarsitis. Injection of the distal tarsal joints should be performed when needed to maintain reasonable soundness and to allow these horses to continue to perform at a high level. Occasionally, a horse with distal tarsitis will begin to have a diminished response to intra-articular therapy. Radiographs are made at that time to determine the extent of arthritic development. If there is evidence of ankylosis, turnout and a temporary discontinuance of training and showing may be required. If the radiographs show a lack of significant arthritis, then a procedure to stimulate ankylosis of the joints may be indicated. There are two described techniques for the induction of ankylosis in the distal tarsal joint: surgical drilling across the joint[7] and injection of sodium monoiodoacetate.[8] In general, both techniques have mixed results and the natural process of ankylosis is preferred. The response to intra-articular injections of hyaluronic acid and corticosteroids in young horses with juvenile arthritis is often insufficient to enable these horses to compete at the lucrative futurities. In these horses, the surgical drilling procedure for hastening ankylosis may offer the best chance for future athletic performance.

Stifle lameness

Both developmental and traumatic conditions of the stifle occur in Western performance horses. Developmental conditions include osteochondrosis of the femoropatellar and/or femorotibial joints and upward fixation of the patella. Osteochondrosis in the femoropatellar joint is most commonly associated with the trochlear ridges of the femur or in the medial femorotibial joint as a cyst within the medial femoral condyle. Upward fixation of the patella is usually observed in younger horses that are conformationally predisposed by being straight through the stifles. Most often this is an intermittent condition with a gait abnormality and, rarely, slight lameness. Trauma can vary from mild inflammation to major soft tissue and cartilage damage associated with the joint.

Horses with stifle lameness are typically lamer than seen with distal tarsal inflammation. There is generally pain palpable in the back musculature and often there is effusion of the femoropatellar or medial femorotibial joint. The horse exhibits a shorter cranial phase of the stride that is especially evident at the gallop or canter most notably when the affected leg is on the outside of a lunged or round pen circle. There is usually a hip rise on the affected leg because of the shortened stride and reluctance to flex the leg fully. A positive res-

ponse to upper hindlimb flexion is evidenced with a further shortening of the stride and a more noticeable hip rise. The lameness is localized to the stifle with the use of intra-articular anesthesia. In general, the femoropatellar and medial femorotibial joints communicate while the lateral femorotibial joint does not.

A comprehensive radiographic study of the affected joint should be performed. A complete study includes lateral, caudal-cranial, and caudolateral-craniomedial views. It is relatively common for lesions to be evident only on one of the views. Recently, ultrasound examination of the stifle to visualize the cranial cruciate ligament, cranial aspect of the meniscus and collateral ligaments has been described and may be useful in determining the extent of the injury in select cases.[9]

Developmental stifle conditions

Intermittent upward fixation of the patella is most commonly observed in 2- and 3-year-old horses and can often be diagnosed with a good clinical history. Occasionally there will be slight effusion of the femoropatellar joint. Conservative management is preferred as transection of the medial patellar ligament can predispose to secondary arthritis.[10] A consistent exercise program is necessary to properly condition the hindlimb musculature. In more severe cases, further therapy is usually necessary and may include a regimen of intramuscular estrone sulfate (TD Swanson, personal communication), injection of the medial and sometimes middle patellar ligaments with a counterirritant, surgical splitting of the medial patellar ligament[11] and, as a last resort, medial patellar ligament desmotomy. Generally the prognosis is good and the horse can be managed with conservative therapy.

Osteochondrosis of the femoropatellar joint is treated with arthroscopic surgery. Lesions are most commonly located on the lateral trochlear ridge. The prognosis is dependent on the size of the lesion with smaller lesions having a superior prognosis, but usually the prognosis is favorable.[12] Lesions within the femorotibial joints are almost always observed on the medial femoral condyle. Lesions will vary from slight flattening or indentation of the articular cartilage to large subchondral cysts. Recommendations for treatment of medial femoral condyle cysts are controversial. Arthroscopic surgery has yielded mixed results and therefore is usually reserved for horses not responding well to more conservative treatment. If the lameness is not severe and the lesions are small, intra-articular injection of the medial femorotibial joint with hyaluronic acid and corticosteroids will often alleviate the lameness and allow the horse to remain in work. If the lameness is more severe and/or the cystic lesion is sizeable with a large communication with the joint, then intra-articular injection is often used in conjunction with confinement and rest. Recent research has been directed towards improving the healing of the defect in an effort to increase surgical success.[13,14] Currently, these methods are mostly experimental and further research and clinical trials are necessary.

Traumatic stifle conditions

Injuries to the stifle most commonly occur in the medial femorotibial joint. In cutting and reining horses, it is not uncommon for mild inflammation of the medial femorotibial joint to occur in conjunction with distal tarsitis. Traumatic injuries will vary from mild inflammation to career-ending soft tissue disruption. In the more severe injuries, rest is required. These horses require strict stall confinement, systemic anti-inflammatories, intramuscular polysulfated glycosaminoglycan (Adequan i.m., Luitpold Pharmaceutical Inc., Animal Health Division, Shirley, NY 11967) and re-examination at a later date. The prognosis is guarded at best and depends on the subsequent development of arthritis. Horses with minimal inflammation and no radiographic abnormalities can often be managed and kept in training and competition. If concurrent distal tarsal inflammation exists, intra-articular injection of the distal tarsal joints is often all that is required for resolution of the stifle inflammation. When more significant inflammation exists, the affected joint should be injected with hyaluronic acid and a short-acting corticosteroid. Further inflammation of the stifles can sometimes be avoided by maintaining the distal tarsal joints as pain free as possible.

References

1. Schumacher J, Schramme M, Schumacher J, et al. Abolition of lameness caused by experimentally induced solar pain in horses after analgesia of the distal interphalangeal joint. Proc Am Assoc Equine Pract 1999; 45:193–194.
2. Herthel DJ. Enhanced suspensory ligament healing in 100 horses by stem cells and other bone marrow components. Proc Am Assoc Equine Pract 2001; 47:319–321.
3. Boening KJ, Loffeld S, Weitkamp K, et al. Radial extracorporeal shock wave therapy for chronic insertion desmopathy of the proximal suspensory ligament. Proc Am Assoc Equine Pract 2000; 46:203–207.
4. Bohanon TC. Contrast arthrography of the distal intertarsal and tarsometatarsal joints in horses clinically affected with osteoarthrosis. Proc Am Assoc Equine Pract 1994; 40:193–194.
5. Kraus-Hansen A, Jann H, Kerr D. Arthrographic analysis of communication between the tarsometatarsal and distal intertarsal joints of the horse. Vet Surg 1992; 21:139–144.
6. Bell B, Baker G, Foreman J, et al. In vivo investigation of communication between the distal intertarsal and tarsometatarsal joints in horses and ponies. Vet Surg 1993; 22:289–292.
7. McIlwraith CW, Turner AS. Arthrodesis of the distal tarsal joints. In: McIlwraith CW, Turner AS, eds. Equine surgery advanced techniques. Philadelphia: Lea and Febiger; 1987:185–190.

8. Bohanon TC. Chemical fusion of the distal tarsal joints with sodium monoiodoacetate in horses clinically affected with osteoarthrosis. Proc Am Assoc Equine Pract 1995; 41:148–149.
9. Reef VB. Musculoskeletal ultrasonography. In: Reef VB, ed. Equine diagnostic ultrasound. Philadelphia: WB Saunders; 1998:160–164.
10. Gibson KT, McIlwraith CW, Park RD, et al. Production of patellar lesions by medial patellar desmotomy in normal horses. Vet Surg 1989; 22:157–163.
11. Tnibar MA. Medial patellar ligament splitting for the treatment of upward fixation of the patella in the horse. Proc Am Assoc Equine Pract 2001; 47:491–493.
12. Foland JW, McIlwraith CW, Trotter GW. Arthroscopic surgery for osteochondritis dissecans of the femoropatellar joint of the horse. Equine Vet J 1992; 24(6):419–423.
13. McIlwraith CW, Frisbie DD, Trotter GW, et al. Use of a subchondral bone plate micropick technique to augment healing of articular cartilage defects. Proc Am Assoc Equine Pract 1998; 44:233–235.
14. Jackson WA, Stick JA, Arnoczky SP, Nickels FA. The effect of compacted cancellous bone grafting on the healing of subchondral bone defects of the medial femoral condyle in horses. Vet Surg 2000; 29:8–16.

CHAPTER 55

Veterinary aspects of training hunter/jumper horses

Duncan F. Peters

Introduction

It has long been recognized that horses have the ability to jump obstacles. This unique characteristic and man's domestication of the horse over time has led to refinement of this ability. The next logical step was the development of a competitive venue for jumping. The sport of showing horses over fences is rooted in England in the mid-nineteenth century. International competitions flourished in Europe and equestrian jumping events were introduced at the 1912 Olympic Games. A unique aspect of showing horses over fences is that men and women riders compete as equals.

The show hunter

The hunter classes at horse shows are intended to demonstrate the grace, elegance and jumping style of the horse and are scored subjectively by one or more judges (Fig. 55.1). Originally, the concept was to show over obstacles that might be encountered in the foxhunting field. Jumps would include natural building materials and mimic gates, coops, walls and a variety of natural brush vegetation. More recently, show hunter courses have the same basic jump style, but now are adorned with bright flowers and foliage which may entice the horse to jump more brilliantly over the jumps.

Hunters are supposed to jump with a style that appears easy to ride while at the same time folding their front legs tightly and squarely with knees elevated above the point of the shoulder. The head and neck should be extended forward and have a flexing curvature over the top of the fence (Fig. 55.2). The horse should appear to clear the required height with ease and the hindquarters should glide smoothly over the fence in a round, arcing style. The entire jumping motion should be fluid, effortless and controlled, and appear to be smoothly connected with the takeoff and landing strides.

Fig. 55.1
Show hunter exhibiting the jumping style, elegance and beauty necessary for success in the show ring.

Fig. 55.2
Classic jumping form in a hunter. Note that the front legs are square and the knees high as horse arcs over the jump. Also note the flexion through the neck and the extension of the hindquarters as the horse leaves the ground.

Fig. 55.3
Power, speed and colorful obstacles mark the showjumper arena.

The movement, pace and general impression of the show hunter around the course is important in the scoring by the judges. Movement at the trot and canter should be fluid, smooth and with a relaxed cadence that covers the ground with a minimum of effort. The horse should appear relaxed and comfortable with minimal noticeable commands by the rider. The horse and rider should approach fences in a balanced position and jump the obstacles 'in stride'. Show hunters compete over jumps of varying height (up to four feet) depending on their age, jumping ability, experience and the capability of the rider.

The showjumper

The showjumper is typically a horse that demonstrates a combination of power and speed. The main requirement is to jump a series of obstacles within a specified, allotted time. The objective is to jump the course with the least number of penalty faults. Scoring is done objectively based on penalty faults given for such things as jumps that are lowered in height by knocking them down, refusals to jump an obstacle, exceeding the time allowed on course, placing a foot in the water jump, and a fall of a horse/rider combination.

The showjumper has to be athletic and have a proclivity for jumping any kind of colored or configured obstacle that may be included in the competition course (Fig. 55.3). The horse must jump with precision and care, whereas the absolute form and style over the obstacles is of lesser importance. It is extremely important that the horse be well schooled and responsive to the rider due to the fact that competition courses have winding turns, combination fences and often varying number of strides between fences. The showjumper can be any breed, color, size and shape as long as the horse demonstrates a desire and willingness to jump the obstacles without incurring faults. The elite showjumpers tend to be naturally well-balanced athletes with an ease of movement that is fluid, loose and appears effortless, especially at the canter. Jumpers compete in a variety of classes based on age, fence height, prize money won and the ability of the rider.

The biomechanics of the jumping style in jumpers varies from that of the hunters. The strides preceding the jump are used to position the horse and to harness its horizontal energy in order to convert it to vertical energy in the takeoff stride. In the stride just prior to takeoff, the horse lowers its center of gravity, decelerates forward movement of the front legs and then thrusts vertically to raise the forequarters off the ground. The hind feet then plant close to the base of the fence and supply further vertical energy to propel the body over the obstacle. There is a rotation of the center of gravity over the top of the fence with extension of the lumbosacral region and the hip joint to allow the hindquarters to clear the obstacle. Landing requires the front legs to land in a staggered arrangement in order to gallop away from the fence (Fig. 55.4). This imparts very large vertical forces that must be absorbed by the structures of the front legs. The higher and wider the fence, the greater the forces involved and the greater the effort required by the horse and rider. When these factors of jumping biomechanics are combined with the variety of pace, obstacles and directional lines of the showjumping course itself, it requires a horse that is well trained, responsive, athletic and properly conditioned to compete successfully.

The demands of show hunting and jumping

As a year-round sport, show hunting and jumping is a demanding sport and it is difficult for owners, trainers and

Fig. 55.4
The soft tissues of the front legs have to withstand tremendous stress during takeoff, landing and tight turns in the jumper ring.

veterinarians to manage these horses such that consistent athletic performance is achieved throughout the year. Many factors must be considered to keep a training and showing program efficient and fresh for the horses while minimizing injuries and the need for veterinary medical intervention.

Show horses must be conditioned adequately to attain a level of 'fitness for the intended task'. Ideally, the required level of fitness is achieved before a horse is taken on the show circuit. Once a horse achieves a desired level of fitness, it is fairly easy to maintain that level with consistent exercise.[1] Hunters do not require the level of fitness demanded of the showjumper. Actually, many show hunters are kept slightly underconditioned and overweight in order to minimize the amount of exercise required to 'take the edge off' prior to entering the show ring. Judges tend to reward this overly relaxed expression in their scoring. Showjumpers, on the other hand, tend to be conditioned in a manner more appropriate to the level of athletic activity.

The show season and individual show schedules can be important to the success and health of hunters and jumpers. Most elite hunters and jumpers are vying for year-end awards, entrance to prestigious horse shows or participation on certain team events. This means that a horse either has to accumulate a large number of points compared with rival horses or has to perform well in specific qualifying shows. The show season may be 9 to 10 months in length with two to three shows per month. When combined with the rigors of travel and regular conditioning, it is clear that there are high demands on the show athlete. Hunters often have two to four jumping classes per show day. If they are entered in amateur rider as well as open hunter classes, these horses may compete on 4–5 consecutive days. These work demands are further increased by participation in warm-up classes and the need to school over fences prior to each class. In contrast, jumpers tend to be managed through a show in a manner that targets one or two specific classes. Most showjumpers either compete in the open classes, with a professional rider, or in the amateur classes. This more restricted performance schedule tends to maintain the showjumper's energy and mental alertness at a desirable level.

Show hunters and jumpers tend to travel more frequently and farther than other sport horses. This makes them susceptible to transit stress and to suppression of their immune system.[2] In this author's opinion, horses are more susceptible to infections for up to 7 days after prolonged transportation. This is especially true when traveling between time zones and internationally. As most large horse shows are scheduled over a 6–7-day period, there is often minimal time for recovery following transportation from one venue/event to the next.

Judging criteria also may contribute to the stresses imposed on show horses, particularly in the hunter classes. In many instances, a horse that is quiet and relaxed in the ring will be favored over a horse with superior jumping ability but a more 'playful' disposition. As a result, hunter horses are often exercised to the point of fatigue (lunging and/or under saddle) to 'take the edge off' before entering the ring to compete. Alternatively or additionally, many owners and/or trainers look toward medications or hormones to alter the 'appearance' of the hunter in the ring. Both practices may predispose these horses to problems that are ultimately performance limiting.

Arena footing has become a primary concern for horse trainers and owners, equestrian governing bodies, show managers and veterinarians. Poor footing (e.g. overly hard surface), both in the main arena and in the schooling and warm-up areas, appears to be a major predisposing factor for musculoskeletal injury. Many federations are now adopting stringent guidelines for the quality of footing at sanctioned events.

Veterinary services

The veterinarian plays a key role in the training, management and medical care of the hunter and jumper. The veterinarian wears many hats and has to coordinate the efforts of many people (e.g. farrier, massage therapist, trainer) in order to provide optimal care to the horses under his or her care. The scope of his/her responsibilities and efforts may be constantly changing to meet the needs of clients, patients and even equestrian governing federations. The veterinarian

must be willing and able to see the total picture from a variety of different vantage points and be adept at keeping all parties focused on the proper care of the horse.

It is also imperative that open and clear lines of communication are nurtured and maintained throughout the diagnosis and treatment of a given problem. In addition to veterinary care, the practitioner must be prepared to act as source of advice concerning nutrition, conditioning programs, equipment (tack), and transportation. This does not mean that he or she needs to have all the answers, but should be able to identify qualified people to assist in the overall management program of the horse. For example, the soliciting of advice from a nutritionist regarding a feeding program, referral to a specialized veterinary facility for advanced diagnostic techniques or surgery, or the acquisition of current research papers relevant to a current problem.

Additionally, the veterinarian should expect in return an open and honest dialogue with the trainer concerning any veterinary problems that arise while the horse is away at competitions. This is extremely important in light of the fact that trainers often travel long distances to compete and spend a large amount of time at competitions not attended by their regular veterinarian. Lameness or metabolic problems incurred at a show should be re-evaluated and discussed once the horse has returned home. Copies of medical records should be obtained from the attending veterinarian at the show. This will ensure proper care of the horse and help to determine if changes in veterinary care or other management of the horse are warranted. The veterinarian should rely on the trainer and his/her employees for day-to-day information concerning the horses under his or her care. It is important to have a good relationship with the grooms because they spend the most time with the horses and can usually provide reliable and timely information concerning an individual horse. For lameness or poor performance problems, insight provided by the rider can be invaluable in localizing subtle gait abnormalities. Similarly, a veterinarian with riding skills may, on occasion, wish to ride a horse as a component of the gait evaluation.

Proper care of hunter and jumper horses is also critically dependent upon a strong relationship between veterinarian and farrier. They must work together to maintain good lines of communication between themselves as well as with the trainer or owner. Ideally, the farrier and veterinarian work together in the development of a shoeing plan, although there are cases in which the veterinarian must request use of a specific shoe or shoeing technique.

Veterinary medical service can be provided to show stables in a variety of ways. In most instances, show stables have a primary ambulatory veterinarian who attends to the general care of the horses when they are not competing on the circuit. He/she maintains a preventive medicine program, works up and treats musculoskelatal problems, attends to emergencies and consults regarding many aspects of show horse care. In addition, this practitioner usually has a network of referral hospitals or their own hospital facility that can be utilized for problems requiring further diagnostic workup or treatment. It is important for the practitioner to provide veterinary referral contacts for their trainer/show stable for the geographic areas in which they compete. Some veterinarians travel with their clients on the show circuit, but this is the exception. More routinely, there are a number of ambulatory veterinarians that routinely travel the show circuit and attend to whichever horses or stables may need their services at a particular competition.

Pre-purchase examinations

The pre-purchase examination provides the potential buyer a 'point in time' veterinary assessment of the horse in the context of its intended use. The intent is to identify problems that may limit or hinder athletic performance. For the show hunter and jumper, this involves a comprehensive physical examination with particular focus on conformation, the musculoskeletal system and the assessment of gait.[3] Problems must be evaluated in light of the intended use of the horse, the potential impact on athletic performance, the prognosis, and the willingness of the buyer to accept risk regarding the problem. Radiology, ultrasound, endoscopy, thermography and clinical hematology are routinely employed in most performance horse pre-purchase examinations. Additional evaluations using acupunture, chiropractic techniques, nuclear scintigraphy, magnetic resonance imaging, computer aided tomography and kinesiology, as well as other evaluation modes, have been employed to aid the buyer in making an 'informed decision'. An important part of any pre-purchase examination is the necessity for accurate, readable records and clear communication with the buyer or buyer's agent.

Lameness examinations

Frequently, horses return from shows with lameness or gait abnormalities. It is imperative to obtain a detailed and accurate history regarding the problem, including the administration of any medications. The history may come from notes from an attending horse show veterinarian or repeated queries to the trainer, rider or groom associated with the horse. The physical examination should include palpation, work on a lunge line, flexion tests and, in some cases, observation under saddle. Regional perineural anesthesia and intra-articular anesthesia can be very helpful in localizing the area of lameness. Further diagnostic procedures to delineate the actual cause of lameness may be conducted at the stable or at a clinic.

Specific disease problems encountered in show hunters and jumpers

Show horses are susceptible to a wide array of veterinary problems, particularly those involving the musculoskeletal system. In many instances, proper identification of the

problem facilitates appropriate treatment and management that allows the athlete to return to competition in a short period of time. The demands on the elite hunter and jumper make them prone to both acute- and chronic-onset musculoskeletal injury. Chronic problems can develop from low-grade, subclinical pain and may compromise performance in the absence of overt lameness. Changes in jumping technique, stride length or work attitude, or an overall decline in performance can be signs of low-grade musculoskeletal problems. Acute-onset problems usually result in a distinct lameness and early diagnosis and treatment is imperative for optimum resolution. Unfortunately, these injuries have the potential to become chronic, thereby requiring recurrent treatment and/or a reduction in workload expectations.

Foot problems

The show hunter and jumper is prone to foot injury as a result of variations in exercise surfaces and excessive wetting and drying cycles due to repeated bathing and application of hoof coatings. It is not uncommon for horses showing in warm climates to be bathed three to four times per day and a commercial hoof oil to be applied to the feet every time the horse leaves the stable area and following schooling just prior to entering the show ring. In addition, the ring areas at horse shows are worked up and watered on a regular basis to provide good footing. These factors contribute to shelly, brittle hoof capsules and the development of cracks that may cause lameness or make it difficult to hold shoes properly. A variety of management tools have been used in an effort to mitigate the effects of repeated cycles of wetting and drying. The application of a clear acrylic coating to the hoof capsule at the time of shoeing and weekly thereafter can help to seal the hoof wall. Attempts should be made to preserve the periople at the time of shoeing. A decrease in the frequency of bathing is also recommended; a thorough grooming can usually achieve the desired appearance.

Quarter cracks and hoof capsule injuries can cause persistent lameness and poor performance. Quarter cracks are usually the result of hoof imbalance coupled with concussive trauma. Accordingly, the veterinarian and farrier should work together to identify and correct foot imbalance. In addition, corrective farriery should move the breakover caudally and unweight the affected area. The crack should be debrided followed by the application of a temporary shoe that evenly distributes weight over the foot (i.e. bar shoe). Systemic medication to curb inflammation may also be indicated. In more severe cases, stabilization of the crack is required to alleviate pain. This can be accomplished by an array of techniques including screw-in plates, glue-on plates, wire and Kevlar laces, acrylic compounds, and cast material. Frog support pads, pour-in soft hoof packing or steel pads also can be used to support the foot. Some reduction in exercise is necessary to prevent destabilization of these support devices. A 2- to 4-month period is often required for complete stabilization of the crack. However, with close monitoring the conditioning load can be slowly increased during this period.

Chronic concussive injury with resultant front foot soreness is a common occurrence in jumping horses performing on firm surfaces. Early indications of soreness may be a shortened, choppy stride, putting in a quick short stride at takeoff to a jump and refusal to jump. Injury may involve the soft tissues of the foot (i.e. bruise, hematoma, low-grade laminitis) and may progress to chronic remodeling of the coffin bone (pedal osteitis). The initial goal of therapy is to alleviate inflammation via the administration of anti-inflammatory drugs and medications purported to increase blood flow to the foot. Adjunct therapies included regional perineural anesthesia, foot soaking, poultice bandages and the use of Styrofoam hoof pads. Corrective foot trimming and shoeing should be undertaken once the inflammation has subsided. The foot must be trimmed and balanced to optimize its ability to absorb concussion. Simple, acute cases may only require the insertion of soft impression material under a flat pad, a rim pad or a soft pour-in pad under a regular shoe. In more severe cases, glue-on shoes, a rigid plastic or steel pad with acrylic impression material, enlarged bar shoes for support or the application of acrylic material to raise the heels may be indicated. It may take weeks to months for a 'sore-footed' horse to return to form. Exercise on soft ground, minimal jumping, lightweight riders and a reduced competition schedule will speed the process.

Caudal heel pain is a common cause of lameness in show hunters and jumpers. The diagnostic dilemma is to determine which structure, or combination of structures, underlies the pain. Regional perineural anesthesia, distal interphalangeal intra-articular anesthesia and navicular bursa anesthesia may help to differentiate the source. Magnetic resonance imaging of the heel region has been helpful and in many instances multiple problems have been identified. Acute cases respond well to therapy that involves the intra-articular or intrabursal administration of corticosteroids or sodium hyaluronate, a period of rest (3 to 6 weeks) followed by controlled light riding (3 to 6 weeks), anti-inflammatory medication and attention to shoeing (caudal heel support). Chronic caudal heel pain can be a challenge to treat and manage. Many affected horses can continue to compete if the condition can be managed such that lameness is no worse than a grade 2. However, the trainer and/or owner must be willing to accept lowered performance expectations, including a decrease in the number of shows and classes within a show expected of the horse. Regular low-intensity exercise to maintain conditioning is important to prevent other musculoskeletal problems. Regular (every 2–3 months) intra-articular therapy and the administration of anti-inflammatory medications at competitions can also aid in the management of these horses. Surgical interventions involving the innervation to or support of the navicular bone are last resort treatment measures.

Joint problems

Joint ailments in show athletes are related to an isolated traumatic incident or to repeated 'wear and tear' on joints. The goals of therapy for acute synovitis are to reduce pain,

swelling and inflammation in order to minimize chemical mediator induced damage to the joint. This is generally accomplished through physical therapy techniques and the administration of systemic and intra-articular medications. The prognosis is good and most affected horses are able to return to their previous level of competition after 3 to 4 weeks. An extended layoff and/or surgical treatment may be required if joint trauma results in chip fracture, cartilage damage or supportive ligament lesions.

Osteoarthritis (OA) and degenerative joint disease are the most common chronic joint problems in show horses. Both high motion/low load joints (metacarpal-phalangeal, metatarsal-phalangeal, carpal, etc.) and high load/low motion joints (interphalangeal, distal tarsal) can be affected. The extent of remodeling damage to the joint can influence treatment and management of the horse. It is important to utilize good shoeing principles in an attempt to reduce stress on joints. The use of rolled or rockered toes with the break-over moved caudally may aid a sore fetlock joint. Horseshoe pads or soft acrylic pour-in pads may help disperse concussive forces. Limiting the use of horseshoe or screw-in heel caulks can reduce shear forces on a joint. Periodic intra-articular injections of corticosteroids and sodium hyaluronate may alleviate inflammation and pain. Osteoarthritis of high load/low motion joints should be managed similarly; it is this author's opinion that intra-articular injections with sodium hyaluronate and/or corticosteroids should be done every 3–4 months. The duration of relief will depend on the severity of the condition, and the success of concurrent therapies and management practices. The systemic administration of hyaluronate and polysulfated glycosaminoglycans appears to be useful in horses with OA, and the judicious use of non-steroidal anti-inflammatory drugs is also recommended for the control of inflammation. The daily oral administration of chondroitin sulfate and glucosamine is now routine, although the efficacy of these treatments is unproven. Exercise should be regular, consistent and geared toward maintaining the necessary fitness for the show ring. For jumpers, tight turns and high-speed exercise should be undertaken sporadically and not when the horse may be fatigued. It is better to school over a few fences more frequently than to put many fences into one schooling session.

Osteochondrosis dissecans (OCD) is prevalent in show hunters and jumpers, perhaps because of the large number of Warmblood horses used in these disciplines. Many OCD lesions are identified during pre-purchase examinations or during the evaluation of an acute lameness associated with moderate to severe joint effusion. When lameness is present, arthroscopic surgical intervention is usually indicated. These horses have a guarded to good prognosis for return to competition depending on the severity of lesion(s). Occasionally, a conservative approach to therapy involving joint injections and extended rest is instituted.

Soft tissue injuries

Most soft tissue injuries to ligaments and tendons are acute in nature. Depending on the extent of that injury and the recovery time involved, they may then be classified as a chronic problem. The soft tissue structures most often injured in hunters and jumpers are the superficial digital flexor tendon, the accessory ligament of the deep digital flexor tendon and the suspensory ligament. Recurrence of these problems is common.

In the author's opinion, fatigue is a major contributing factor to superficial flexor tendon injury in hunters. Most hunters are overweight and underconditioned. Nonetheless, these horses are routinely worked to the point of fatigue just prior to entry into the show ring, often on uneven and inconsistent footing. It is likely that this fatigue contributes to the stress on this tendon with resultant tendinitis.[4] Diagnostic ultrasound should be performed to determine the extent of tendon damage and to aid selection of an initial treatment plan. An injury with peritendinous swelling and no major fiber damage should be managed with physical therapy (ice or hypertonic hydrotherapy), bandage support, systemic anti-inflammatory medication, rest and a follow-up ultrasound in 2 to 4 weeks. Light exercise can be incorporated into the rehabilitation program if the subsequent ultrasound examination demonstrates improvement. Cold laser or therapeutic ultrasound may be incorporated at this stage, if available. The rate of healing is variable but affected horses may be ready for a return to competition in approximately 2 to 3 months. An injury that results in a core lesion should initially be evaluated and treated as above, with re-evaluation of the injury in 45 to 60 days. A decision to continue rest, inject the lesion or perform a surgical procedure should be based on the change in appearance of the lesion. Most horses that develop a significant core lesion within the superficial digital flexor tendon require 6 to 8 months for recovery, after which a return to the previous level of exercise may be possible.

Inflammation and lameness associated with the accessory ligament of the deep digital flexor tendon (distal check ligament) is more common in the showjumper than the hunter. This is most likely due to the size of fences involved and the different jumping styles. The check ligament adjunctively aids the deep flexor tendon at takeoff to convert horizontal energy into vertical energy and to elevate the forequarters of the horse off the ground. In addition, during landing from a jump, the suspensory ligament and the check ligament of the front legs act as 'stops', converting vertical energy to horizontal energy as the deep flexor tendon loads and helps to move the horse away from the fence. In most instances of injury to the check ligament, there is an incident of a 'funny feeling' jump or a stumbling on landing. The initial management is directed at physical therapy with cold treatment and cooling gel bandage support, systemic non-steroidal anti-inflammatory medication, rest with hand walking, and evaluation of the injury by use of ultrasonography. A relatively minor sprain with fiber pattern edema and minimal amount of overall thickening is treated with medicated poultice bandages, continued anti-inflammatory medications, mildly raised heels, cold laser or ultrasound therapy, and a slow return to exercise over a 4-week period. For the first 4–6 weeks of training, it is generally wise to follow a conservative training and competition schedule, avoiding excessive

speed in jump-offs and utilizing supportive bandages or boots during work. The prognosis for this type of injury is favorable.

Chronic, recurrent thickening, inflammation, soreness and lameness attributed to the check ligament carries a poorer prognosis and can require a forced reduction in the level of competition or retirement. Affected horses will show some improvement following palliative treatment with corrective shoeing, rest, anti-inflammatory medications and other therapies. However, persistent lameness can occur due to the buildup of scar tissue in the check ligament. Surgical intervention with check ligament desmotomy has been beneficial, but generally more as a salvage procedure to make the horse comfortable in retirement or as a pleasure horse.

Suspensory ligament injuries are a cause of poor performance in hunters and jumpers.[5] The three distinct regions of the ligament (high or origin, body, and branches) can be affected. Injury to the suspensory ligament of the show hunter generally occurs more frequently in the front legs as a result of the aforementioned fatigue factors. Exercise in deep, heavy footing also increases the risk for this injury. In jumpers, about two-thirds of cases of suspensory desmitis occur in the fore legs. It is the opinion of this author that the increase in prevalence of suspensory desmitis in jumpers can be attributed to the desire for more 'grab' with the use of more and larger caulks or studs on shoes. The latter may cause the horse to load their support apparatus in a jerky, uneven and inconsistent manner, putting peak loads on the suspensory ligament over very short time periods as the caulks 'grab'. The increase in running speed that the rider feels is attainable with better traction also may predispose to suspensory ligament injury. Many of the hindlimb suspensory problems can be attributed to strain during takeoff biomechanics, while front limb desmitis is usually the result of injury during landing or while completing fast turns.

The suspensory ligament tends to heal slowly due to poor vascularization and the density of fibers. Even in cases in which there is minimal ultrasonographic evidence of injury, an 8- to 12-month period of rehabilitation can be required before a return to full exercise. Generally, desmitis that occurs at attachment regions (proximal metacarpal or metatarsal, abaxial sesamoids) has a poorer prognosis for return to previous level of competition compared with injuries at other sites. Therapeutic plans should focus on the next 8-week period, with re-evaluation of progress and treatment plans at the end of each period. For the first 4 weeks, treatment should focus on resolution of heat, pain, and swelling, along with rest. Then, adjunctive therapy (laser, ultrasound, extracorporeal shock wave), local injections (hyaluronate, corticosteroids, sclerosing agents), herbal preparations, and light exercise can be instituted. If clinical or ultrasound findings do not improve from one examination to another, a more aggressive therapeutic approach may be indicated. This may involve surgery for local fiber splitting or furage, bone marrow autograft injection, transplantation injection of stem cells, carbon/silicone injections or hyperbarometric oxygen treatment. Light exercise of walk and trot for a couple of months can slowly be increased over time to include some short canter work. Foot care should include attention to medial/lateral balance, caudal heel support, and a slight lowering of the heels to reduce stress on the injured ligament and ease breakover. In horses with good response to treatment, consistent exercise under saddle on the flat is generally possible around 7 to 8 months post-injury. Cavalletti and pole work can be started and progress to small jumps over the subsequent 6- to 8-week period, with an increase in jump height and training intensity over the next month. Return to the show ring should be gradual and great attention should be paid to footing, foot care, any changes in jumping style, swelling or heat of the suspensory, and any indication of gait abnormality or lameness.

Back problems

Back soreness is a frequent complaint in hunters and jumpers. The biomechanics and stresses placed on the bony vertebral column and the associated muscles and ligaments while jumping are not completely understood or documented.[6] Nonetheless, observation of horses jumping large fences with a rider suggests that considerable strain is placed on these structures. In hunters and jumpers, back soreness is often attributed to muscle problems, specifically muscle fatigue, muscle spasm or some neuromuscular interaction. Back pain can be precipitated by a sudden increase in the level of competition, a change in rider or rider ability, a change in saddle or other equipment, exercise on a lunge line, deep dry or wet ground conditions, or secondary to other lameness or muscle problems. For example, lower lumbar and gluteal muscle soreness is a fairly common finding in horses with distal tarsitis. Chronic, low-grade discomfort of the forelimb fetlock region may result in nagging lower lumbar and sacroiliac soreness. Therefore, effective management of muscle pain over the back region requires identification and treatment of these underlying primary problems.

Several treatments are effective for the palliative relief of back pain and inflammation. Ice and cold therapy can be effective in the management of acute pain or directly following exercise. Electromagnetic blankets, acupuncture, light therapy, massage and chiropractic techniques, stretching exercises, therapeutic ultrasound and liniments or poultices may also be beneficial. It also is important to ensure that the horse undergoes proper warm-up and cool-down when exercising. Horses that are reported to be stiff or tight through the thoracolumbar or the lumbosacral regions while ridden should be given 20 to 25 minutes of walk and slow trot together with bending and suppling exercises at the beginning and end of each strenuous flatwork or jumping session. Jumping sessions may involve more repetitions of an exercise but at a lower intensity and/or shorter duration. Although difficult and time-consuming for many riders, this approach is effective in the prevention of recurrent back pain. Quarter sheets or blankets over the large muscles of the lower back and hindquarters, while riding, are helpful in cold or inclement riding conditions. Other therapies that may be used include the local injection of corticosteroid and homeopathic preparations and the systemic administration of muscle relaxants, non-steroidal anti-inflammatory drugs, immune modulators or antioxidant supplements.

Back soreness caused by primary skeletal problems of the thoracic, lumbar or iliosacral regions is difficult to diagnose, treat and manage. An experienced rider may be able to detect subtle changes in gait, movement or jumping style subsequent to the infiltration of local anesthetic into suspect areas. Imaging studies (ultrasound, radiology, nuclear scintigraphy) can help in the localization of back lesions. In addition to the treatment and management measures discussed above, therapy often involves the use of local corticosteroid injections. Recently, epidural administration of corticosteroids has been used for the treatment of pain related to osteoarthritic changes between vertebrae or associated with nerve root inflammation.

Stress-related diseases

Frequent and prolonged transport, housing in confined areas with large numbers of horses, irregular exercise programs, changes in feeding management, continuous activity around the stable area, and heavy use of medications are some factors that may predispose show horses to disease conditions. Although there have been no epidemiologic studies, diseases that may occur at a higher incidence in show horses than in other groups include viral respiratory disease, pleuritis, laminitis, colitis and gastric ulcers.

Miscellaneous conditions

From a judging perspective, laryngeal hemiplegia is regarded as unsoundness in a show horse. Originally, the thought was that a field hunter with a restricted airway problem would develop exercise intolerance over the course of a day of fox hunting. Realistically, most show hunters are performing in the ring for approximately 90 to 120 seconds at a submaximal level in which laryngeal hemiplegia is highly unlikely to restrict performance. Nonetheless, some form of surgical intervention is generally recommended for treatment of laryngeal hemiplegia. The technique selected depends on the degree of hemiplegia and the inspiratory noise present when the horse performs.

Pneumovagina can adversely affect jumping style in some hunter and jumper mares. The main clinical signs are a clamping down of the tail during jumping and a tendency to drop the hindquarters and jump flat over the fence and to hit or knock down jump rails with the hind legs. Treatment involves closure of the vulval lips below the level of the brim of the pelvis by use of a Caslick procedure.

Owners and trainers of female show horses are often concerned about behavioral changes associated with the estrous cycle. Behavioral signs of estrus can render some mares reluctant to perform and otherwise difficult to move around the show grounds. Oral or injectable hormone therapy can mitigate this behavior. A glass ball device placed in the uterus shortly after ovulation will suppress behavioral estrus for up to 3 months.[7] In some cases, an ovariectomy may be the appropriate course of action. This is only contemplated if the mare is not to be used for future breeding or she develops an ovarian tumor that is causing behavioral problems.

Intact male horses can also develop behavioral and performance problems. Many stallions become hard to handle and a challenge to keep focused on exercise performance. Some stallions develop testicular and/or scrotal inflammation and pain related to irritation during exercise under saddle or while jumping. These horses will tend to move with their hind legs placed wider than usual, 'stick' off the ground at takeoff, and constantly tail swish, buck or kick out with their hind legs while exercising. The application of lubricating gels to the scrotum to minimize irritation, a reduction in exercise intensity or duration, or castration are possible approaches to this problem.

References

1. Clayton H. Conditioning sport horses. Mason, MI: Sport Horse Publications 1991:77–94.
2. Smith BL. Effects of road transport on indices of stress in horses. Equine Vet J 1996; 28:446–454.
3. Marks D. Prepurchase examination of jumpers and dressage horses. Proc Am Assoc Equine Pract 1999; 45:4–12.
4. Smith RK, Birch HL, Patterson-Kane J, et al. A review of the etiopathogenesis and current proposed strategies for prevention of superficial digital flexor tendinitis in the horse. Proc Am Assoc Equine Pract 2000; 46:54–58.
5. Stashak T. Diseases of joints, tendons, ligaments and related structures. In: Adams' Lameness in horses, 5th edn. Philadelphia: Lippincott, Williams and Wilkins; 2002:621–624.
6. Cauvin E. Assessment of back pain in horses. In Practice 1997; 19:522–533.
7. Nie G, Johnson KE, Wenzel JGW. Use of a glass ball to suppress behavioral estrus in mares. Proc Am Assoc Equine Pract 2001; 47:246–248.

CHAPTER 56

The older athletic horse

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Demographics of the older or geriatric athletic horse

The definition of 'older' or geriatric horse varies, but 20 years of age or older has been suggested as a guideline.[1] The average horse is reported to have a life expectancy of 25 years.[1] While it is difficult to determine accurately the number of older or geriatric horses, it is estimated that between 10 and 20% of the horse population is geriatric.[1,2] The total horse population in the USA is estimated to be 5 to 8 million.[2] Therefore, there may be roughly 500 000 to 1.5 million horses in the USA that are considered older or geriatric. The population of geriatric horses is likely to have increased over the last several decades. Many of these older horses perform various athletic activities well into their twenties.[1] Today, horses are valued for companionship rather than just their ability to compete or perform work. In addition, modern horse owners are willing to spend more money on health care and optimal nutritional management. Consistent with these trends, at one veterinary teaching hospital in the USA there was a 55% increase in the number of horses 20 years of age or older between 1990 and 1995.[3]

The effects of aging on the body systems in horses

Cardiovascular system

It is well documented that aging results in a decrease in aerobic capacity in humans.[4–7] Older human athletes have decreased maximal oxygen consumption ($\dot{V}O_{2max}$) and decreased cardiac output.[4–6] The decrease in maximal cardiac output appears to be the result of a decrease in both maximal stroke volume and heart rate.[6] Training in older humans can help maintain aerobic capacity and stroke volume.[6,8–10] However, the age-related decline in maximal heart rate is not affected by training.[6]

A similar decrease in exercise and aerobic capacity also occurs in older horses.[11] Older horses are not able to run as fast on a high-speed treadmill (mean ± standard error: 8.7 m/s ± 0.5 versus 10.8 m/s ± 0.5) or as long (275 ± 31 versus 419 ± 31 seconds) as are younger horses.[11] The $\dot{V}O_{2max}$ of unfit, older horses is 24% lower than that of unfit, younger horses.[11] In addition, the treadmill velocity at which $\dot{V}O_{2max}$ occurs is lower in older than in younger horses (8 m/s ± 0.4 versus 10 m/s ± 0.7).[11] Maximal heart rate appears to decrease with age.[12] The treadmill velocity at which blood lactate concentrations of 4 mmol/L occur (indicative of the anaerobic threshold) is lower in older horses (7.5 m/s ± 0.4 versus 10.2 m/s ± 0.7).[11] Unfit, older horses do not thermoregulate as well as unfit, younger horses because of aging-related decreases in resting plasma volume and central cardiac mechanisms.[13,14] Unfortunately, the effects of training on these variables have not been determined in horses.

Respiratory system

Aging results in several changes in respiratory function in humans, including lower partial pressures of arterial oxygen (Pao_2) and carbon dioxide ($Paco_2$) and a higher alveolar to arterial oxygen gradient ($P(A–a)o_2$).[15] Aging results in similar findings in horses. Older horses tend to have lower Pao_2, $Paco_2$, and higher $P(A–a)o_2$, and arterial pH values (Table 56.1).[16] A lower Pao_2 is reported in older horses during anesthesia.[17] The decrease in the $Paco_2$ in humans is thought to be secondary to metabolic acidosis.[18] In contrast, the low $Paco_2$ and higher pH in older horses may be due to hyperventilation in order to maintain Pao_2.[16] The increase in $P(A–a)o_2$ indicates that older horses have impaired transfer of oxygen from alveoli to capillaries.[16] The effects of exercise on the respiratory system have not been determined in older horses.

Table 56.1 Arterial blood gas values, hematologic and serum chemistry values (mean ± standard error or standard deviation) of young and geriatric horses

	Young horses	Geriatric horses	Reference
pH	7.404 ± 0.005	7.428 ± 0.007*	16
Pa_{O_2} (mmHg)	101.7 ± 1.6	90.2 ± 2.2*	16
Pa_{CO_2} (mmHg)	43 ± 0.7	41.5 ± 1.0*	16
$P(A–a)_{O_2}$ (mmHg)	7.2 ± 1.7	22.1 ± 2.5*	16
Mean cell volume (MCV) (fL)	47.8 ± 2.2	49.7 ± 2.2*	3
Mean cell volume (MCV) (fL)	43 ± 1	49 ± 2*	19
Mean cell hemoglobin (MHC) (pg)	16.3 ± 0.9	17.1 ± 0.8*	3
Lymphocytes ($\times 10^9$/L)	3.1 ± 1.1	2.2 ± 0.8*	3
$CD4^+/CD8^+$ cell ratio	4.07 ± 1.54	3.30 ± 1.31*	25
Ionized calcium (mEq/L)	3.00 ± 0.02	3.18 ± 0.05*	16
Ionized calcium pH corrected (mEq/L)	2.98 ± 0.03	3.14 ± 0.05*	16

* Significant difference between young and geriatric horses ($P < 0.05$).

Hematologic and serum chemistry values

The effects of aging of horses on hematologic and serum chemistry values are described in several studies. Older horses have significantly higher erythrocyte mean cell volume (MCV) and mean cell hemoglobin (MCH) than do younger horses[3,19] (Table 56.1), although none of these values in older horses exceeded the reference range.[3] The increase in MCH is thought to reflect the large red blood cell size rather than a true increase in MCH concentration.[3] An increase in MCV is also reported in older humans, and may be associated with decreased serum folate and vitamin B_{12} concentrations, as supplementation will often result in a decrease in the MCV.[3] Horses do not have an absolute dietary requirement for these vitamins because of their extensive synthesis and absorption from the large intestine. However, older horses may have decreased digestive capacity, which may limit their ability to produce or absorb some of these nutrients.[20] Total lymphocyte counts are decreased in geriatric horses when compared with younger horses (Table 56.1).[3] In this particular study, 17% of the geriatric horses had lymphocyte counts that were lower than the established lower limits reference range (1500 cells/μL).[3] An increase in ionized calcium (even with pH correction) is reported in older horses (Table 56.1).[16]

Immune system

The age-related decrease in immune function is termed immunosenescence, and occurs in humans and other animals.[21] Immunosenescence could reflect alterations in the function of T cells (responsible for cell-mediated responses), B cells (responsible for antibody-mediated responses) or nonspecific or innate immunity. It appears that older horses have decreased immunocompetency.[22–24] Older horses infected with equine viral arteritis develop more severe clinical signs than do younger horses housed under similar situations.[22] The ability of horses to produce antibodies to equine influenza virus vaccination gradually decreases with age.[23] Older horses have a 10-fold lower antibody titer to equine influenza virus vaccination than do younger horses.[24]

Older horses have lower lymphocyte numbers (mean ± standard deviation; 2.2×10^9/L ± 0.81 versus 3.1×10^9/L ± 1.1) and lower lymphocyte function when compared with younger horses (Table 56.1).[24,25] Total lymphocyte count and lymphocyte subset cell counts (including T cells, $CD4^+$ and $CD8^+$ cells, and B cells) decrease with age in horses.[25] There is a significant decrease in the percentage of $CD8^+$ lymphocytes, and an increase in the ratio of $CD4^+$ to $CD8^+$ lymphocytes in older horses compared with younger horses (Table 56.1).[25] The increase in CD4:CD8 cell ratio may indicate a pro-inflammatory state in geriatric horses.[25] However, serum concentrations of fibrinogen, an acute phase protein, production of which increases with inflammation, and albumin, which decreases with inflammation, are unchanged in older horses.[25] Older horses have a significantly lower lymphoproliferative response to phytohemagglutinin (PHA), concanavalin A, and pokeweed mitogens compared with younger horses.[24] Serum concentrations of IgG, IgG(T), IgM, and IgA do not differ with age.[25]

The age-related decline in somatotrophin, or growth hormone, secretion may at least be partially responsible for the functional impairment of humoral and cell-mediated immune responses in older humans.[26] Daily administration of equine somatotrophin results in an increase in total leukocyte numbers in geriatric horses.[27] However, only the granulocyte counts were increased, not the lymphocyte numbers.[27] The effect was transient, and not dose related. Granulocytic oxidative burst activity was not affected by equine somatotrophin administration. However, the lymphoproliferative response to mitogens (including PHA and pokeweed) was increased at 2 weeks following cessation of treatment.[27]

Exercise has been shown to substantially alter cell-mediated immune responses in younger horses.[28] However, even though older horses have reduced immune function,[25] geriatric horses are more resistant to exercise-induced immune suppression than younger horses.[24] Exercise adversely affects the lymphoproliferative responses of peripheral blood mononuclear cells of young horses, but not old horses.[24]

Endocrine system

Age does not appear to affect endocrine function or values in normal, older horses at rest.[24,29] Plasma renin activity, atrial natriuretic peptide, arginine vasopressin, aldosterone, and endothelin-1 concentrations are similar in young and aged horses.[29] Aged horses have similar resting cortisol concentrations to younger horses.[24] There are no apparent changes in oral glucose tolerance, insulin secretion, dexamethasone suppression tests, or adrenocorticotrophin (ACTH) concentrations that can be attributable to age alone.[19]

Age-related differences in the endocrine responses to exercise do occur in horses. Exercise increases plasma renin activity, atrial natriuretic peptide, arginine vasopressin, and aldsosterone, but not endothelin-1 concentrations in both young and old horses.[29] Older horses have a greater exercise-induced increase in plasma renin activity and aldosterone concentrations than do younger horses.[29] However, older horses have a smaller exercise-induced increase in atrial natriuretic peptide and arginine vasopressin concentrations than do younger horses.[29] Younger horses have a greater exercised-induced increase in cortisol concentrations than do older horses.[29] The significance of these findings are unclear as all these values are within the reported reference range.[29]

Somatotrophin's role in slowing or even reversing the effects of aging can be documented in younger humans, where somatotrophin deficiency results in changes in appearance, decreased body mass, decreased immune function, and other sequelae of aging.[30] Chronic administration of somatotrophin increases strength and may improve the 'quality of life' in aged humans.[30,31] However, somatotrophin administration to humans does not affect maximal aerobic capacity or endurance performance.[30–32]

The effects of exogenous administration of equine somatotrophin to geriatric horses on feed intake, body score, digestion, aerobic capacity, and immunocompetence is reported, and the results are mixed.[29,33,34] Bodyweight, body condition scores, and feed intake are not affected by administration of equine somatotrophin to older horses.[33,34] However, greater 'muscle definition' was reported in one study.[33] Daily administration of equine somatotrophin to older horses may improve nitrogen balance and fiber digestion.[34] Somatotrophin administration does not affect aerobic capacity (measured by $\dot{V}o_{2max}$, maximum running velocity, or total running time) in older horses.[33] However, administration of equine somatotrophin to older horses appears to have a beneficial immune effect, by increasing the number of granulocytes, and the lymphoproliferative response to mitogens following treatment.[29]

Musculoskeletal system

There is less known about the effects of aging on the skeletal system in horses. Degenerative joint disease is reported to be a frequent cause of death in older horses.[35] Osteoarthritis is commonly observed in joints of older horses.[36] There is a loss of biomechanical function of human articular cartilage with increasing age.[36] However, the biochemical characteristics of the collagen component of equine cartilage are not influenced by age of the horse.[36] The effects of aging, calcium and phosphorus supplementation, and exercise are investigated in a few studies. Skeletal systems of horses of different ages respond differently to calcium and phosphorus supplementation.[37] Younger horses may have the ability to respond to inactivity and exercise more quickly than mature or aged horses.[37]

The effects of age on muscle in humans are responsible for a number of physical impairments, such as a decrease in muscle strength and impaired mobility. The decrease in muscle function is attributed to a decreased ability to generate and sustain power output in association with changes in muscle structure and function.[38,39] A decrease in muscle mass is attributed to a decrease in diameter of the muscle fiber. The slow (type I) to fast twitch (type II) muscle fiber ratio appears to increase with age, due to motor unit remolding.[40]

The effects of age on MHC isoform distribution and activity of marker enzymes of fuel metabolism in horses have been addressed in a few studies. In contrast to humans, older trained horse have a greater percentage of fast myosin heavy chain (MHC) fibers (type II) than do younger trained horses.[41] Among five age groups of trained horses (the oldest group ranging in age from 11 to 24 years of age), the oldest group had a greater percentage of fast MHCs than did younger horses.[42] In contrast, untrained Thoroughbred horses have an increase in the percentage of type I fibers and a decrease in type IIb fibers associated with aging.[43] However, the horses only ranged in age from 1 to 6 years in this particular study and could not be considered old.[43] The effects of age on MHC isoform distribution, activity of marker enzymes of fuel metabolism, and effect of exercise have not been investigated in horses.

Equine Cushing's disease (pituitary adenoma, pituitary pars intermedia dysfunction)

- Equine Cushing's disease is a common disease in older horses.
- Clinical signs range from delayed shedding, muscle wasting, abnormal fat distribution, and laminitis.
- Diagnosis is best based on an overnight dexamethasone suppression test.
- Dysfunction of the pars intermedia is due to loss of dopaminergic innervation and increased production of pro-opiomelanocortin.
- Recommended therapy in most cases is improved husbandry.
- Pergolide is the recommended medical treatment in horses with more severe clinical signs.

Recognition of the disease

Pituitary pars intermedia dysfunction, also known as equine Cushing's disease (ECD), is probably the most common endocrine disease of geriatric horses. The clinical signs vary widely, but can result in either loss of use of an athletic individual or need for humane euthanasia.

History and presenting complaint

Equine Cushing's disease is recognized in horses, ponies, and donkeys ranging in age from 12 to 30 years.[44–46] Presenting complaints include delayed hair shedding, weight loss, laminitis, lethargy, hyperhidrosis, polyuria, and polydipsia.[44–46]

Physical examination

The majority of horses with ECD have a normal temperature, heart and respiratory rate. Hair coats can vary from very long and curly, to only a few longer hairs on the limbs, withers, thorax, and croup.[44] Muscle wasting is often noted by the 'sway-backed' or 'pot-bellied' appearance of the horse.[44] Abnormal fat distribution is often apparent as bulging supraorbital fat pads.[44] Owners often complain of exercise intolerance, excessive sweating, and lethargy. Immunosuppression may be recognized by various infections such as sole abscesses, skin infections, periodontal disease, and sinusitis.[46] Laminitis is a serious clinical sign associated with ECD, which often results in the loss of use of the horse, or even the need for humane euthanasia. Other clinical signs include delayed wound healing, infertility, pseudolaction, bilateral blindness, and seizures.[46]

Special and laboratory examination

A complete blood count in horses with ECD may reveal a stress leukogram, characterized by a mature neutrophila and lymphopenia.[46] Abnormalities on the serum chemistry may include mild increases in serum activity of liver-derived enzymes (including aspartate aminotransferase, alkaline phosphatase, sorbitol dehydrogenase, and gamma-glutamyl transferase).[44,46] Between 25% and 75% of horses with ECD are reported to have hyperglycemia.[46] However, Couetil reports that hyperglycemia occurs in 45% of horses with ECD and in 33% of normal (control) horses.[47] Insulin concentrations are increased in 70% of horses with ECD.[48] However, elevated serum insulin concentrations also occur in horses that do not have ECD.[4]

Necropsy examination and diagnostic conformation

The gold standard for diagnosis of ECD is necropsy and histopathology.[45,49,50] At post-mortem examination there is usually evidence of pituitary hyperplasia or an adenoma. The adenoma appears as a firm, lobulated mass several centimeters in diameter on the ventral aspect of the brain. Visual evidence of compression of the hypothalamus or optic nerves may be evident.[45] Thirteen of 26 horses with ECD had macroadenomas of the pars intermedia that replaced most of the pars distalis.[49] The adenomas were sharply delineated without a defined capsule, causing varying degrees of compression and atrophy of the pars distalis or pars nervosa.[45,49]

An ante-mortem diagnosis of ECD is most often based on endocrinologic testing of the pituitary–adrenal axis.[50–56] Endocrine function tests of the pituitary–adrenal axis include the overnight dexamethasone suppression test (DST),[50] thyrotrophin-releasing hormone stimulation test (TRH stimulation test),[51] combined DST/ACTH (adrenocorticotrophin hormone) stimulation test,[50] or DST/TRH stimulation test.[54] Other tests reported include measurement of serum ACTH,[53,55,56] insulin,[57] and glucose concentrations,[57] glucose tolerance tests,[57] and resting or serial cortisol concentrations.[50]

The overnight DST has excellent sensitivity and specificity (100%) when the post-cortisol blood sample is obtained 19 to 20 hours after administration of the dexamethasone.[50] Dexamethasone (40 μg/kg) is administered intramuscularly at 5 p.m. Blood is collected for measurement of plasma cortisol concentration, immediately before and 19 hours after administration of the dexamethasone. Plasma cortisol concentrations greater than 1 μg/dL 19 hours after dexamethasone concentration are diagnostic of ECD. The DST has been compared to the gold standard (post-mortem examination) in both diseased and healthy horses.[50] Due to infrequent association between corticosteroids and laminitis, and frequent existence of laminitis in affected horses, some clinicians prefer to use other tests.[51,53,55,56] However, for the majority of these tests the sensitivity and specificity is unknown.[51,55,57] Even the reported sensitivity and specificity should be questioned, as the presence or absence of the disease was based on clinical signs of ECD, not post-mortem examination.[53–56] Therefore, despite the concerns of inducing laminitis, which have not been substantiated, the DST is considered to be the diagnostic test of choice.

One of the earliest diagnostic tests, the TRH stimulation test, was reported by Beech and Garcia in 1985.[51] Plasma cortisol concentrations 15 to 90 minutes after TRH stimulation, are higher in horses with ECD when compared with normal horses.[51] In contrast, Eiler et al reported that TRH stimulation did not result in any significant differences in plasma cortisol concentration between ECD and normal horses.[54] However, the diagnosis of normal and ECD was based on clinical signs, not the gold standard (histopathology) in both studies.[51,54] Examination of circadian rhythm in cortisol concentrations, the ACTH stimulation test, a combined ACTH/DST test did not discriminate between normal and ECD horses (the diagnosis was confirmed at necropsy).[50]

The use of plasma ACTH concentrations for the diagnosis of ECD was recently reported.[53,55,56] The sensitivity ranges from 82 to 100% and the specificity ranges from 78 to 100%.[53,55,56] The majority of the reports based the diagnosis of disease or control on clinical signs, not post-mortem exam-

ination.[53,55] There are several reported 'normal' ranges for plasma ACTH concentrations (18.68 ± 6.79 pg/mL[53] to 30 ± 5 pg/mL[56]). The ACTH concentrations considered to be diagnostic of ECD also range from > 27 pg/mL for ponies,[53] > 35 pg/mL,[55] > 50 pg/mL for horses,[53] and > 55 pg/mL.[56] The differences may be due to differences in types of assays used (chemiluminiscent enzyme immunoassay or radioimmunodiffusion assay),[53,55] differences between ACTH concentrations for different breeds (ponies versus horses),[53] and delay in sample processing (plasma ACTH is only stable for 3 hours in whole blood).[53] There is no significant difference in ACTH concentrations between 'clinically normal' older and younger horses.[3] However, the authors noted that ACTH concentrations exceeded 100 pg/mL in both groups of the normal younger and older horses.[3]

Treatment and prognosis

Therapeutic aims

There is no cure for ECD. Therefore, the therapeutic aims are to reduce the clinical signs associated with the disease first through careful management, and in the more severely affected cases through medical management of the disease. The most important aspects in dealing with ECD are excellent basic husbandry and vigilance for any concurrent disease complications. In mildly affected horses regular dental care, deworming, regular foot care, responsive nutritional management, and close attention to clean stable conditions are generally sufficient. Body clipping may be necessary in some affected horses in the summer.

Medical therapy is indicated in horses that have persistent recurrent infections, are hyperglycemic, or develop laminitis. The goal of the medical therapy is to reduce the production of pro-opiomelanocortin (POMC)-related peptides that are responsible for the clinical signs (see 'Etiology and pathogenesis' section). Use of a dopamine agonist is recommended based on the fact that loss of dopaminergic innervation of the pars intermedia results in increased production of POMC-related peptides. Pergolide and bromocriptine are both long-acting type 2 dopamine agonists. The low oral bioavailability of bromocriptine makes it impractical for use on a long-term basis.[58] Therefore, pergolide administered orally is more frequently used.

Therapy

Cyproheptadine has antihistaminic, anticholinergic, and antiserotonin effects. Cyproheptadine was initially recommended because serotonin had been shown to be a potent secretagogue of ACTH in rat pars intermedia tissue.[59] The importance of serotonin in ECD is unknown, as levels within the pars intermedia do not differ from control horses.[60] There is no basic pharmacokinetic information about this drug in horses. Anecdotal clinical information indicates that a positive response to therapy is achieved in 35% of affected horses.[61] Treatment with cyproheptadine in 16 horses with ECD resulted in improved clinical signs in 75% of the horses, but plasma ACTH concentrations rarely returned to normal.[52] Cyproheptadine treatment resulted in improvement in the DST or TRH stimulation test in only 1 out of 7 horses.[48] The recommended doses vary from 0.25 to 0.5 mg/kg orally,[61] 0.25 mg/kg twice a day,[61] or 0.6 to 1.2 mg/kg$^{0.75}$.[44,48]

Pergolide is the treatment of choice for ECD in horses. Controlled studies to establish the bioavailability, pharmacokinetics, and metabolism of this drug have not been reported for the horse. Therefore the dose and frequency of administration is based on anecdotal information. Some recommended doses are: 0.0017 mg/kg divided in two daily doses,[62] 0.25 to 1 mg/horse/day,[63] or 0.002 mg/kg once a day.[48] Beech reports an improvement in clinical signs in 22 out of 25 horses treated with pergolide mesylate after several weeks of therapy.[63] The dose of pergolide was increased over several weeks, if there was no 'clinical response' to treatment.[63] Dybdal reported clinical improvement in more than 25 horses treated with pergolide over a 1-year period.[64] Monitoring of blood glucose concentrations is recommended to determine the dose and response to pergolide therapy.[61] The pergolide dose is increased 0.25 mg to 0.5 mg/day/horse every 4 to 6 weeks until normal blood glucose concentration is obtained.[61] The use of clinical signs (laminitis and obesity) and hyperglycemia to initially diagnose and then follow response to therapy may result in erroneous information.[48,65] There is a newly recognized endocrine disease (termed peripheral Cushing's disease) which results in clinical signs (laminitis and obesity) and laboratory data (hyperglycemia and hyperinsulinemia) that are similar to ECD.[48,65,66] In these reports ECD was ruled out based on post-mortem examination, or a normal DST.[48,65,66]

Several investigators have attempted to provide more objective assessment of the effects of pergolide and cyproheptadine for treatment of ECD. A single dose of pergolide resulted in a decrease in plasma POMC concentrations in a mare with ECD.[67] Unfortunately, measurement of plasma POMC concentrations is not commercially available at this time to assess response to therapy. Some investigators recommend repeating the DST to confirm the return of a functional pituitary–adrenal feedback loop.[61] Pergolide treatment resulted in a normal DST in 2 out of 9 horses with ECD, and the DST 'became closer to normal' in 7 horses after several months of therapy.[62] However, another author reports that pergolide treatment, in 10 horses, resulted in improvement in clinical signs, but insulin concentrations, TRH stimulation or DST test results did not return to normal.[44] The data, unfortunately, were not reported.[44] It is difficult to critically determine the effects of therapy, as none of these reports compared the treated horses with an untreated control group. There is only one report in which a small group of control horses were compared with treated horses.[48] Horses with ECD (diagnosed by TRH stimulation or DST) were treated with cyproheptadine (n = 7), pergolide (n = 20) and no treatment (n = 5) for 6–12 months.[48] Clinical improvement occurred in most of the pergolide-treated group, some of the cyproheptadine-treated group, but not in the

untreated control group. The DST or TRH stimulation test returned to normal in 7 out of 20 horses treated with pergolide, 1 out of 7 horses treated with cyproheptadine, and 1 out of 5 in the untreated control group.[48]

Prognosis

There is no published information regarding prognostic indices for this condition. From clinical experience it would appear that the prognosis of ECD depends on the clinical signs. Horses with hyperglycemia, persistent secondary infections, and laminitis tend to have the worst prognosis. Laminitis frequently results in the end of the horse's athletic career and in most situations progresses to the need for humane euthanasia. There are no published reports about progression of the disease. It is unknown if all horses with ECD will eventually develop the more serious clinical signs.

Etiology and pathogenesis

Equine Cushing's disease has been previously described as a pars pituitary ademona, but it may be more correctly due to hyperplasia or dysfunction of the pars intermedia.[49,60,67,68] The hyperplasia or dysfunction of the pars intermedia has been shown to be due to loss of dopaminergic innervation of the pars intermedia, resulting in increased production of POMC.[46,49,67,68] Post-translational processing of POMC in the pars intermedia results in increased plasma concentrations of ACTH, α- and β-melanocyte stimulating hormone (MSH), corticotrophin-like intermediate peptide (CLIP) and β-endorphin.[49,67,68] Horses with ECD are highly resistant to glucocorticoid negative feedback inhibition of plasma ACTH secretion as glucocorticoids inhibit the pars distalis, but not pars intermedia.[67] However, dopamine infusion resulted in a decrease in ACTH, β-MSH, CLIP and β-endorphin concentrations.[67,68]

The clinical signs of ECD are often attributed to the effects of ACTH and subsequent cortisol production. Muscle wasting, laminitis, insulin-resistant hyperglycemia, and immunosuppression are often attributed to ACTH and loss of the diurnal variation of cortisol. Polyuria and polydipsia can be attributed to hyperglycemia or diabetes insipidus. Diabetes insipidus may be peripheral, due to antagonism of antidiuretic hormone (ADH) at the collecting duct, or central and due to reduced ADH synthesis and/or secretion following compression of the supraoptic nuclei and infundibulum by the space-occupying hyperplastic pars intermedia.[46] While plasma concentrations of ACTH are greater in affected horses, the levels of α-MSH, β-MSH, CLIP and β-endorphin are disproportionally increased.[67] The role of these other hormones in development of the clinical signs of ECD is not well understood. It has been proposed that abnormal behavior (such as docility) may be attributable to increased β-endorphin production.[60] Corticotrophin-like intermediate peptide (CLIP) may be involved in the pathogenesis in hyperinsulinemia detected in some horses with ECD, as it is known to be an insulin secretagogue in obese mice.[68] The pathogenesis of the hyperhidrosis and hirsutism is not known, but may be due to compression of the thermoregulatory center of the hypothalamus.

Peripheral Cushing's disease

Recognition of the disease

There is a well-recognized syndrome in middle to older aged horses characterized by laminitis, obesity, and hyperglycemia.[65] These horses have previously been identified as having 'hypothyroidism', or being diagnosed with ECD.[65,66] However, necropsy examination, thyroid stimulation tests or overnight DST have failed to confirm these diagnoses.[48,65,66] These horses appear to have a disorder in cellular cortisol metabolism. This syndrome has been termed 'peripheral Cushing's disease'.[65] A similar syndrome exists in humans, which is called central (or visceral) obesity, or the metabolic syndrome.[69,70]

History and presenting complaint

Middle to older aged horses may present with a complaint of obesity and chronic laminitis. The distribution of body fat involves the neck and gluteal muscles. Geldings may present for a swollen sheath. Owners frequently complain that it is difficult to reduce the weight of these horses by diet restriction. Many of these horses have been diagnosed with 'hypothyroidism' or even with ECD.

Laboratory examination

A complete blood count and serum chemistry often reveals hyperglycemia. Elevated insulin concentrations[48,65,66] and an abnormal glucose tolerance test (documenting insulin resistance) are described.[65] These horses will often have low circulating concentrations of thyroid hormone.[65] However, thyroid-stimulating tests fail to support the diagnosis of hypothyroidism.[65] Moreover, experimentally induced hypothyroidism does not produce horses with obesity and laminitis. Confirmatory testing for ECD, using either a DST or TRH stimulation test, is normal in these horses.[48,65,66]

Necropsy examination

Necropsy examination fails to reveal pars intermedia hyperplasia or adrenal gland pathology in horses with peripheral Cushing's disease.[65,66]

Diagnostic confirmation

The diagnostic confirmation of peripheral Cushing's disease at present is recognition of clinical signs and laboratory data, and ruling out of either ECD or hypothyroidism.[48,65,66]

Treatment and prognosis

Therapeutic aims

At the present there is no specific treatment for peripheral Cushing's syndrome in horses. Therapeutic aims are to reduce the clinical signs associated with the disease by management. Exercise may help improve glucose tolerance and insulin function. Laminitis should be treated as necessary. Dietary supplement with chromium (5 mg/day) may improve peripheral insulin function and glucose tolerance.[65,71]

Prognosis

There are no published reports on prognosis of this syndrome in horses.

Epidemiology and pathogenesis

The exact etiology of peripheral Cushing's disease in horses is unknown, but it is proposed these horses have a disorder in cellular cortisol metabolism similar to the human syndrome.[48,65] Central obesity or the metabolic syndrome in humans is associated with hypertension, dyslipidemia, diabetes, accumulation of intra-abdominal (visceral) rather than subcutaneous fat, and premature death.[69,70] There is an increase in the 24-hour cortisol production, but circulating basal cortisol concentrations and a DST are normal in these patients.[69] Corticosteroid action is in part regulated by 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) which converts active cortisol to inactive cortisone.[69] Adipose stromal cells from omental fat, but not subcutaneous fat, can generate active cortisol from inactive cortisone.[69] In addition, the expression of 11β-HSD1 in adipose fat is further increased after exposure to cortisol and insulin.[69] Johnson and Ganjam report that horses with peripheral Cushing's syndrome have increased blood pressure, insulin resistance, and hyperlipidemia.[65] Other clinical signs in horses include abnormal fat deposits, reduced fertility, laminitis, and difficulty in losing weight.[48,65] The lowered circulating thyroid hormone levels may be due to elevated cortisol production that can lead to inhibition of the thyroid-stimulating hormone (TSH) produced by the pituitary gland.[65]

References

1. Hintz HF. The geriatric horse. Equine Pract 1995; 17:8–10.
2. Harper F. The geriatric horse. Large Anim Vet 1992; 6:10–12.
3. McFarlane D, Sellon DC, Gaffney D, et al. Hematologic and serum biochemical variables and plasma corticotropin concentration in healthy aged horses. Am J Vet Res 1998; 59:1247–1251.
4. Pollock ML, Foster C, Knapp D, et al. Effects of age and training on aerobic capacity and body composition of master athletes. J Appl Physiol 1987; 62:725–731.
5. Holloszy JO, Kohrt WM. Exercise. In: Masoro EJ, ed. Handbook of physiology, section 11, aging. New York: Oxford University Press; 1995:633–666.
6. Lakatta EG. Cardiovascular system. In: Masoro EJ, ed. Handbook of physiology, section 11, aging. New York: Oxford University Press; 1995:413–474.
7. Dempsey JA, Seals DR. Aging, exercise, and cardiopulmonary function. In: Lamb DR, Gisolfi CV, Nadel E, eds. Perspectives in exercise and sports medicine, Vol. 8: Exercise in older adults. Carmel, IN: Cooper Publishing; 1995:237–304.
8. Seals DR, Habberg JM, Hurley BF, et al. Endurance training in older men and women: I. Cardiovascular responses to exercise. J Appl Physiol 1984; 57:1024–1029.
9. Haskell WL, Phillips WT. Exercise training, fitness, health, and longevity. In: Lamb DR, Gisolfi CV, Nadel E, eds. Perspectives in exercise and sports medicine, vol. 8: Exercise in older adults. Carmel, IN: Cooper Publishing; 1995:11–52.
10. Kenney WL. Body fluid and temperature regulation as a function of age. In: Lamb DR, Gisolfi CV, Nadel E, eds. Perspectives in exercise and sports medicine, vol. 8: Exercise in older adults. Carmel, IN: Cooper Publishing; 1995:305–351.
11. McKeever KH, Malinowski K. Exercise capacity in young and old mares. Am J Vet Res 1997; 58:1468–1472.
12. Goetz TE, Manohar M. Isoproterenol-induced maximal heart rate in normothermic and hyperthermic horses. Am J Vet Res 1990; 51:743–746.
13. McKeever KH, Easton TL, Geiser S, et al. Thermoregulation in old and young horses during exercise. Med Sci Sports Exerc 2000; 32:S156.
14. McKeever KH, Kearns CF. Ageing-induced alterations in plasma volume in horses. Med Sci Sports Exerc 2001; 33:S257.
15. Ceveri I, Zoia MC, Fanfulla F, et al. Reference values of arterial oxygen tension in the middle aged and elderly. Am J Res Crit Care Med 1995; 152:934–941.
16. Aguilera-Tejero E, Estepa JC, Lopez I, et al. Arterial blood gases and acid–base balance in healthy young and aged horses. Equine Vet J 1998; 30:352–354.
17. Whitehair KJ, Willits NH. Predictors of arterial oxygen tension in anesthetized horses: 1,610 cases (1992–1994). J Am Vet Med Assoc 1999; 215:978–981.
18. Frassetto L, Sebastian A. Age and system acid–base equilibrium. Analysis of published data. J Gerontol 1996; 51:B91–B99.
19. Ralston SL, Nockels CF, Squires EL. Differences in diagnostic tests results and hematologic data between aged and young horses. Am J Vet Res 1988; 49:1389–1392.
20. Ralston SL, Squires EL, Nockels CF. Digestion in the aged horse. Equine Vet Sci 1989; 9:203–205.
21. Miller RA. Immune system. In: Masoro EJ, ed. Handbook of physiology, section 11, aging. New York; Oxford University Press; 1995:551–590.
22. Traub-Dargatz JL, Collins JK, Bennet DG, et al. Comp Contin Educ Pract Vet 1985; 7:s490–s496.
23. Goto H, Yamamoto Y, Ohta C, et al. Antibody responses of Japanese horses to influenza viruses in the past few years. J Vet Med Sci 1993; 55:33–37.
24. Horohov DW, Dimock A, Guirnalda P, et al. Effect of exercise on the immune system of young and old horses. Am J Vet Res 1999; 60:643–647.
25. McFarlane D, Sellon DC, Gibbs SA. Age-related quantitative alterations in lymphocyte subsets and immunoglobulin isotypes in healthy horses. Am J Vet Res 2001; 62:1413–1417.
26. Kelley KW. Growth hormone, lymphocytes, and macrophages. Biochem Pharmacol 1989; 38:705–711.

27. Malinowski K, Christensen RA, Konopka A, et al. Feed intake, bodyweight, body condition score, musculation, and immunocompetence in aged mares given equine somatotrophin. J Anim Sci 1997; 75:755–760.
28. Keadle TL, Pourciau SS, Melrose PA, et al. Acute exercise stress modulates equine immune function. J Equine Vet Sci 1993; 13:225–231.
29. McKeever KW, Malinwski K. Endocrine response to exercise in young and old horses. Equine Vet J Suppl 1999; 30:561–566.
30. Nelson JF. The potential role of selected endocrine systems in aging processes. In: Masoro EJ, ed. Handbook of physiology, section 11, aging. New York: Oxford University Press; 1995:377–394.
31. Yarasheki KE. Growth hormone effects on metabolism, body composition, muscle mass, and strength. In: Holloszy JO, ed. Exercise and sport science reviews. Philadelphia: Williams and Wilkins; 1994:285–312.
32. Lombardo JA, Hickson RC, Lamb DR. Anabolic/androgenic steroids and growth hormone. In: Lamb DR, Gisolfi CV, Nadel E, eds. Perspectives in exercise and sports medicine, vol. 8: Exercise in older adults. Carmel, IN: Cooper Publishing; 1995:11–52.
33. McKeever KH, Malinowski K. Christensen RA, et al. Chronic recombinant equine somatotrophin (eST) administration does not affect aerobic capacity or exercise performance in geriatric mares. Vet J 1998; 155:19–25.
34. Ralston SL, Christensen RA, Malinowski K. Chronic effects of equine growth hormone (eGH) on intake, digestibility and retention of nutrients in aged mares. J Anim Sci 1996; 74(Suppl 1):194.
35. Leblond A, Villard I, Leblond L, et al. A retrospective evaluation of the causes of death of 448 insured French horses in 1995. Vet Res Comm 2000; 24:85–102.
36. Brama PAJ, TeKoppele JM, Bank RA, et al. Influence of site and age on biochemical characteristics of the collagen network of equine articular cartilage. Am J Vet Res 1999; 60:341–345.
37. Mansell BJ, Baker LA, Pipkin JL, et al. The effect of calcium and phosphorus supplementation on bone metabolism in young, mature, and aged horses during inactivity and subsequent aerobic training. J Equine Vet Sci 2001; 21:445–450.
38. Jassen I, Heymsfield SB, Wang S, et al. Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. J Appl Physiol 2000;89:81–88.
39. White TP. Skeletal muscle structure and function in older mammals. In: Lamb DR, Gisolfi CV, Nadel E, eds. Perspectives in exercise and sports medicine, vol. 8: Exercise in older adults. Carmel, IN: Cooper Publishing; 1995:115–174.
40. Larson L. Motor units: remodeling in aged animals. J Gerontol A Biol Sci 1995;50a:91–95.
41. Barrey E, Valette JP, Jouglin M, et al. Heritability of percentage of fast myosin heavy chains in skeletal muscle and relationship with performance. Equine Vet J Suppl 1999; 30:292–298.
42. Rivero JLL, Galisteo AM, Aguera E, et al. Skeletal muscle histochemistry in males and female Andalusian and Arabian horses of different ages. Res Vet Sci 1993;54:160–169.
43. Roneus M. Muscle characteristics in Standardbreds of different ages and sexes. Equine Vet J 1993;25:143–146.
44. Beech J. Diseases of the pituitary gland. In: Colahan PT, Mayhew IG, Merrit AM, et al, eds. Equine medicine and surgery, 5th edn. St. Louis: Mosby; 1999:1951–1956.
45. Love S. Equine Cushing's disease. Br Vet J 1993;149:139–153.
46. Kolk JH van der. Diseases of the pituitary gland including hyperadrenocorticism. In: Watson TDG, ed. Metabolic and endocrine problems of the horse. New York: WB Saunders; 1998:41–59.
47. Couetil LL. New developments in equine Cushing's disease. Equine Pract 1996; 18:28–32.
48. Schott HC, Coursen CL, Eberhart SW, et al. The Michigan Cushing's project. Proc Am Assoc Equine Pract 2001; 47:22–24.
49. Heinrichs M, Baumgarter W, Capen CC. Immunocytochemical demonstration of proopiomelanocortin-derived peptides in pituitary adenomas of the pars intermedia in horses. Vet Pathol 1990; 27:419–425.
50. Dybdal NO, Hargreaves KM, Madigan JE, et al. Diagnostic testing for pituitary pars intermedia dysfunction in horses. J Am Vet Med Assoc 1994; 204:627–632.
51. Beech J, Garcia M. Hormonal responses to thyrotropin-releasing hormone in healthy horses and horses with pituitary adenomas. Am J Vet Res 1985; 46:1941–1943.
52. Couetil L. Clinical response and plasma adrenocorticotropin concentrations in horses with equine Cushing's disease treated with cyproheptadine. Proc Am Assoc Equine Pract 1996; 42:297–298.
53. Couetil L, Paradis MR, Knoll J. Plasma adrenocorticotropin concentrations in healthy horses and horses with clinical signs of hyperadrenocorticism. J Vet Intern Med 1996; 10:1–6.
54. Eiler H, Oliver JW, Andrews FM, et al. Results of a combined dexamethasone suppression/thyrotropin-releasing hormone stimulation test in healthy horses and horses suspected to have a pars intermedia pituitary adenoma. J Am Vet Med Assoc 1997; 211:79–81.
55. Perkins G, Lamb S, Erb HN, et al. Plasma adrenocorticotropin (ACTH) concentrations and clinical response in horses treated with equine Cushing's disease with either cyproheptadine or pergolide.(abstr) J Vet Intern Med 2001; 15:286.
56. Kolk JH van der, Wensig T, Kalsbeek HC, et al. Laboratory diagnosis of equine pituitary pars intermedia. Domest Anim Endocrinol 1995; 12:35–39.
57. Garcia MC, Beech J. Equine intravenous glucose tolerance test: Glucose and insulin responses of healthy horses fed grain or hay and of horses with pituitary adenoma. Am J Vet Res 1986; 47:570–572.
58. Beck DJ. Effective long-term treatment of a suspected pituitary adenoma with bromocriptine mesylate in a pony. Equine Vet Educ 1992; 4:119–122.
59. Fisher JL, Moriarity CM. Control of bioactive corticotropin release from the neurointermediate lobe of the rat pituitary *in vitro*. Endocrinology 1977; 100:1047–1054.
60. Millington WR, Dybdal NO, Dawson R Jr, et al. Equine Cushing's disease: Differential regulation of β-endorphin processing in tumors of the intermediate pituitary. Endocrinology 1988; 123:1598–1604.
61. Levy M, Sojka JE, Dybdal NO. Diagnosis and treatment of equine Cushing's disease. Comp Cont Educ Vet 1999; 21:766–769.
62. Peters DF, Erfle JB, Slobojan GT. Low-dose pergolide mesylate treatment for equine hypophyseal adenomas (Cushing's syndrome). Proc Am Assoc Equine Pract 1995; 41:154–155.
63. Beech J. Treatment of hypophyseal adenomas. Comp Cont Educ Vet 1994; 16:921–923.
64. Dybdal NO. Anterior lobe (pars intermedia) dysfunction. In: Smith BP, ed. Large animal internal medicine, 2nd edn. St Louis: Mosby; 1996:1445–1449.
65. Johnson PJ, Ganjam VK. Laminitis, 'hypothyroidism', and obesity: A peripheral Cushingoid syndrome in horses. In: Proceedings 17th Annual American College of Veterinary Internal Medicine Forum; 1999:192–194.
66. Ruoff WW, Baker DC, Morgan SJ, et al. Type II diabetes mellitus in a horse. Equine Vet J 1986; 18:143–144.

67. Orth DN, Holscher MA, Wilson MG, et al. Equine Cushing's disease: Plasma immunoreactive proopiolipomelanocortin peptide and cortisol levels basal and in response to diagnostic test. Endocrinology 1982; 110:1430–1441.
68. Wilson MG, Nicholson WE, Holscher MA, et al. Proopiolipomelanocortin peptides in normal pituitary, pituitary tumor, and plasma of normal and Cushing's horses. Endocrinology 1982; 110:941–953.
69. Bujalska IJ, Kumar S, Stewart PM. Does central obesity reflect 'Cushing's disease of the omentum'? Lancet 1997; 349:1210–1213.
70. Mansuzaki H, Paterson J, Sinyama H, et al. A transgenic model of visceral obesity and the metabolic syndrome. Science 2001; 294:2166–2170.
71. Ott EA, Kivipelot J. Influence of chromium tripicolinate on growth and glucose metabolism in yearling horses. J Anim Sci 1999; 77:3022–3030.

CHAPTER 57

General principles for the vaccination of equine athletes

Hugh Townsend

In addition to aiding in the prevention of devastating and life-threatening diseases, vaccination programs for equine athletes should be directed towards the prevention of diseases known to have significant adverse effects upon athletic performance. The emphasis should be on those diseases that place individual or group performance at substantial risk. Wherever possible, decisions on vaccination and its timing should be based on published data, such as reports of vaccine safety, efficacy and duration of immunity as well as current disease surveillance data. In those cases where the data required for evidence-based decisions are not available, decisions on vaccination must be taken based on expert, practitioner and client experience, opinions and objectives. Steady improvement in the effectiveness of these decisions can be achieved through the application of knowledge gained through ongoing vaccine and epidemiologic research.

Reaching the best decisions on the vaccination of the equine athlete requires knowledge of the timing and circumstance of significant risk of disease. Our incomplete understanding of the epidemiology, pathogenesis and immunology of all infectious diseases, combined with limited information about the efficacy and duration of immunity of existing vaccines, makes this a challenging process. This is further complicated by the highly variable response of individual horses to all vaccines. Nonetheless, if used strategically, some vaccines are capable of reducing the risk and severity of disease at both the individual and herd or group levels.

Currently, many vaccines are marketed for use in horses in North America. Most are multivalent, designed to meet a market that wishes to provide wide and convenient protection against a broad spectrum of diseases. Generally, the intent is to achieve this through yearly vaccination following an initial prime and boost series. In reality, however, it is difficult to stimulate a serviceable immunity against most diseases, particularly the important contagious diseases, that will last for more than 6 months. In fact, the desire to provide protection against several diseases with a single, yearly administration puts unrealistic expectations upon all current multivalent vaccines. Vaccination programs in all horses, including the athletic horse, could be much improved through acceptance of reasonable expectations for their role in the prevention of disease and by accommodating these limitations in the design of disease prevention programs.

The wide array of equine vaccines currently on the market in North America has resulted in considerable confusion in our attempts to develop appropriate vaccination programs. However, this process can be simplified by limiting consideration to those diseases that pose real and significant risk and for which we possess vaccines of known efficacy. The logic of this approach is supported by the recognition that vaccination is never completely without risk and can, in some situations, be completely without benefit. Vaccination on the sole premise that it 'might do some good' may provide psychological support for horse owners and veterinarians but it is unlikely to benefit the horse. Designing programs without due attention to the requirements and claims of the manufacturer as well as the cost, benefit and risks of vaccination may lead to procedures that are either oversimplified and ineffective (e.g. one multivalent vaccine per year) or unduly complex and expensive.

Each of the major infectious diseases of the athletic horse along with preventive strategies, including vaccination, are described in other chapters of this book. Taken one by one, developing an appropriate vaccination strategy should be fairly straightforward, especially when we have some data upon the epidemiology of the disease (circumstance and timing of significant risk), vaccine efficacy,

Table 57.1 Vaccination against common diseases of horses

Disease	Agent	Vaccine	Program	Vaccination rate[69]	*Justification/comment*[a]
Influenza	Equine influenza virus A2			63%	*High prevalence, predictable periods of risk, herd immunity critical in preventing outbreaks of disease*
		Killed	Prime and boost, then every 6 months or 2 weeks prior to risk		Efficacious (European vaccines)
		Modified-live (intranasal)	Every 6 months or 2 weeks prior to risk		Efficacious (North America)
		ISCOM	Prime and boost, then every 6 months or 2 weeks prior to risk		Efficacious (European vaccine)
Equine herpes virus	EHV1, 2 and 4	No commercial vaccine against EHV2		43%	*Limited – prevalence of EHV respiratory disease is not known*
		Killed (EHV1 and 4)	Prime and boost followed by revaccination every 6 months		Efficacious (European vaccines)
		Modified-live (EHV1 and 4)	Prime and boost followed by revaccination every 6 months		No published data on efficacy
Strangles	*Streptococcus equi*			13%	*Limited – equine athletes not usually at high risk*
		M protein	Prime and boost and then every 6 months or 2 weeks prior to risk		Efficacy demonstrated in challenge and field trials
		Live attenuated (intranasal)			Challenge data not published
Tetanus	*Clostridium tetani*	Tetanus toxoid	Prime and boost and yearly revaccination and/or at time of deep wound or surgery	70%	*Clinical disease tends to be severe with a high case fatality rate* No published efficacy in horses
Rabies	Rabies virus	Killed	Prime and boost and yearly revaccination or prior to risk	24%	*Fatal disease* No published efficacy in horses
Viral encephalitis	EEE	Killed	Prime and boost and yearly or 6-monthly revaccination	63%	*High disease prevalence in some regions – high case fatality rate* No published efficacy data
	WEE	Killed	Prime and boost and yearly revaccination prior to risk		*Traditional in areas where disease is or has been prevalent* No published efficacy data
	West Nile	Killed		n/a	*High incidence in endemic regions – prolonged treatment and high case-fatality rate* Results of challenge trials not published
EPM	*Sarcocystis neurona*	Killed	Prime and boost and yearly revaccination	n/a	*High prevalence in endemic regions, potentially devastating disease. Treatment prolonged and expensive* No published efficacy data – multicenter trial in progress
EVA	EVA virus	Modified-live	Prime and boost and yearly revaccination	1.8%	*Limited – low prevalence of clinical disease* Published efficacy data
Potomac horse fever	*Neorickettsia risticii* (formerly *Ehrlichia risticii*)	Killed	Prime and boost and yearly revaccination prior to known period of risk	18%	*Acute severe disease with high complication rate and cost of treatment* Published evidence suggests vaccines are not effective

[a] Logically, only vaccines for which there is published evidence of efficacy are likely to provide benefit to the equine athlete and then only when those animals are at significant risk (see justification/comment).

safety and duration of immunity. The real challenge is how to combine these various strategies into a program that will provide real benefit to horse and owner.

The following paragraphs cover diseases of potential importance for the equine athlete for which vaccines are available (Table 57.1). The focus of the material is principally upon North America but the general approach to the assessment and use of vaccines is meant to be applicable on an international scale. This chapter is based upon the premise that there is no such thing as a fully effective 'one size fits all' vaccination program for the equine athlete. In each case, the costs, risks and the benefits of vaccination must be carefully considered with both the individual animal and the group in mind. Clearly, the combined effect of all of the factors involved in the effective use of vaccines will change over time. The unique and critical role of the veterinary practitioner in this process is not the physical delivery of vaccine to the animal but the careful and considered monitoring of each situation and the ability to make informed, effective program modifications as conditions change and new information becomes available.

Influenza

Influenza is the most commonly diagnosed infectious disease of horses against which vaccination is currently possible. Outbreaks among large groups of young equine athletes, particularly race horses, occur regularly and such populations are frequently and predictably at risk.[1–12] More is known about the epidemiology, diagnosis, strategies for prevention, utility of vaccination, efficacy of the vaccines and the effectiveness of vaccine strategies in the control of equine influenza than any other disease of the horse. Efficacious killed and immunostimulating complex (ISCOM) vaccines are marketed in the European Community[13–15] and an efficacious, cold-adapted, temperature-sensitive, modified live, intranasal vaccine is marketed in North America.[16–19] Based on current published reports, all these types of vaccines reduce rates of infection, amounts of virus shed and rates of clinical disease among individuals and within groups of animals for at least 6 months. A number of killed influenza vaccines are also marketed in North America. Although these vaccines may be useful, neither the manufacturers nor independent investigators have published data demonstrating their efficacy.

Prevention of influenza outbreaks is dependent upon appropriate control measures including regular and constant surveillance, use of rapid, point of care diagnostic tests,[3,20–22] national and international disease surveillance and the institution of effective vaccination programs at the level of the individual and the group.[2,4,6,23,24] The principal reason for occurrence of regular outbreaks of influenza in North America and elsewhere is almost certainly the failure to apply existing knowledge about this disease and its prevention. At most large facilities, particularly racetracks, the risk factors for disease outbreaks and the likely time of their occurrence are reasonably well understood. For example, a 3-year study at a racetrack where few precautions were taken to prevent introduction or spread of disease showed that outbreaks of influenza occurred once each year, in the middle of the racing season, when the horse population at the track was near its maximum.[25] According to the results of another study, movement of weanlings, not vaccinated within the previous 6 months, from the sales ring into racing yards in Newmarket resulted in outbreaks of influenza in those yards.[3]

Co-mingling of young equine athletes significantly increases the risk of outbreaks of influenza. Often, this occurs in controlled environments where preventive strategies could be instituted with little difficulty. All horses entering an athletic venue should have received a vaccine of published efficacy within the previous 6 months. In doing so, the risk of disease in the individual and more importantly, among the group of animals comingling in the environment, will be reduced. Horses that exceed this 6-month limit while resident in the environment should be revaccinated. The risk of adverse responses to these vaccines is small and the potential benefit to the population of this regime is large.

Perfect protection of individual animals following vaccination cannot be expected. Response to vaccination and duration of immunity among individual animals is varied and unpredictable following the administration of even the most effective vaccines. For this reason, vaccination must be combined with other strategies, including regular surveillance of the population, rapid diagnosis of disease, quarantine or removal of affected animals from the group and revaccination of the group at the first sign of an outbreak. Finally, any outbreaks that do occur should be properly documented. A plan should be in place for collection of the appropriate data needed to determine the cause and chart the course of any significant outbreak of disease.

Equine herpesvirus

Experimental infection of susceptible horses with equine herpesvirus 1, 2 or 4 results in typical signs of respiratory tract infection; malaise, fever, cough and nasal discharge.[26–37] Vaccination prior to experimental challenge can reduce the occurrence and severity of clinical signs and the amount of virus shed, but does not prevent viremia or persistent infection.[30,33,38–42] There is good evidence to show that most horses become infected with these viruses by the time they are weaned[43,44] and should therefore be capable of recurrent viral recrudescence and shedding for the rest of their lives. It is not known if any vaccination is capable of influencing either EHV infection or recrudescence.

Although it is commonly held that EHV1 and EHV4 are important causes of respiratory disease among equine athletes, particularly young race horses, there are no published studies to show that this is true. Although there is evidence of seroconversion of horses to both EHV1 and EHV4 during the course of racing seasons,[45–49] there are no descriptions of outbreaks of EHV respiratory disease that follow an epidemic curve typical of a contagious disease. In all published

longitudinal epidemiologic studies, seroconversions to EHV occurred sporadically and in some cases were clearly associated with concurrent equine influenza infections.[45,50,51]

Clearly, until more information upon the epidemiology of EHV respiratory disease and the efficacy the EHV vaccines becomes available it will prove difficult to provide clear recommendations on the use of vaccination against these diseases. At the present time, most of these vaccines are marketed as a component of a multivalent vaccine, often in combination with influenza antigens. Certainly there is no evidence that these vaccine combinations are harmful, but there may be no benefit in selecting multivalent respiratory vaccines based upon the EHV antigens they contain.

Strangles (*Streptococcus equi* infections)

Under most circumstances, equine athletes should not be at high risk of developing clinical signs of strangles. Classical outbreaks were first described in army remounts.[51,52] More recent epidemics have involved brood mare farms,[53–58] rescue farms,[59] groups of experimental animals,[60,61] horse feedlots[62] and riding stables[63] but there are no recent reports of strangles outbreaks among groups of equine athletes.

Horses suffering from classical strangles are easily identified. The signs are well known to all veterinarians and most knowledgeable horse owners and trainers. The identification of non-clinical carriers does provide a challenge but more sensitive methods for detecting these animals are being developed. The key to prevention and control of strangles rests with the early identification of both clinically diseased and non-clinical carrier animals and the institution of appropriate control procedures including appropriate quarantine and sanitation procedures.[63] Using this approach it should be possible to limit or prevent direct contact between infected animals and susceptible equine athletes.

There is reasonable experimental and field trial data to show that the use of intramuscular vaccines containing the M protein of *Streptococcus equi*[64,65] or submucosal injection of a live attenuated vaccine[66] will reduce both the occurrence and severity of clinical signs of disease. However, because strangles in equine athletes is uncommon, the rate of vaccination among these animals is low. As well, the strangles vaccines have been dogged by the perception that severe local reactions may occur following their use, even though published safety data show that these reactions may be infrequent.[65]

Use of the live, attenuated intranasal strangles vaccine has been associated with some reports of abscess formation at the site of other injections given on the same day as well as reports of classical disease from which the vaccine strain of the organism has been isolated.[67] Importantly, although the manufacturer has conducted experimental challenge trials of this vaccine, none of the details of these studies have been presented in peer review publications.

Increasing knowledge about the pathogenesis and epidemiology of equine strangles and the development and testing of control procedures based upon identification of non-clinical carriers, sanitation and quarantine may result in decreased urgency to develop safe and efficacious vaccines against this disease. Based on our current understanding, there appears to be no clear justification for vaccination of equine athletes against strangles unless it is known that these horses are likely to be placed at high risk of exposure and disease. At best, current vaccines reduce the rate and severity of clinical disease in vaccinated animals by approximately 50%.[65,68] Under most circumstances, instituting other preventive procedures should provide a higher likelihood of success in the prevention and containment of outbreaks of this disease among equine athletes.

Equine rabies

Rabies is a rare but fatal disease of horses. The National Animal Health Monitoring Scheme (NAHMS) survey[69] reports that approximately 25% of horses in the USA over 12 months of age are vaccinated annually against this disease. Despite a widespread conviction that the equine rabies vaccines are highly efficacious, as well as verbal and written assurances from the vaccine industry and regulatory authorities, the only published information upon the efficacy of rabies vaccination in horses relates to instances when vaccinated animals developed the disease.[70,71] Assuming that successful challenge trials have been conducted, it is highly regrettable that there are no published data on the serologic or protective response of horses to the vaccines presently on the market. Paradoxically, the use of rabies immunoglobulin, including equine rabies immunoglobulin, is considered an essential component of post-exposure treatment in people and there are published field trials demonstrating the efficacy of this procedure.[72–76] This appears to provide clear evidence that protecting horses through vaccination should be possible.

The duration of immunity following administration of an efficacious vaccine against equine rabies will vary among individual animals but based on data from humans and other animals, it should exceed 12 months. Assuming a close correlation between serologic status and protection against this disease, those seriously interested in preventing equine rabies might be advised to focus some of their efforts upon developing a commercially available serologic test for protective antibody in horses. Knowing whether or not individual horses possess protective concentrations of serum antibody would be extremely useful. If vaccines were administered on this basis, the rate of revaccination would probably be reduced and it would soon become evident which vaccines on the market gave the best response. The cost of such a service might prove comparable to the cost of annual vaccination programs, and would be more useful.

Tetanus

Like rabies, equine tetanus is a rare disease, even amongst horses that have not been vaccinated. Tetanus toxoid is the most commonly used vaccine in horses 12 months of age and older. In North America, approximately 70% of horses in this age range are vaccinated on an annual basis.[69] To be judged satisfactory by the United States Department of Agriculture, Center for Biologics, tetanus vaccines must provide a serologic response in guinea pigs that is at least four times higher than that thought necessary to protect them against a natural challenge.

Experimental challenges showing protection following vaccination of horses have been reported[77] but these studies were not conducted using commercial vaccines. There is no published information upon the magnitude or duration of serologic response or protection against toxin challenge among horses vaccinated with any of the tetanus toxoids currently marketed in North America. Equine tetanus has been reported among vaccinated animals[78] although these animals were less likely to die than non-vaccinates.

The decline in the incidence of equine tetanus since vaccination became common practice and the fact that equine tetanus antitoxin is effective in the treatment of the disease in people[79–81] has naturally led to the conclusion that most, if not all, of the current tetanus toxoid vaccines are effective. Arguably, some of the decline in incidence of the disease may be related to other factors, including improvements in general husbandry practices and methods of wound management, including the common use of antibiotics.

The duration of immunity following vaccination with any of the currently marketed toxoids is not known. There is some evidence to suggest that it is likely to exceed 1 year[14] and perhaps be as long as 8.[77] Data on the serologic status of vaccinated and unvaccinated horses of different ages and an assessment of variation among the different vaccines would be very useful in helping us refine current vaccination programs. Until this information becomes available, the practice of yearly vaccination of horses, following an initial prime and boost vaccination, will continue to be standard practice for equine athletes.

Eastern and western equine encephalomyelitis

There is little information on the efficacy of the eastern (EEE) and western equine encephalomyelitis (WEE) vaccines. Virtually every manufacturer of equine vaccines in North America produces at least one vaccine against equine encephalomyelitis and most textbooks and articles on the prevention of these diseases claim that vaccination is key. However, there are no results from well-designed challenge or even serologic studies to support this claim.

Eastern equine encephalomyelitis is prevalent in the south and east of North America, particularly the southern USA. The case fatality rate is high. Until the critical challenge experiments, field trials, outbreak or case control studies are done to assess vaccine efficacy, it is likely that horses in endemic regions, or traveling to them, will continue to receive vaccine once or twice each year.

Clarifying the impact of vaccination upon the occurrence of western equine encephalomyelitis will likely prove even more difficult than it will for EEE. Appropriate challenge models have not been published so experimental studies upon which to gauge the potential efficacy of existing vaccines cannot be performed. Similar to EEE, vaccination programs against this disease have become ingrained in our disease prevention strategies. The practice of annual WEE vaccination prior to the mosquito season continues in regions of North America where extensive surveillance programs have not detected the presence of virus or disease for over 20 years. At this time, there appears to be no evidence to suggest that routine vaccination against this disease is providing any benefit to equine athletes.

West Nile virus

At the time of preparation of this book, West Nile virus was spreading rapidly across North America and resulting in alarming numbers of clinical cases and subsequent death of horses in both the USA and Canada. There is tremendous public concern regarding this disease and because it is a zoonosis, there are large-scale programs in place to track the spread of the virus. These data are important to the prevention of the disease in horses as they permit realistic assessment of risk of exposure of horses maintained or traveling in different regions. The first and probably the most effective strategy for prevention is related to decreasing exposure of horses to the mosquito vector. This is accomplished through programs to reduce or eliminate sources of standing water in areas where horses are kept, spraying the environment, stabling horses in screened facilities, and the application of insect repellents to horses.

In response to this crisis in North America, a commercial vaccine has been licensed for use in the USA and Canada. Experimental challenges of susceptible horses with live virus have not resulted in clinical signs of disease but have caused infection and detectable viremia. At least two challenge studies assessing the ability of the vaccine to prevent viremia and a field safety trial have been conducted by the manufacturer. The full results of these studies have not yet been published but reports from the manufacturer state that local reactions to the vaccine are mild and uncommon and that in comparison to controls, vaccinated animals experienced a significant decrease in the occurrence of viremia in both studies.

It may be some time before accurate estimates can be made regarding the benefit of vaccination of athletic horses against

this disease. There is an urgent need to conduct both retrospective and prospective studies aimed at providing accurate estimates of the rate of clinical signs of disease among herds of horses maintained under various levels of risk of exposure. Due to the circumstances of their general care and management, equine athletes should be at or near the lowest risk of exposure and disease. However, until more is known about the vaccine and the current epidemic, vaccination of valuable animals will be a common practice. Hopefully, veterinary practitioners and scientists will seize the opportunity to study this disease and the effectiveness of control procedures throughout the present epidemic. With careful assessment of the evidence, vaccination programs should not become fully entrenched without the data to support this practice.

Equine protozoal myelitis

Equine protozoal myelitis (EPM) is an infectious disease of horses requiring prolonged and expensive treatment. Serologic studies show high prevalence of infection in endemic regions and although almost certainly overdiagnosed, the incidence of this disease is much greater than the combined incidence of rabies and tetanus. Equine athletes are at risk in endemic regions through contamination of their feed. A killed vaccine has been provisionally licensed and marketed in the USA and Canada. The efficacy of vaccination is currently under study through a large-scale multicenter study. Research is also proceeding on the development of an experimental challenge model. There seems to be a reasonable prospect that published results will one day become available, providing the critical data upon which informed decisions on vaccination can be made. In the mean time, the decision whether or not to vaccinate will be made on a case-by-case basis by individual owners and their veterinarians.

Equine viral arteritis

Infection with equine viral arteritis (EVA) virus may be followed by clinical signs of respiratory disease. EVA should be included in the differential diagnosis of viral respiratory disease, particularly when combined with evidence of vasculitis (subcutaneous edema, petechial hemorrhages and thrombocytopenia). Occasional outbreaks of the disease may occur in athletic animals[82] but most infections are subclinical. Serologic surveys performed in a number of countries have generally shown relatively low numbers of seropositive horses, particularly among equine athletes.[83–88] Vaccination with a modified live vaccine is followed by seroconversion and one challenge study provides evidence of protection against clinical signs of disease.[89] However, given the infrequency of outbreaks of clinical disease, routine vaccination of equine athletes should not be recommended. Vaccination should be considered for stallions destined to become breeding animals.[90] However, antibody responses stimulated by commercial vaccines cannot be distinguished from natural infection with the virus. This is relevant to management of the equine athlete, as some countries do not permit importation of seropositive animals.

Potomac horse fever

Infections caused by *Neorickettsia risticii* (*Ehrlichia risticii*) are capable of causing acute endotoxemia, colic, diarrhea and hypoproteinemia in horses. Laminitis is a common and sometimes fatal complication.

Although the epidemiology of the disease has not been completely described, substantial progress has been made in understanding the seasonality, distribution and modes of transmission. All published evidence indicates that the disease is not contagious. Infection follows ingestion of infected snail metacercariae. Regions and farms of high prevalence have been identified and equine athletes traveling to or kept in these regions are logically at some risk of infection and disease, particularly when kept at pasture.

Several killed vaccines against *N. risticii* are marketed in the USA and Canada. Data from an experimental challenge of one of these vaccines showed a significant decrease in disease among vaccinates as compared with control animals.[91] However, subsequent studies failed to demonstrate field efficacy.[92,93]

Efforts aimed at limiting disease and fatalities directly related to infection with *N. risticii* should include close attention to limiting exposure, careful monitoring of animals in endemic regions and prompt diagnosis and treatment of individuals developing signs of disease. In the face of questionable evidence of vaccine efficacy, the decision to initiate a program will depend on the experience, judgment and opinions of individual horse owners and their veterinarians. If vaccination is effective, the duration of immunity would not be expected to exceed 6 months. If horses are to be vaccinated, the initial prime–boost strategy should be completed shortly before the onset of the expected period of risk and followed by similar timing of annual revaccination.

However well reasoned the above approach may turn out to be, it is clear that further studies should be conducted to test these and other logical strategies. Horse owners and veterinary practitioners should encourage vaccine manufacturers, research scientists and regulatory agencies to perform more studies aimed at developing a better understanding of the prevention and control of this disease.

Summary

Vaccination programs for all horses, athletes included, should be based upon an understanding of the risk of disease, vaccine efficacy, the concepts of herd immunity, duration of

immunity, variation in response to vaccination among vaccines and among horses and a cost–benefit analysis. There is no doubt that veterinarians wishing to design vaccination programs for equine athletes are hampered in their efforts due to lack of adequate information upon which to base many of their decisions. However, this situation is improving. Regulatory authorities are gradually refining and increasing their demands for relevant efficacy data during the process of vaccine registration and there are many individuals within the vaccine industry seeking to meet or exceed these requirements. Veterinarians and educators have a critical role to play in this process. We must do a better job of teaching and understanding the principles of vaccinology and the strengths and limitations of vaccination as a method of disease control. Practicing veterinarians should be more insistent upon obtaining relevant data on the efficacy, duration of immunity and safety of the vaccines that they recommend and use. The effectiveness of all equine vaccination programs could be substantially improved through more appropriate use of vaccines based on the rigorous application of current knowledge; through realistic assessment of risk, efficacy, costs and benefits of vaccination; and by making sure that all reasonable, alternate strategies of disease prevention are used in combination with vaccination.

References

1. van Maanen C, Cullinane A. Equine influenza virus infections: an update. Vet Q 2002; 24(2):79–94.
2. Glass K, Wood JL, Mumford JA, et al. Modelling equine influenza 1: a stochastic model of within-yard epidemics. Epidemiol Infect 2002; 128(3):491–502.
3. Newton JR, Townsend HG, Wood JL, et al. Immunity to equine influenza: relationship of vaccine-induced antibody in young Thoroughbred racehorses to protection against field infection with influenza A/equine-2 viruses (H3N8). Equine Vet J 2000; 32(1):65–74.
4. Guthrie AJ, Stevens KB, Bosman PP. The circumstances surrounding the outbreak and spread of equine influenza in South Africa. Rev Sci Tech 1999; 18(1):179–185.
5. Lany P, Pospisil Z, Zendulkova D, et al. An epidemiological study on an outbreak of equine influenza in the Czech Republic in the autumn of 1995. Vet Med (Praha) 1997; 42(2):39–42.
6. Powell DG, Watkins KL, Li PH, Shortridge KF. Outbreak of equine influenza among horses in Hong Kong during 1992. Vet Rec 1995; 136(21):531–536.
7. Wood J, Mumford J. Epidemiology of equine influenza. Vet Rec 1992; 130(6):126.
8. Burrows R, Goodridge D, Denyer M, et al. Equine influenza infections in Great Britain, 1979. Vet Rec 1982; 110(21):494–497.
9. Sherman J, Mitchell WR, Martin SW, et al. Epidemiology of equine upper respiratory tract disease on standardbred racetracks. Can J Comp Med 1979; 43(1):1–9.
10. Morley PS, Townsend HGG, Bogdan JR, Haines DM. Descriptive epidemiologic study of disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):535–544.
11. Morley PS, Townsend HG, Bogdan JR, Haines DM. Risk factors for disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):545–550.
12. Rua-Domenech RdL, Reid SWJ, Gonzalez ZAE, et al. Modelling the spread of a viral infection in equine populations managed in Thoroughbred racehorse training yards. Prev Vet Med 2000; 47(1–2):61–77.
13. Newton JR, Townsend HGG, Wood JLN, et al. Immunity to equine influenza: relationship of vaccine-induced antibody in young Thoroughbred racehorses to protection against field infection with influenza A/equine-2 viruses (H3N8). Equine Vet J 2000; 32(1):65–74.
14. Mumford JA, Jessett DM, Rollinson EA, et al. Duration of protective efficacy of equine influenza immunostimulating complex/tetanus vaccines. Vet Rec 1994; 134(7):158–162.
15. Mumford JA, Wilson H, Hannant D, Jessett DM. Antigenicity and immunogenicity of equine influenza vaccines containing a Carbomer adjuvant. Epidemiol Infect 1994; 112(2):421–437.
16. Townsend HG, Penner SJ, Watts TC, et al. Efficacy of a cold-adapted, intranasal, equine influenza vaccine: challenge trials. Equine Vet J 2001; 33(7):637–643.
17. Lunn DP, Hussey S, Sebing R, et al. Safety, efficacy, and immunogenicity of a modified-live equine influenza virus vaccine in ponies after induction of exercise-induced immunosuppression. J Am Vet Med Assoc 2001; 218(6):900–906.
18. Chambers TM, Holland RE, Tudor LR, et al. A new modified live equine influenza virus vaccine: phenotypic stability, restricted spread and efficacy against heterologous virus challenge. Equine Vet J 2001; 33(7):630–636.
19. Youngner JS, Whitaker-Dowling P, Chambers TM, et al. Derivation and characterization of a live attenuated equine influenza vaccine virus. Am J Vet Res 2001; 62(8):1290–1294.
20. Adam EN, Morley PS, Chmielewski KE, et al. Detection of cold-adapted vaccine-strain influenza virus using two commercial assays. Equine Vet J 2002; 34(4):400–404.
21. Chambers TM, Shortridge KF, Li PH, et al. Rapid diagnosis of equine influenza by the Directigen FLU-A enzyme immunoassay. Vet Rec 1994; 135(12):275–279.
22. Morley PS, Bogdan JR, Townsend HG, Haines DM. Evaluation of Directigen Flu A assay for detection of influenza antigen in nasal secretions of horses. Equine Vet J 1995; 27(2):131–134.
23. Mumford JA, Wernery U, Wade JF, Kaaden OR. Control of influenza from an international perspective. Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, 23–26 March 1998:11–24.
24. Shortridge KF, Watkins KL, Powell DG, et al. Steps to prevent entry of equine influenza into Hong Kong: application of Directigen FLU-A enzyme immunoassay. In: Equine infectious diseases VII: Proceedings of the Seventh International Conference, Tokyo, Japan, 8–11 June; 1994:308–309.
25. Morley PS, Townsend HGG, Bogdan JR, Haines DM. Risk factors for disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):545–550.
26. Heldens JG, Hannant D, Cullinane AA, et al. Clinical and virological evaluation of the efficacy of an inactivated EHV1 and EHV4 whole virus vaccine (Duvaxyn EHV1,4). Vaccination/challenge experiments in foals and pregnant mares. Vaccine 2001; 19(30):4307–4317.
27. Heldens JG, Kersten AJ, Weststrate MW, van den Hoven R. Duration of immunity induced by an adjuvanted and inactivated equine influenza, tetanus and equine herpesvirus 1 and 4 combination vaccine. Vet Q 2001; 23(4):210–217.

28. Stokes A, Corteyn AH, Murray PK. Clinical signs and humoral immune response in horses following equine herpesvirus type-1 infection and their susceptibility to equine herpesvirus type-4 challenge. Res Vet Sci 1991; 51(2):141–148.
29. Tewari D, Gibson JS, Slater JD, et al. Modulation of the serological response of specific pathogen-free (EHV-free) foals to EHV-1 by previous infection with EHV-4 or a TK-deletion mutant of EHV-1. Arch Virol 1993; 132(1–2):101–120.
30. Matsumura T, O'Callaghan DJ, Kondo T, Kamada M. Lack of virulence of the murine fibroblast adapted strain, Kentucky A (KyA), of equine herpesvirus type 1 (EHV-1) in young horses. Vet Microbiol 1996; 48(3–4):353–365.
31. Matsumura T, O'Callaghan DJ, Kondo T, Kamada M. Lack of virulence of the murine fibroblast adapted strain, Kentucky A (KyA), of equine herpesvirus type 1 (EHV-1) in young horses. Vet Microbiol 1996; 48(3–4):353–365.
32. Sutton GA, Viel L, Carman PS, Boag BL. Pathogenesis and clinical signs of equine herpesvirus-1 in experimentally infected ponies in vivo. Can J Vet Res 1998; 62(1):49–55.
33. Hannant D, Jessett DM, O'Neill T, et al. Responses of ponies to equid herpesvirus-1 ISCOM vaccination and challenge with virus of the homologous strain. Res Vet Sci 1993; 54(3):299–305.
34. Chong YC, Duffus WPH. Immune responses of specific pathogen free foals to EHV-1 infection. Vet Microbiol 1992; 32(3–4):215–228.
35. Mumford JA, Hannant D, Jessett DM, et al. Evaluation of protective efficacy of equid herpesvirus type 1 ISCOM vaccine for the abortigenic form of disease. Equine Reproduction V: Proceedings of the Fifth International Symposium on Equine Reproduction 1991; 730–731(Journal of Reproduction and Fertility):Supplement No. 44.
36. Coignoul FL, Bertram TA, Cheville NF. Pathogenicity of equine herpesvirus 1 subtype 2 for foals and adult pony mares. Vet Microbiol 1984; 9(6):533–542.
37. Palfi V, Molnar T, Belak S. Viral (EHV-2) respiratory disease in foals. Magyar Allatorvosok Lapja 1979; 34(10):687–690.
38. Mumford JA, Bates J. Trials of an inactivated equid herpesvirus 1 vaccine: challenge with a subtype 2 virus. Vet Rec 1984; 114(15):375–381.
39. Burki F, Rossmanith W, Nowotny N, et al. Viraemia and abortions are not prevented by two commercial equine herpesvirus-1 vaccines after experimental challenge of horses. Vet Q 1990; 12(2):80–86.
40. Schrag D, Floss G, Koene M. Efficacy and tolerability of early intranasal immunizations of foals with Prevaccinol. Praktische Tierarzt 1997; 78(2):108–119.
41. Jessett DM, Schrag D, Mumford JA, et al. Protection provided by an attenuated EHV-1 vaccine against challenge with the virulent EHV-1 AB4 isolate. Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, 23–26 March 1998:414–415.
42. Klein N, McMillen J, Wedman EE, et al. Recombinant EHV-4/equine influenza virus constructs induce immunity against EHV-4 and equine influenza. Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, 23–26 March 1998:417.
43. Gilkerson JR, Love DN, Drummer HE, et al. Seroprevalence of equine herpesvirus 1 in Thoroughbred foals before and after weaning. Aust Vet J 1998; 76(10):677–682.
44. Doll ER, Bryans JT. Epizootiology of equine viral rhinopneumonitis. J Am Vet Med Assoc 1963; 142(1):31–37.
45. Morley PS, Townsend HG, Bogdan JR, Haines DM. Descriptive epidemiologic study of disease associated with influenza virus infections during three epidemics in horses. J Am Vet Med Assoc 2000; 216(4):535–544.
46. Sherman J, Thorsen J, Barnum DA, et al. Infectious causes of equine respiratory disease on Ontario standardbred racetracks. J Clin Microbiol 1977; 5(3):285–289.
47. Matsumura T, Sugiura T, Imagawa H, et al. Epizootiological aspects of type 1 and type 4 equine herpesvirus infections among horse populations. J Vet Med Sci 1992; 54(2):207–211.
48. Yasunaga S, Maeda K, Matsumura T, et al. Diagnosis and sero-epizootiology of equine herpesvirus type 1 and type 4 infections in Japan using a type-specific ELISA. J Vet Med Sci 1998; 60(10):1133–1137.
49. Wood JLN, Newton JR, Chanter N, et al. A longitudinal epidemiological study of respiratory disease in racehorses: disease definitions, prevalence and incidence. In: Equine infectious diseases VIII: Proceedings of the Eighth International Conference, Dubai, 23–26 March 1998. 1999:64–70.
50. Mumford EL, Traub-Dargatz JL, Salman MD, et al. Monitoring and detection of acute viral respiratory tract disease in horses. J Am Vet Med Assoc 1998; 213(3):385–390.
51. Hofer B, Steck F, Gerber H, et al. An investigation of the etiology of viral respiratory disease in a remount depot. In: Bryans JT, Gerber H, eds. Equine infectious diseases III: Proceedings of the Third International Conference, Paris 1972. Basel; Karger; 1973:527–545.
52. Todd KG. Strangles. J Comp Pathol Ther 1910; 23:212–229.
53. Berthelon M, Rampin D. [Course of an outbreak of influenza due to the A/Equi 1 type of virus in a Thoroughbred stud.]. Revue de Medecine Veterinaire 1972; 123(3):293–304.
54. Itoh H, Kudoh H, Kidoguchi K, Miyake Y. *Streptococcus equi* subspecies *equi* infection in grazing horses. Tohoku J Vet Clin 1997; 20(1):18–20.
55. Anzai T, Nakanishi A, Wada R, et al. Isolation of *Streptococcus equi* subsp. *equi* from thoroughbred horses in a racehorse-breeding area of Japan. J Vet Med Sci 1997; 59(11):1031–1033.
56. Uppal PK, Yadav MP, Manchanda VP. Observations on strangles and purpura haemorrhagica as a sequelae to equine influenza infection. Indian J Anim Sci 1990; 60(10):1149–1153.
57. Sweeney CR, Benson CE, Whitlock RH, et al. Description of an epizootic and persistence of *Streptococcus equi* infections in horses. J Am Vet Med Assoc 1989; 194(9):1281–1286.
58. Piche CA. Clinical observations on an outbreak of strangles. Can Vet J 1984; 25(1):7–11.
59. Newton JR, Wood JLN, Dunn KA, et al. Naturally occurring persistent and asymptomatic infection of the guttural pouches of horses with *Streptococcus equi*. Vet Rec 1997; 140(4):84–90.
60. George JL, Reif JS, Shideler RK, et al. Identification of carriers of *Streptococcus equi* in a naturally infected herd. J Am Vet Med Assoc 1983; 183(1):80–84.
61. Dalgleish R, Love S, Pirie HM, et al. An outbreak of strangles in young ponies. Vet Rec 1993; 132(21):528–531.
62. Hoffman AM, Staempfli HR, Prescott JF, Viel L. Field evaluation of a commercial M-protein vaccine against *Streptococcus equi* infection in foals. Am J Vet Res 1991; 52(4):589–592.
63. Newton JR, Verheyen K, Talbot NC, et al. Control of strangles outbreaks by isolation of guttural pouch carriers identified using PCR and culture of *Streptococcus equi*. Equine Vet J 2000; 32(6):515–526.
64. Hoffmann AM, Staempfli HR, Prescott JF, Viel L. Field evaluation of a commercial M-protein vaccine against *Streptococcus equi* infection in foals. Am J Vet Res 1991; 52(4):589–592.

65. Bryant S, Brown KK, Lewis S, et al. Protection against strangles with an enzymatic *Streptococcus equi* extract. Vet Med 1985; 80(9):58–70.
66. Jacobs AAC, Goovaerts D, Nuijten PJM, et al. Investigations towards an efficacious and safe strangles vaccine: submucosal vaccination with a live attenuated *Streptococcus equi*. Vet Rec 2000; 147(20):563–567.
67. Al-Ghamdi GM, Ames TR, Valberg S, et al. Molecular characterization of *Streptococcus equi* isolates cultured from horses experiencing post-vaccinal reaction. In: 18th Annual Veterinary Medical Forum, 25–28 May, 2000; Seattle, WA; 2000:708.
68. Hoffman A, Staempfli H, Viel L, et al. Field evaluation of a commercial M-protein vaccine (Strepvax II) in a feedlot for foals with epidemic strangles. J Vet Intern Med 1989; 3(2):115.
69. Equine '98 Part III: Management and Health of Horses: United States Department of Agriculture, National Animal Health Monitoring Scheme; 1999.
70. Hudson LC, Weinstock D, Jordan T, Bold-Fletcher NO. Clinical presentation of experimentally induced rabies in horses. Zentralbl Veterinarmed [B] 1996; 43(5):277–285.
71. Green SL, Smith LL, Vernau W, Beacock SM. Rabies in horses: 21 cases (1970–1990). J Am Vet Med Assoc 1992; 200(8):1133–1137.
72. Wilde H, Khawplod P, Hemachudha T, Sitprija V. Postexposure treatment of rabies infection: can it be done without immunoglobulin? Clin Infect Dis 2002; 34(4):477–480.
73. Pancharoen C, Thisyakorn U, Lawtongkum W, Wilde H. Rabies exposures in Thai children. Wilderness Environ Med 2001; 12(4):239–243.
74. Lang J, Attanath P, Quiambao B, et al. Evaluation of the safety, immunogenicity, and pharmacokinetic profile of a new, highly purified, heat-treated equine rabies immunoglobulin, administered either alone or in association with a purified, Vero-cell rabies vaccine. Acta Trop 1998; 70(3):317–333.
75. Jaiiaroensup W, Lang J, Thipkong P, et al. Safety and efficacy of purified Vero cell rabies vaccine given intramuscularly and intradermally. (Results of a prospective randomized trial). Vaccine 1998; 16(16):1559–1562.
76. Chutivongse S, Wilde H, Supich C, et al. Postexposure prophylaxis for rabies with antiserum and intradermal vaccination. Lancet 1990; 335(8694):896–898.
77. Lohrer J, Radvila P. [Active tetanus prevention in the horse and the duration of immunity]. Schweiz Arch Tierheilkd 1970; 112(7):307–314.
78. Green SL, Little CB, Baird JD, et al. Tetanus in the horse: a review of 20 cases (1970 to 1990). J Vet Intern Med 1994; 8(2):128–132.
79. Blake PA, Feldman RA, Buchanan TM, et al. Serologic therapy of tetanus in the United States, 1965–1971. JAMA 1976; 235(1):42–44.
80. Sanders RK, Martyn B, Joseph R, Peacock ML. Intrathecal antitetanus serum (horse) in the treatment of tetanus. Lancet 1977; 1(8019):974–977.
81. Thomas PP, Crowell EB, Jr, Mathew M. Intrathecal anti-tetanus serum (ATS) and parenteral betamethasone in the treatment of tetanus. Trans R Soc Trop Med Hyg 1982; 76(5):620–623.
82. Monreal L, Villatoro AJ, Hooghuis H, et al. Clinical features of the 1992 outbreak of equine viral arteritis in Spain. Equine Vet J 1995; 27(4):301–304.
83. Hullinger PJ, Gardner IA, Hietala SK, et al. Seroprevalence of antibodies against equine arteritis virus in horses residing in the United States and imported horses. J Am Vet Med Assoc 2001; 219(7):946–949.
84. Newton JR, Wood JL, Castillo-Olivares FJ, Mumford JA. Serological surveillance of equine viral arteritis in the United Kingdom since the outbreak in 1993. Vet Rec 1999; 145(18):511–516.
85. Huntington PJ, Forman AJ, Ellis PM. The occurrence of equine arteritis virus in Australia. Aust Vet J 1990; 67(12):432–435.
86. Kaaden OR, Haas L, Klopries M. [Equine viral arteritis]. Tierarztl Prax 1990; 18(3):277–282.
87. Kolbl S, Schuller W, Pabst J. [Serological studies of the recent infections of Austrian horses with the equine arteritis virus]. Dtsch Tierarztl Wochenschr 1991; 98(2):43–45.
88. Fukunaga Y, Matsumura T, Sugiura T, et al. Use of the serum neutralisation test for equine viral arteritis with different virus strains. Vet Rec 1994; 134(22):574–576.
89. McCollum WH. Responses of horses vaccinated with avirulent modified-live equine arteritis virus propagated in the E. Derm (NBL-6) cell line to nasal inoculation with virulent virus. Am J Vet Res 1986; 47(9):1931–1934.
90. Timoney PJ, McCollum WH. Equine viral arteritis. Vet Clin North Am Equine Pract 1993; 9(2):295–309.
91. Ristic M, Holland CJ, Goetz TE, Powell DG. Evaluation of a vaccine for equine monocytic ehrlichiosis (Potomac horse fever). Equine infectious diseases V: Proceedings of the Fifth International Conference. Lexington, KY: University Press of Kentucky; 1988:206–213.
92. Dutta SK, Vemulapalli R, Biswas B. Association of deficiency in antibody response to vaccine and heterogeneity of *Ehrlichia risticii* strains with Potomac horse fever vaccine failure in horses. J Clin Microbiol 1998; 36(2):506–512.
93. Atwill ER, Mohammed HO. Evaluation of vaccination of horses as a strategy to control equine monocytic ehrlichiosis. J Am Vet Med Assoc 1996; 208(8):1290–1294.

CHAPTER 58

Parasite control for the athletic horse

Cliff Monahan

Introduction and background

Parasite control programs for performance horses will differ from those for pleasure horses in two principal areas: they will differ in intensity by virtue of the need to maximize the performance horse's athletic abilities, and could shift in scope of parasite targets because travel to events may expose a performance horse to a wider spectrum of parasitic infections than encountered by a sedentary horse. These may be ectoparasites serving as vectors for bacterial and viral pathogens; thus avoidance of the disease is predicated on the parasite control program.

This chapter will begin with coverage of three universally prevalent equine gastrointestinal parasites that define the most important concepts of anthelmintic control programs. Control of all other gastrointestinal parasites of horses will be achievable within a framework to control these three parasites. *Parascaris equorum* is an age-related nematode problem and defines the need to treat prophylactically at regular intervals related to its life cycle. The strongyles, both large and small, are the principal nematode targets of equine parasite control programs worldwide. *Anoplocephala perfoliata* is a common cestode of Equidae worldwide and is susceptible to a limited spectrum of available drugs, thus defining the need to understand how to shift drug choices when necessary.

This chapter will then address ectoparasites and their control, which include management or husbandry practices coupled with a few chemicals having a broad spectrum of activity. The intensity of the ectoparasite control program is based on the importance of the potential transmission. All permanent equine facilities should employ ectoparasite control programs, but the intensity would increase when hosting an event. Extreme measures would be warranted for the sponsors of an international event where horses could be carriers of foreign diseases.

The reader must be cognizant of additional differences between programs designed for all residents of a large training facility as compared to programs for individual horses while traveling off-premises to events. Both styles of control program must be based on rational expectations of management practices and antiparasitic compounds, coupled with a rational list of the anticipated parasites that need to be controlled. As a brief example, a trainer traveling with a small number of performance horses to an international event could employ a labor-intensive and costly preventive program that would be unreasonable to implement for all the residents of a large training facility where residents are exposed only to a local parasite fauna. The traveling horse will usually be stabled, which greatly reduces exposure to parasites ingested on pasture. The residents of a training facility may graze significantly or recreationally; thus the focus shifts to protection of the pastures from heavy contamination through a comprehensive, herd deworming program.

Although parasitism is undesirable because it can drain nutrients and energy otherwise applied to growth or performance, a parasite-free horse is an anomaly and is not a realistic goal of a parasite control program. Many of the equine parasites are prevalent worldwide, so exposure to infective stages should be viewed as inevitable unless the horse remains in a very controlled environment. Horses should develop an acquired resistance to the normal, anticipated spectrum of equine parasites (ascarids and cyathostomes as examples), through controlled exposure.[1–3] Anthelmintic programs are intended to manage these parasitic diseases, not eliminate them completely.

In contrast to the anticipated spectrum of gastrointestinal parasites, there are regional or sporadic infections for which no immunity would be expected to develop. For these, a prevention program is desirable and rational, but not always possible. Many viral, bacterial, rickettsial and protozoal diseases are transmitted by biting arthropods; thus an ectoparasite control program would become the front-line of defense against exposure. This type of prevention program should be

applied while horses are traveling to events even if these potential diseases are not endemic in that area because there is a chance that another competitor is a carrier.

Our understanding of the relative contribution to equine disease by gastrointestinal parasites has evolved since the advent of the macrocyclic lactones (ML) during the early 1980s. *Strongylus vulgaris* is the cause of verminous arteritis or thromboembolic colic,[4] thus the most pathogenic of the horse parasites, but *S. vulgaris* has been tremendously reduced in prevalence through regular use of ivermectin.[1] Without *S. vulgaris* to shoulder the blame for the incidence of colic, we learned of the contribution by the small strongyles or Cyathostominae, previously considered of minimal pathogenicity.[5,6] Widespread benzimidazole resistance of the cyathostomes[7,8] led to reliance on ivermectin as the backbone of anthelmintic control programs. Ivermectin and the entire class of macrocyclic lactones have no activity against tapeworms, and *Anoplocephala perfoliata* is the most important tapeworm of equids. In identical fashion as seen with the cyathostomes, *A. perfoliata* was dismissed as insignificant until the evidence became undeniable.[9,10] As history has demonstrated, our perception of the important equine parasites has been influenced tremendously by the activity of our anthelmintics. Control programs must be designed to target the parasites of importance and shift the choice of anthelmintic as appropriate.

Gastrointestinal parasitic diseases

Parascaris equorum

Parascaris equorum is a common and important parasite of foals, weanlings and yearlings before they can be considered true performance horses, but ineffective control of this infection can result in damage during the growth phase with ramifications for later performance.

Infection and pathogenesis

Ingested ascarid eggs hatch in the small intestine where the larvae penetrate the wall. Their migration follows the path of least resistance because the larvae are swept by the venous blood flow through the portal system to the liver. The larvae are trapped first in the liver and migrate within the parenchyma for several days before reaching vessels that carry them into the caudal vena cava to the heart, then to the lungs. Clinical signs stemming from migration through the liver may be more vague than those of pulmonary migration.

Following passage through the liver, the pulmonary capillary beds next trap the larvae. Most *P. equorum* larvae find their way through the thin walls of the alveoli into the lumen. *Parascaris equorum* can cause an eosinophilic pneumonitis with ramifications on pulmonary function that extend beyond the duration of larval migration.[11,12] Pulmonary changes can range from a mild cough to bacterial pneumonia accompanied by a purulent nasal discharge, typically bilateral. A peripheral neutrophilia or eosinophilia is often observed on a complete blood count (CBC).[11,12]

Ascarid larvae in the lungs are coughed up the trachea to the pharynx and swallowed. Larvae arrive in the small intestine measuring just millimeters in length, but grow eventually as long as 50 centimeters when mature. Their contact with the mucosal surface leads to truncation and thickening of the villi and alteration of the cellular components of the mucosal lining. These changes reduce digestion and absorption of nutrients. Large masses of ascarid larvae and adults can lead to impactions and intussusceptions when ascarids develop unchecked by regular anthelmintic administration.[13]

Diagnosis

During the prepatent, migratory phase, diagnosis of *P. equorum* infections is problematic because confirmation by a fecal examination is not possible for at least 70 days after infection. A provisional diagnosis can be made based on the age and associated clinical signs. Clinical chemistry changes associated with liver damage include elevated serum activity of aspartate transaminase (AST), but this enzyme is not specific for liver damage. Serum activity of sorbitol dehydrogenase (SDH) and gamma-glutamyl transaminase (GGT) are likely to be elevated secondary to the hepatic damage by the larvae, and are more specific for liver involvement. For diagnosis of patent infections by a fecal examination, both passive flotations and centrifugation techniques are effective, but centrifugation techniques are more sensitive. The eggs will be characteristic of ascarids: thick-shelled, brown in color, usually with a proteinaceous coating, and will measure 90–100 μm in diameter.

Treatment and control

Treatment and control of *P. equorum* infections should be achievable with the benzimidazoles, pyrantel salts or piperazine. A recent report from Europe indicates that *P. equorum* populations have developed resistance to both ivermectin and moxidectin.[14] Published reports of this resistance have not yet been made from other regions of the world, but recent personal experience in North America with several yearlings carrying patent infections of *P. equorum* included a recent history of ivermectin treatments. These experiences are indicative that the macrocyclic lactone class is no longer reliable for *P. equorum* treatment or control. Clinicians are advised to perform follow-up fecal examinations at 14 days after treatment to verify success or failure.

A major consideration in choice of anthelmintic is the absorption from the intestine for systemic activity against migrating larvae. Pyrantel pamoate and fenbendazole have limited absorption, so would not be the first choice for targeting the migratory larval stages in either the liver or lungs. Fenbendazole could be given over 5 days for activity against migrating larvae. Ivermectin and moxidectin both have systemic activity against migratory larvae at the therapeutic

dosage, but the recent drug resistance question of *P. equorum* must be answered. Moxidectin should not be used for foals less than 4 months of age, nor for debilitated horses.

Preventive anthelmintic treatments should be initiated by 6 weeks of age and not delayed until a fecal examination confirms the presence of *P. equorum*. These treatments should be repeated at 6-week intervals and are aimed at removing larval ascarids before their adult size becomes problematic or egg production begins. As mentioned previously, contamination of the soil will lead to years of ascarid transmission. At 6-week intervals, an anthelmintic with systemic activity is not necessary as the immune response will develop and block further migration.

Colic, impaction and intussusception can occur following anthelmintic administration to heavily infected young horses, but the root cause of this sequela is the inadequate parasite control program rather than the drug administration. Many practitioners feel that half doses of anthelmintics are safer to use in this situation, as if this would only affect half of the ascarids. Clinicians are advised to use the label dosage and prepare for the potential with such precautions as mineral oil. Piperazine is contraindicated in this setting.

Epidemiology

Ascarid infections of most animals are diseases of neonates and juveniles that will develop resistance or immunity through exposure. Infections in 2-year-old horses are rare. Ascarid eggs have a thick, proteinaceous shell that resists desiccation and protects the infective larva, facilitating survival in the environment for years.[15] Because the egg is infective, transmission of *P. equorum* can occur in any season, and can occur in young horses confined to stalls or paddocks.[15,16] This transmission is in contrast to strongyle infections that require warm temperatures for activity of the infective larvae and pasture settings for grazing transmission.

Strongyle infections

The large and small strongyles are associated taxonomically by morphological characteristics, but differ significantly in their development in the horse. The large strongyles include three most important species within the genus *Strongylus*: *S. vulgaris*, *S. edentatus* and *S. equinus*. The cyathostomes, or small strongyles, constitute several genera with over 40 species worldwide; thus the terms 'small strongyles' or 'cyathostomes' are preferred for convenience.

Large strongyles

Infection and pathogenicity

Strongylus vulgaris has, historically, been regarded as the most pathogenic nematode parasite of Equidae worldwide due to its migration through the cranial mesenteric artery (CMA), causing verminous arteritis or thromboembolic colic. This migration follows the arterioles of the cecal and colonic submucosa moving craniad along the arterial system. Damage to the endothelium promotes platelet adherence. When sufficient numbers of *S. vulgaris* larvae are funneled to the CMA, their numbers destroy the normal, elastic architecture of the artery, disrupting laminar flow of blood. Turbulent flow promotes clot formation, seeding the distal capillary beds with thrombi of varying sizes. The size of the distal artery blocked by a thrombus will affect the size of the ischemic area of the intestine. If the area is small, collateral circulation can be established and the horse may suffer a transient bout of colic. If large, ischemia will lead to an intractable colic, endotoxemia and death. Resolution of small lesions can result in serosal attachments between loops of the intestine, which can be associated with future entrapments. Architectural changes of the CMA remain for the life of the horse; thus an active infection is not required for repeated bouts of thromboebolic colic. The elastic nature of the CMA will not return.

Diagnosis

Fecal examinations easily recover both large and small strongyle eggs. This typical strongyle-type egg cannot be differentiated morphologically as either a large or small strongyle. Today, the assumption that any eggs recovered are all small strongyles is justified by the sporadic to rare appearance of large strongyles in well-managed horses.

Treatment and control

The large strongyles are best controlled by regular deworming with a macrocyclic lactone because of their potent systemic effects against migrating larvae. Due to their prepatent period (6–11 months), the large strongyles can be eliminated from a well-managed horse farm by semiannual use of ivermectin or moxidectin, although *S. vulgaris* does still occur.[17] Daily deworming with a pyrantel tartrate feed additive is useful while traveling, but does not replace regular deworming with a macrocyclic lactone.[18] Daily deworming is intended to kill the larvae as they exsheath before penetrating the intestinal wall; however, a single, morning feed additive may not have sufficient concentration in the lumen if horses graze later in the day. Nonetheless, daily dewormers are a useful product for horses traveling to events where they may be allowed recreational grazing on pastures of unknown contamination. For maximum protection, the product should be fed just prior to grazing.

Epidemiology

As mentioned previously, the prevalence of large strongyles has been reduced by ivermectin usage and the cyathostomes are now the focal point of equine deworming programs. Transmission requires grazing for exposure to infective larvae. For the athletic horse, the greatest risk of exposure will come off premises at events, where recreational grazing may expose horses to pastures of unknown infectivity. Age-related resistance to the large strongyles does develop

through exposure, but is not complete and owners or trainers should be diligent to protect horses off premises.

Cyathostomes

Infection and pathogenicity

The life cycle of the cyathostomes is complex and reviewed elsewhere.[19,20] The small strongyles do not migrate through the body as do the large strongyles; instead, they penetrate no further than the mucosa or submucosa of the cecum and ventral colon where they encyst for variable periods of time. During encystment, the small strongyles are hypobiotic, rendering them less susceptible to normal anthelmintic treatments. Over 90% of the million or more cyathostomes will be hypobiotic or encysted larval stages.[21,22] Their presence in the wall of the cecum or ventral colon causes thickening of the mucosa, which decreases absorption of nutrients. Their presence also disrupts the myoelectrical conduction of the smooth muscle, which can manifest as spasmodic colic.

There are two manifestations of cyathostome infections, both related to the larval stages. The acute form, larval cyathostomosis, is better known and stems from a synchronous emergence of larval stages analogous to type II ostertagiasis in cattle. Synchronous activation can destroy the cecal and colonic mucosa, resulting in severe, protein-losing, life-threatening diarrhea. This is a medical emergency with a guarded prognosis.[23] The mechanism triggering the emergence of encysted cyathostomes is not well characterized and is multifactorial.[23,24]

The second manifestation is also due to the larval stages, is subtle, develops slowly over a grazing season, and is difficult to diagnose because fecal examinations may be negative as few adult cyathostomes may be present in the lumen. This condition will also be seen most commonly in horses less than 6 years of age.[24] When a horse grazes an infected pasture, the mucosal population of hypobiotic larvae grows daily, which develops into a progressive thickening of the cecal and ventral colonic mucosa until a point at which absorption of nutrients is impaired. Afflicted horses typically show a progressive loss of body condition in spite of sufficient feed intake. Typically, regular anthelmintic treatments remove the egg-laying adults with limited activity against the mucosal stages. This leads to the misconception that a horse receiving regular anthelmintics and negative on a fecal examination could not be suffering from parasitism.

Diagnosis

The small strongyle egg-laying adults in the lumen of the cecum or ventral colon produce a typical strongyle-type egg during patent infections. These eggs are easily recovered by normal fecal examination techniques. Unfortunately, the clinical signs associated with cyathostome infections are secondary to the encysted or hypobiotic larvae. Acute cyathostomosis can be differentiated from other causes of acute diarrhea by the presence of blood-red larvae in the feces or on a palpation sleeve. High numbers of strongyle-type eggs would not be recovered on a fecal examination of acute cyathostomosis because few adults are present in the lumen. Diagnosis may be aided by a CBC demonstrating an eosinophilia, or by finding low plasma protein values and normal to elevated levels of fibrinogen in the face of a protein-losing enteropathy.

Treatment and control

The most important distinction to make is between treatment of the lumen-dwelling adults and the mucosal-dwelling encysted larvae. Treatment of acute cyathostomosis is a medical emergency to replace the fluid and protein losses. Anthelmintics are of secondary importance for these cases.

Anthelmintic programs are aimed at control of the egg-laying adults, which should translate into lower mucosal burdens through reduction of pasture contamination. Small strongyles have developed widespread benzimidazole resistance, which is widely reported,[7,8] thus the benzimidazole class of anthelmintics should be reserved for the 5-day course of daily treatments at elevated dosages to remove the encysted larvae.[25] Cyathostomes have also developed resistance to pyrantel salts, although not as widely reported as for the benzimidazoles. Their periodic use is rational and effectiveness should be confirmed with a fecal examination.

This leaves the macrocyclic lactone class as the backbone of an anthelmintic control program. Both ivermectin and moxidectin have excellent activity against the lumen-dwelling adults. Ivermectin has little or no reported activity against the mucosal larvae, probably due to its short plasma half-life.[26] Moxidectin, in contrast, has an extended half-life with measurable levels at 80 days post-treatment.[26] This extended activity does provide additional protection to grazing horses,[27] but may select for drug-resistant cyathostomes.[28,29] The author prefers the exclusive use of ivermectin for cyathostome control, with elevated benzimidazole treatments for 5 days to target mucosal stages. Since the advent of ivermectin in the early 1980s, there has never been a report of macrocyclic lactone-resistant cyathostomes. Recent reports of ascarid resistance highlight the importance of avoiding drug-resistant horse nematodes.

The 5-day course of benzimidazole treatments should be useful in horses under 6 years of age during the later part of a grazing season. They would be beneficial when a young horse enters training where stabling may reduce or eliminate exposure on pasture. By killing the larvae in situ within the mucosa, larval degeneration should seed the immune system with antigens in the fashion of a drug-abbreviated vaccination, theoretically engendering a level of acquired resistance at an earlier age.

The periodicity of anthelmintic treatments will depend on the drug employed, and is important to horses with access to pasture, not those confined to stalls. Use of pyrantel salts would require retreatment at 4- to 6-week intervals. Use of ivermectin or moxidectin allows 8- to 12-week intervals before egg shedding recurs. Regardless of the anthelmintic, fecal examinations should be used to verify the effectiveness of treatments, then to identify the egg reappearance time

that will dictate subsequent treatments.[30] Excessive drug treatments are not necessary and are likely to speed the development of drug resistance.[29]

Epidemiology

In contrast to *P. equorum*, both large and small strongyles are transmitted seasonally during the grazing season through ingestion of the infective larvae on pasture. Cyathostome infections are of greatest severity or risk in horses less than 6 years of age with access to pasture.[1,6,24,31] Acute cyathostomosis also has an association with season (late winter or early spring), and a recent history of deworming that apparently triggers the synchronous emergence of larvae. Older horses should have developed an acquired resistance through controlled exposure, but will still carry infections and serve as a source for pasture contamination. Encysted larvae survive for years past ingestion. Gibson[32] demonstrated that the encysted population was sufficient to repopulate the lumen after anthelmintic treatments for almost 3 years when the experiment was terminated. This finding highlights that acute diarrhea in a stall-confined athletic horse could stem from larval cyathostomosis even when previous exposure to pasture is a year or more in the past. All horses, regardless of age, will experience some degree of larval emergence but few will reach the magnitude necessary to trigger acute cyathostomosis. Athletic horses confined to stalls and fed hay are still at risk of acute cyathostomosis if they have grazed on pasture earlier in life. Any young horse turned out to pasture for rest or rehabilitation after an athletic campaign would be at higher risk and should receive regular monitoring by fecal examinations and appropriate anthelmintic treatments. On large farms or boarding facilities, the efficacy of the control program will have a direct effect on the incidence of colic seen on that farm.[5]

Equine tapeworm infections

The importance of tapeworm infections to the owner or trainer of performance horses lies less in their degree of pathogenicity, but more from an understanding of the life cycle and transmission, and then the requirement for a shift in anthelmintic choice for treatment and control.

Infection and pathogenesis

Tapeworms utilize an indirect life cycle that requires an orbatid mite as the intermediate host for transmission to horses. These tiny, free-living mites live and feed on fecal debris or other organic matter, whether on pasture or in stalls, so transmission to a stabled performance horse can occur. The prepatent period for *Anoplocephala perfoliata* is 4 to 6 weeks following ingestion of an infected mite.

Anoplocephala perfoliata is the most pathogenic horse tapeworm because its predilection site ranges from the terminal ileum into the cecum, with particular clustering at the ileocecocolic valve.[33] Erosive lesions can penetrate into the submucosa and smooth muscle of the valve, affecting its function, which will promote spasmodic colic and intussusception.[9,10,34–36]

Diagnosis

Tapeworm infections of horses are diagnostic problems for two reasons: (1) because progottids break down in the intestinal tract rather than being passed intact, thus a gross examination of the feces rarely reveals the presence of the tapeworms; (2) the eggs liberated by a degenerating proglottid are unevenly distributed in the feces. The eggs can be recovered from a fecal sample with several examination techniques. However, the concentration or uneven distribution of eggs within feces decreases the confidence in negative results. Coprological examinations are not a reliable indicator of the infection status; only 50–60% of tapeworm-infected horses (positive identification at necropsy examinations) will be positively identified by normal fecal examination techniques.[33,37] Centrifugation techniques using larger quantities of feces increase sensitivity somewhat, but never to a heightened level of confidence. A quantitative technique, such as the McMasters or modified Stolls is definitely contraindicated as the sensitivity would be lower. Both sugar and zinc sulfate flotation media of 1.20 specific gravity can be used; sodium nitrate should be avoided because it will disrupt the egg more than will sugar or zinc solutions. The anoplocephalid eggs recovered on an examination are asymmetrically shaped and can easily be mistaken for debris, particularly when few eggs are present.

Treatment and control

Anthelmintic choices for tapeworm treatments are limited. The benzimidazoles as a class have activity against tapeworms in other domestic animals, but fenbendazole was reported as ineffective using a 5-day regimen at 10 mg/kg.[38] Pyrantel salts have cestocidal activity.[39,40] Pyrantel tartrate as a daily dewormer is effective at 2.6 mg/kg given daily for 30 days, and reported to be more effective than a single dose of pyrantel pamoate at 19.8 mg/kg.[41,42] Praziquantel and epsiprantel are related compounds with excellent cestocidal activity. Praziquantel is highly effective against *A. perfoliata*,[43] and will be marketed worldwide in combination with ivermectin. This single combination will be effective for treatment of the most important parasitic infections of horses, which suggests that moxidectin will soon be formulated with epsiprantel in the near future to remain competitive.

Due to the low reliability of ante-mortem diagnosis, control is better achieved through scheduled, periodic treatments with an effective compound. At the present time, treatments twice yearly with a pyrantel salt should be adequate for tapeworm control, as well as activity against nematodes, such as small strongyles.

Epidemiology

Anoplocephala perfoliata has a worldwide distribution, and should be anticipated in horses regardless of the housing

conditions. Mite activity, essential for transmission, will be temperature-dependent, so tapeworm transmission can have a seasonal component in colder climates.[44] Year-round transmission has been reported in more temperate regions.[45] In colder climates, heated barns may support mite activity during cold periods. Transmission can certainly occur in stables; thus an athletic horse in training can become infected. There is some acquired resistance through exposure to tapeworm infections; however, many or most athletic horses are within the younger population.

As a final note to owners and trainers of athletic horses, the author advises that all feeds be protected from access by other animals, domestic, feral or wild. The author has recovered cat ascarid eggs passed by horses that ingested contaminated feeds, as barn cats will defecate in grain bins and hay barns. Contaminated feeds represent a route of infection for *Toxoplasma gondii* spread by barn cats, or *Sarcocystis* spp., such as *Sarcocystis neurona* passed by opossums in North America. Both grain and hay should be protected.

Ectoparasite control for athletic horses

Athletic horses will be exposed to a wider spectrum of ectoparasites than sedentary horses by virtue of travel to different regions, or contact with other participating horses. The importance of such exposure can span from contact transmission of a nuisance ectoparasite to the potential exposure of a life-threatening arthropod-borne infection at an event, such as an encephalitis virus. Most ectoparasite problems are irritating, not life-threatening, but a night spent under a relentless attack by biting midges or mosquitoes may drain the energy or focus otherwise available for performance.

Control programs and procedures will differ as significantly as the spectrum of disease or pests of concern, ranging from those applied to an individual competitor, to procedures employed by the sponsors of an international event concerned with prevention of arthropod-borne diseases. Facilities personnel can employ management practices directed towards controlling the habitats of important ectoparasites, whereas a trainer traveling with horses has little or no influence over the environment where the event is held, and instead, must rely on treatments applied directly to their competitors.

Equine facilities, whether a permanent training or boarding facility, or the temporary sponsors of an event, should address the ectoparasite habitat at their location rather than rely solely on chemical control. Simple management practices can reduce the ectoparasite potential, such as mowing, improving drainage, and effective composting of manure and bedding as examples. Fans, baited traps and lights can be added to barns. Rodent control can have a profound influence on the local ectoparasite population and arthropod-borne disease risk, as rodents serve both as a source of blood meals and as amplification hosts of several arthropod-borne diseases. Management practices should be implemented and improved annually, as these physical interventions will reduce the need for chemical interventions, and will improve their efficacy when applied. Within a reasonable timeframe before the start of an event, chemical control measures could be implemented as an adjunct to the management practices employed continuously. The degree of this chemical control may increase in proportion to the level of risk, as in the case of an encephalitis outbreak, or hosting an international event. An understanding of the biology and habits of these vectors or pests is essential for implementation of rational control measures, as is an appreciation of the effects that area sprays may have on an ecosystem.

Environmental insecticides and acaricides cannot discriminate between the parasitic or the beneficial arthropods, such as bees or the various insects responsible for natural recycling of manure. Chemical sprays can translate into damaging effects on the fish, reptile, amphibian and bird populations that act as natural forces balancing the arthropod populations. Most ectoparasiticides for environmental use are long-acting synthetics that accumulate progressively up the food chain. Alterations of this balance can be self-defeating for an equine facility. Priority should be given to environmental improvements that decrease the reproductive potential of ectoparasites and foster an increase of the insectivorous populations. Indiscriminate use of area insecticides has led to the development of drug-resistant pests rather than their elimination.

Situations do arise, however, that warrant the rational and controlled use of area chemicals, such as an outbreak of mosquito-borne encephalitis, or hosting an international event where carriers of a foreign, arthropod-borne disease may be a realistic concern. The 1996 Olympic Games held in Atlanta, Georgia, represent one case in point, when extensive measures were implemented over the concern that *Babesia* spp. could become introduced into the local *Dermacentor* population through feeding on carriers in competition.[46] The sponsors of the Olympic games began with environmental measures to reduce the tick habitat before using chemicals prior to the arrival of competitors.

In all situations where environmental sprays or fogs will be employed, the facilities managers must follow the local, state or federal regulations concerning the use of such compounds, and follow the safety precautions for specific formulations. If unusual circumstances dictate extensive, environmental measures, permits may be required and the application process may require months or more before a ruling.

In contrast to the environmental control measures are those that can be applied directly to the horse. There are just a few classes of effective insecticides and acaricides available, most of which are also formulated as environmental sprays. One very important rule of thumb is that the active ingredient may be identical in two formulations, but the vehicle or propellant will differ. Formulations made for area or environmental sprays should never be used directly on animals as toxicity or blistering of the skin may occur based on the propellant or vehicle.

The remainder of this chapter will focus on the ectoparasites and their control rather than on the arthropod-borne diseases because those diseases are not unique to the performance horse. A thorough knowledge of these ectoparasite control measures will be important to trainers and riders while traveling, and to facilities managers, particularly when hosting an equestrian event.

Mosquitoes

Mosquitoes are best known as the vectors of many equine encephalitis viruses. All mosquito genera and species require standing water in varying quantities for their replication, ranging from ponds or puddles to seemingly insignificant quantities in a hoof print or remaining in the axillae of leaves and branches of plants. The principal management practice for their control resides in the identification of possible replication sites at an equine facility because the majority of mosquitoes move only a few hundred meters from their hatching sites to feed on animals. This will become an important radius for chemical treatments immediately prior to the arrival of participants at events. These sites can be areas of tall grass, irrigation ditches, ponds, puddles, small accumulations around the roots of trees or rain gutters with leaf clutter blocking complete drainage. Regular and critical inspection of the premises can reveal many inapparent sites that will be important for both the physical interventions and to identify these sites if environmental sprays are to be used. As insignificant as these sites may seem, these small sites do not support fish or amphibian species that would devour the developing larval stages, and thus may contribute more feeding mosquitoes than the obvious, larger sites. The edges of ponds, lakes or canals where vegetation blends into water are much more important than the open water of these larger bodies. Walls or banks can be constructed at these interfaces such that the transition is sharply divided between vegetation and water.

Several of the most important species of *Aedes* and *Ochlerotatus* (formerly designated as a subspecies of *Aedes*), lay eggs in temporarily dry areas that will accumulate water after a rain or irrigation. The eggs of these genera can withstand varying degrees of desiccation and may remain dormant for months before activation. Improving drainage and filling depressions are obvious interventions. Mowing tall grass and weedy areas will increase sunlight penetration, which will speed drying where replication occurs.

Mosquitoes are weak fliers and the addition of fans to barns can prevent mosquito feeding on stabled horses. Many but not all mosquito species are evening or night feeders, so stabling horses during crepuscular periods can reduce their exposure. Many mosquito species are attracted to sodium vapor lights but not towards yellow light; thus sodium lights can be placed at the periphery and yellow lights used inside and around stables and arenas. Several devices that electrocute flying insects use appropriate light or bait, such as carbon dioxide (CO_2), and are worthwhile additions to mosquito control. Several vertebrates are well known for their consumption of large quantities of flying mosquito adults. Thus the addition or promotion of bat housing or bird-nesting sites is beneficial, as is nurturing the frog populations in ponds or lagoons on or near the premises.

Chemical control of mosquitoes will have three approaches: environmental sprays or fogs over exterior sites; environmental sprays with residual activity on the interior structures of barns or stables; direct application of repellents or insecticides to horses. Fogs are formulated to produce microscopic droplets that remain in airborne suspensions, extending their potential contact time with flying adults. These should never be used indoors when animals are present. Fogs kill flying adults through contact, so logic dictates their dispersal only at mosquito feeding times, only when calm wind conditions permit, and only near important mosquito sites. Fogs are the most toxic formulations for birds and bats, and thus require caution and rational use. Because fogs have limited duration as aerial suspension, potent but short-acting insecticides such as pyrethrins are sensible choices. Although a seemingly semantic difference, sprays are intended to disperse droplets over some solid substrate, whether vegetation or facilities. Insecticidal sprays can be applied to breeding sites when needed, and long-acting compounds with weeks of activity are available, but these will have the greatest impact on the non-parasitic fauna. Formulations containing pyrethroids have the lowest mammalian toxicity but can have adverse effects through accumulation in reptile, fish and bird populations. *Bacillus thuringiensis* is a bacteria that produces an insecticidal compound and is available as a dust that can be applied to areas of mosquito larvae development and this may be more environmentally sound than long-acting synthetic compounds. If permitted in specific localities, organophosphate sprays such as malathion or diazinon could be employed when conditions warrant. Imidacloprid is a potent insecticide approved in many countries for use on crops intended for human consumption or as topical flea control on pets, implying excellent tolerance by vertebrate species. Insect growth regulators, such as methoprene, pyriproxyfen or diflubenzuron, can inhibit development of mosquito larvae, have little or no vertebrate toxicity, but have little residual activity, and thus require repeated application. Any of these environmental treatments should be applied only to those sites where the problem exists rather than as an indiscriminant broadcast of chemicals.

Mosquito females will rest on a physical structure following a blood meal; thus environmental sprays can be applied to the walls and doors of a barn or arena. Compounds with residual activity, such as the synthetic pyrethroids or the organophosphates, are logical choices in this situation as they can provide several weeks of activity. While this strategy does not prevent mosquito feeding, it plays an important role in halting transmission of mosquito-borne diseases by killing replete females that may have ingested an equine pathogen.

Appropriate repellents and insecticides can be applied directly to the skin of horses if so directed. If not formulated specifically for horses, these compounds should be used with caution. The identical active ingredients on the label of two

products can be misleading because differences in the vehicle suspension may be a toxic factor for horse skin. Repellent formulations with botanical derivatives, such as citronella, limonene and linolool, are available but not highly effective repellents. The synthetic repellent butoxypolypropylene glycol is formulated for horses. Several pyrethroids approved for use as wipes on horses, such as cypromethrin, resmethrin and permethrin, are attributed with repellent qualities that may stem from rapid killing of the mosquitoes that alight on the treated skin. The pyrethroids are the backbone of on-horse ectoparasite control as they have potent activity against mosquitoes, biting flies, midges, ticks, mites and lice. Many pyrethrin or pyrethroid formulations contain piperonyl butoxide, which is not itself insecticidal but which inhibits the arthropod enzymes that inactivate pyrethrins. Piperonyl butoxide, therefore, potentiates the action of pyrethrins. Wipes applied to horses for mosquito control should be applied to the entire body due to their more indiscriminate feeding pattern, whereas ticks tend towards feeding in protected areas of the ventrum or head and ears.

Ticks

Ticks are best known as vectors of *Babesia caballi*, *Theileria equi* and *Anaplasma phagocytophilum* as well as several other arthropod-borne viral and bacterial diseases, and tick paralysis. Tick-borne diseases will have a regional distribution and seasonal pattern of occurrence directly related to those patterns of the vector tick, and vary from year to year according to environmental factors and cycles, including weather and influences on the host populations.[47,48] Ticks themselves do not travel far from their hatching sites but can be carried great distances by the roaming of animals or the migration of birds. Survival or establishment at the new site will be dependent on hospitable climatic and environmental characteristics. Equine facilities can make reasonable, physical or environmental changes that reduce this hospitality but management of climatic changes are beyond the scope of this chapter.

Ticks favor habitat of grasses and shrubs with sufficient moisture that their egg masses can develop before desiccation. Several genera populate the interface between forest and meadow. As a generality, ticks favor turf and cross-country terrain over dirt and arenas; thus the risk of tick-borne diseases is reduced but not eliminated at urban facilities. Mowing areas of scrub, brush and long grass will aid the overall control program by reducing the tick reproductive potential, reducing the vegetation they climb while questing for hosts, and by removing the excessive vegetation that would diminish the efficacy of a chemical spray if or when necessary in the control program. These areas should be cleaned of fallen branches or logs that could serve as reproductive sites or impede effective mowing. As questing ticks will climb to the top of vegetation and wait for a host, the height and density of vegetation will influence the number of ticks and their success in contacting hosts. The height of this vegetation will also influence the height on the legs of horses where acaricidal wipes must be applied. These areas can be monitored for tick populations by dragging a cotton or muslin sheet over the ground and collecting ticks for identification and enumeration. Tick traps can be made that use CO_2 release as a bait. Questing ticks are lured towards the CO_2 and climb into a collecting sack, sheet of muslin or an adhesive pad. Monitoring will help demonstrate the effectiveness of the control program and highlight those areas that may need additional modification or receive an area spray of acaricide. Such monitoring may be required of the sponsors for an international event, but should be practiced occasionally at all permanent horse facilities where ticks exist.

Larval and nymphal tick stages often rely on nestling and neonatal rodents or rabbits for their first blood meals. These mammalian populations also serve as the reservoir or amplification hosts for many bacterial or viral diseases for which ticks serve as vectors. Therefore, rodent control is a particularly important facet of tick control. Along with rodent control, equine facilities should make every effort to exclude wildlife from their premises due to the risk of importing ticks attached to those hosts, as well as the other problems that wildlife can create.

Chemical control measures include applications to the horse or the environment, bearing in mind that these different formulations should not be interchanged even though the active ingredient may be identical. Pyrethrins, pyrethroids, organophosphates and carbamates are commonly used as active ingredients. Pyrethroid and organophosphate compounds have been developed that will provide 3–5 weeks of residual activity following application. Pyrethrin formulations owe much of their safety on the horse or in the environment to the fact that pyrethrin is metabolized or oxidized quickly. Organophosphates and carbamates share a mechanism of action and can have additive effects that can lead to toxicity if used concurrently with other acetylcholinesterase inhibitors, particularly when long-acting compounds are used.

Sprays can be applied to areas of scrub, brush or grass that have been mowed. Wipes or sprays can be applied to horses, particularly covering the legs, ventrum and neck, head and ears, as ticks tend to congregate in these areas rather than spread across broad, exposed areas of the flanks and back. Several pyrethroid compounds in these formulations can provide 3–4 weeks of residual activity on the horse, and are effective against ticks and insect pests, such as mosquitoes, biting flies, gnats and midges.

Face flies, house flies and stable flies

These flies, *Musca autumnalis*, *M. domestica* and *Stomoxys calcitrans* respectively, are widespread pests and vectors of disease in and around barns and stables, and are daytime feeders. Stable flies actively bite, painfully, usually around the legs, and have been implicated as mechanical or biological vectors of several arthropod-borne diseases of equids, surra and equine infectious anemia being examples. Face flies and house flies are attracted to secretions and transmit diseases by contact, for the most part. They can serve as the intermediate

host of several nematodes of horses. Collectively, these three flies utilize manure and decaying materials of different types for egg laying and larval development. Thus the most important measure in their control is hygiene within and around the stable area, and composting effectively the bedding, manure and decaying vegetation that supports their larval development. These flies may travel from neighboring farms where conditions are more favorable, but this potential does not alter the need to maintain a high level of sanitation at a stable.

Face flies both feed and rest on the faces of cattle and horses; thus topical repellents and insecticides can be applied to the face for the most effective chemical control, which will also work for house flies. Both are attracted to wounds as well as nasal or lacrimal secretions, implying that wounds should be dressed and the bandage treated with a topical insecticide, or small wounds treated directly with an appropriate repellent or insecticide. Stable flies bite the lower legs, so repellents and insecticides can be applied directly to these susceptible areas. House flies and stable flies rest on a solid surface when not feeding; thus barn walls, doors, windows and screens can be sprayed with long-acting insecticides that kill these flies on contact. Likewise, they can be lured to baited traps impregnated with insecticide, or composed of an adhesive. Manure or compost piles could be treated with an insecticide to kill developing maggots, but such treatment will also kill the beneficial arthropod fauna responsible for manure degradation. Manure piles can be covered with plastic to increase the pile temperature and speed composting.

Tabanid flies

The tabanids include the horse flies (*Tabanus*) and deer flies (*Chrysops*). These are significantly different from the house, face and stable flies in both their feeding habits and their sites of replication. The tabanids are best known as vectors of equine infectious anemia and implicated in the transmission of other blood-borne infections. The tabanids have slashing mouthparts to draw blood and feed, and it is the interrupted feeding that is implicated in the mechanical transmission of several diseases as they fly to another animal to continue a blood meal.

The tabanids are more difficult to control than the other flies because their larval stages occur in the leaf litter of forested areas that are not reasonably accessible for environmental or chemical interventions. Tabanids fly some distance to feed, in contrast to mosquitoes. As such, their sites of replication may be miles from an equine facility. Tabanids are daytime feeders and prefer hosts outside of barns, so stabling horses during the peak tabanid season will help prevent bites. Tabanids target moving objects in pastures or paddocks, a characteristic exploited by traps made of moving parts, usually wind-driven but sometimes mechanized. These traps have an adhesive surface, which could be augmented by application of a contact insecticide. Repellents and insecticidal wipes, such as those containing pyrethroids, will also have some effect, though it may be negligible, against tabanids.

Black flies and biting midges

Black flies or buffalo flies are fierce biters within the genus *Simulium*, and the biting midges or 'no-see-ums' are members of the genus *Culicoides*. Both have been implicated as vectors of various filarial diseases of humans and animals, and *Culicoides* is also well known as a vector of several important viral diseases, the most important for international events being African horse sickness.

Both the black flies and midges are ferocious blood-feeders that inflict very painful bites relative to their small size, and many horses develop hypersensitivity reactions to the saliva. *Simulium* is a daytime feeder, principally early mornings, whereas *Culicoides* is an evening or early nightfall feeder. Both feed in swarms that are extremely irritating to afflicted horses. Neither pest is a strong flier, and both prefer open spaces for feeding. Thus stabling horses with fans creating a light breeze is an effective measure, perhaps more than repellents.

Both *Simulium* and *Culicoides* require water in some form for their larval stages, but differ tremendously in the type of water source. *Simulium* requires moving water and can utilize both raging currents or slow. *Culicoides*, in contrast, requires stationary water, such as marshes, ditches and irrigated pastures, and some species can utilize moist soil. This makes control measures directed at the sites of larval development more difficult if not impossible. Both have a seasonal occurrence that could allow sponsors of an event to avoid those peak times when scheduling the event. Chemical control on horses can be attempted with repellents and insecticides, but those horses with hypersensitivity reactions should be stabled at the respective feeding times and provided with a fan to inhibit swarms from reaching the horse. During an outbreak, or to prevent an outbreak of a viral disease as devastating as African horse sickness, environmental sprays or fogs could be delivered over larger areas that serve as the breeding grounds of *Culicoides*.

References

1. Klei TR. Recent observations on the epidemiology, pathogenesis, and immunology of equine helminth infections. In: Ploughwright W, Rossdale PO, Wade JF, eds. Equine infectious diseases, IV. Newmarket, UK: R and W Publications; 1992:129–136.
2. Klei TR. Equine immunity to parasites. Vet Clin North Am Equine Pract 2000; 16(1):69–79.
3. Klei TR, Chapman MR. Immunity in equine cyathostome infections. Vet Parasitol 1999; 85:123–133.
4. Georgi JR. The Kikuchi-Enigk model of *Strongylus vulgaris* migration in the horse. Cornell Vet 1973; 63:220–263.
5. Uhlinger C. Effects of three anthelmintic schedules on the incidence of colic in horses. Equine Vet J 1990; 4:251–255.
6. Uhlinger CA. Equine small strongyles: Epidemiology, pathology, and control. Comp Cont Educ Pract Vet 1991; 13(5):863–869.
7. French DD, Klei TR. Benzimidazole resistant strongyle infections: A review of significance, occurrence, diagnosis and control. Proc Am Assoc Equine Pract 1983; 29:313–317.

8. Boersema JH, Borgsteede FHM, Eysker M, et al. The prevalence of anthelmintic resistance of horse strongyles in the Netherlands. Vet Q 1991; 13(4):209–217.
9. Proudman CJ, French NP, Trees AJ. Tapeworm infection is a significant risk factor for spasmodic colic and ileal impaction colic in the horse. Equine Vet J 1998; 30(3):194–199.
10. Proudman CJ, Trees AJ. Tapeworms as a cause of intestinal disease in horses. Parasitol Today 1999; 15(4):156–159.
11. Darien BJ. Eosinophilic pneumonitis in foals and horses – Case notes and commentary. Comp Cont Educ Pract Vet 1994; 16(9):1210–1212.
12. Burks BS. Parasitic pneumonitis in horses. Comp Cont Educ Pract Vet 1998; 20(3):378–384.
13. Southwood LL, Baxter GM, Bennett DG, et al. Ascarid impaction in young horses. Comp Cont Educ Pract Vet 1998; 20(1):100–108.
14. Boersema JH, Eysker M, Nas JWM. Apparent resistance of *Parascaris equorum* to macrocylic lactones. Vet Rec 2002; 150(9):279–281.
15. Ihler CF. The distribution of *Parascaris equorum* eggs in the soil – Profile of bare paddocks in some Norwegian Studs. Vet Res Commun 1995; 19(6):495–501.
16. Lyons ET, Swerczek TW, Tolliver SC, et al. Natural superinfection of *Parascaris equorum* in a stall-confined orphan horse foal. Vet Parasitol 1996; 66:119–123.
17. DeLay J, Peregrine AS, Parsons DA. Verminous arteritis in a 3-month-old Thoroughbred foal. Can Vet J Rev Vet Can 2001; 42(4):289–291.
18. Monahan CM, Chapman MR, Taylor HW, et al. Foals raised on pasture with or without daily pyrantel tartrate feed additive: comparison of parasite burdens and host responses following experimental challenge with large and small strongyle larvae. Vet Parasitol 1997; 73:277–289.
19. Ogbourne CP. Pathogenesis of cyathostome (Trichonema) infections of the horse. A review, Farnham Royal, Slough SL2 3BN, England:Commonwealth Agricultural Bureaux, 1978:1–25.
20. Reinemeyer CR. Small strongyles: recent advances. Vet Clin North Am Equine Pract 1986; 2:281–312.
21. Eysker M, Boersema JH, Kooyman FNJ. Emergence from inhibited development of cyathostome larvae in ponies following failure to remove them by repeated treatments with benzimidazole compounds. Vet Parasitol 1989; 34:87–93.
22. Eysker M, Boersema JH, Kooyman FNJ. The effect of ivermectin treatment against inhibited early third stage, late third stage and fourth stage larvae and adult stages of the cyathostomes in Shetland ponies and spontaneous expulsion of these helminths. Vet Parasitol 1992; 42:295–302.
23. Love S, Murphy D, Mellor D. Pathogenicity of cyathostome infection. Vet Parasitol 1999; 85:113–121.
24. Reid SWJ, Mair TS, Hillyer MH, et al. Epidemiological risk factors associated with a diagnosis of clinical cyathostomiasis in the horse. Equine Vet J 1995; 27:127–130.
25. DiPietro JA, Klei TR, Reinemeyer CR. Efficacy of fenbendazole against encysted small strongyle larvae. Proc Am Assoc Equine Pract 1997; 43:343–344.
26. Perez R, Cabezas I, Carcia M, et al. Comparison of the pharmacokinetics of moxidectin (Equest) and ivermectin (Equalan) in horses. J Vet Pharmacol Ther 1999; 22:174–180.
27. Vercruysse J, Eysker M, Demeulenaere D, et al. Persistence of the efficacy of a moxidectin gel on the establishment of cyathostominae in horses. Vet Rec 1998; 143:307–309.
28. Sangster NC. Pharmacology of anthelmintic resistance in cyathostomes: will it occur with the avermectin/milbemycins? Vet Parasitol 1999; 85:189–204.
29. Sangster NC, Gill J. Pharmacology of anthelmintic resistance. Parasitol Today 1999; 15:141–146.
30. Uhlinger C. Preliminary studies into factors affecting the variability of egg reappearance period and anthelmintic treatment intervals in the control of equine cyathostomes. In: Ploughwright W, Rossdale PO, Wade JF, eds. Equine infectious diseases, IV. Newmarket, UK: R and W Publications; 1992:157–161.
31. Paul JW. Equine larval cyathostomosis. Comp Cont Educ Pract Vet 1998; 20:509–513.
32. Gibson TE. The effect of repeated anthelmintic treatment with phenothiazine on the faecal egg counts of housed horses with some observation on the life cycle of *Trichonema* spp. in the horse. J Helminthol 1953; 27:29–40.
33. Williamson RMC, Beveridge I, Gasser RB. Coprological methods for the diagnosis of *Anoplocephala perfoliata* infection of the horse. Aus Vet J 1998; 76(9):618–621.
34. Rodriguez-Bertos A, Corchero J, Castano M, et al. Pathological alterations caused by *Anoplocephala perfoliata* infection in the ileocaecal junction of equids. J Vet Med, Series A – Physiol Pathol Clin Med 1999; 46(5):261–269.
35. Little SE. Adult tapeworms in horses: Clinical significance. Comp Cont Educ Pract Vet 1999; 21(4):356–360.
36. Jordan ME, Courtney CH. Equine tapeworm. Equine Pract 1999; 21(4):10–13.
37. Meana A, Luzon M, Corchero J, et al. Reliability of coprological diagnosis of *Anoplocephala perfoliata* infection. Vet Parasitol 1998; 74(1):79–83.
38. Lyons ET, Drudge JH, Tolliver SC. Fenbendazole in equids – further controlled tests with emphasis on activity of multiple doses agains naturally occurring infections of migratory large strongyles. Am J Vet Res 1986; 47:317–321.
39. French DD, Chapman MR. Tapeworms of the equine gastrointestinal tract. Comp Cont Educ Pract Vet 1992; 44:655–662.
40. Lyons ET, Tolliver SC, Drudge JH. Further evaluation of pyrantel pamoate at the therapeutic dose rate (6.6 mg base/kg) against *Anoplocephala perfoliata* in horses. J Helminthol 1997; 64(2):285–287.
41. Kivipelto J, Nicklin C, Asquith RL. A comparison of two programs (pyrantel tartrate administered daily and 3X pyrantel pamoate administered at 8-week intervals) for the reduction of tapeworm EPG in the horse. J Equine Vet Sci 1998; 18(2):125–128.
42. Lyons ET, Tolliver SC, McDowell KJ, et al. Field test of activity of the low dose rate (2.64 mg/kg) of pyrantel tartrate on *Anoplocephala perfoliata* in Thoroughbreds on a farm in central Kentucky. J Helminthol 1997; 64(2):283–285.
43. Lyons ET, Tolliver SC, Ennis LE. Efficacy of praziquantel (0.25 mg kg^{-1}) on the cecal tapeworm (*Anoplocephala perfoliata*) in horses. Vet Parasitol 1998; 78(4):287–289.
44. Lyons ET, Tolliver SC, Collins SS, et al. Transmission of endoparasites in horse foals born on the same pasture on a farm in central Kentucky (1996–1999). Vet Parasitol 2001; 97(2):113–121.
45. Chapman MR, French DD, Klei TR. Seasonal transmission of gastrointestinal parasites of equids in southern Louisiana. J Parasitol 2001; 87(6):1371–1378.
46. Brooks LM. The equine piroplasmosis control programme at the 1996 Summer Olympic Games. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases, VIII. Newmarket, UK: R and W Publications; 1999:371–375.
47. Jones CG, Ostfeld RS, Richard MP, et al. Chain reactions linking acorns to gypsy moth outbreaks and Lyme disease risk. Science 1998; 279:1023–1026.
48. Kaiser J. Ecology – of mice and moths – and Lyme disease. Science 1998; 279:984–985.

CHAPTER 59

Anesthesia of the equine athlete

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The initial question when discussing anesthesia of the equine athlete is 'Are there any horses that aren't athletes?' Compared with many other species, such as cows and cats, the answer is probably no. Having answered this initial question, there are suggestions in the literature that 'fit' horses, particularly 'fit' Thoroughbred horses, are more difficult to anesthetize than other horses.[1,2] Anecdotally, this increased level of difficulty seems to center on lower respiratory rates in 'fit' horses and issues of temperament. A search of the literature reveals few differences in respiratory and cardiovascular function in horses at rest, whether untrained, trained, or detrained. Training increases peak oxygen uptake without changing peak minute ventilation, thus the ratio of minute volume to oxygen uptake (the ventilatory equivalent for oxygen) decreases.[3] A reduction in the ventilatory equivalent indicates that a fit horse exchanges a smaller ventilatory volume to maintain a given oxygen uptake than the same horse when detrained. Further, the respiratory pattern in trained and untrained horses is similar, implying increased efficiency of oxygen extraction at the pulmonary level. This increased efficiency of oxygen extraction may partially account for the decreased respiratory rates observed in anesthetized 'fit' horses. Alveolar tensions of anesthetic gases rise at a slower rate in horses with slow respiratory rates, potentially delaying the attainment of brain anesthetic gas tensions sufficient for anesthesia. The potential decreases in respiratory function could be further exacerbated by the effects of anesthetic drugs and body position on the function of respiratory muscles and interruption of the normal, unique breathing strategy seen in this species.[4] Training does not alter resting heart rate, stroke volume, or cardiac output in the resting horses, but total red cell volume increases and plasma volume increases as much as 29%.[5–7] The increase in plasma volume may increase preload and enhance cardiac output in exercising 'fit' horses.[8] Other changes potentially pertinent to anesthesia include an apparent increase in muscle glycogen, muscle capillarization, and muscle mitochondrial density in fit horses.[9]

History

These questions should be asked of the responsible party prior to anesthesia:

1. Has the horse been anesthetized previously? If so, what were the circumstances and were there any problems associated with the anesthetic period? Many athletic horses have been previously anesthetized, most without incident. Potential problems that could be uncovered by this question include untoward reactions to drug administration, excitement during induction or recovery, prolonged recovery, or rhabdomyolysis.
2. Is the horse tolerant of exercise? Horses that are intolerant of exercise may not tolerate anesthesia. Potential causes of exercise intolerance include respiratory insufficiency, upper airway obstruction, and cardiac insufficiency, including atrial fibrillation or other arrhythmia, or rhabdomyolysis.
3. Has the horse recently experienced any respiratory disease? Anesthesia compromises resistance to respiratory disease in a number of ways including depression of mucociliary and immune function, loss of the cough reflex, drying of the airway, and inhibition of nasal and laryngeal function. In normal animals these changes are short-lived, but in horses incubating respiratory disease, anesthesia may predispose to worsening signs and exacerbation of disease.
4. Does the horse make a respiratory noise at rest or during exercise? Anesthetic agents, notably the α_2-adrenoreceptor agonists, cause relaxation of the upper airway.[10,11] This relaxation may augment a pre-existing condition resulting in partial or full respiratory obstruction. Such obstructions can be overcome with endotracheal intubation but may be problematic during recovery.
5. Has the horse ever tied up (rhabdomyolysis)? There is considerable evidence of genetic, gender, and breed predilection for rhabdomyolysis.[12] Anesthesia can be a triggering event.

6. How does the horse react to new experiences? There is considerable variation amongst equines in their ability to adapt to new situations and experiences. Some horses are apparently calm despite being placed in stimulus-intensive environments while others become agitated without apparent provocation. The demeanor of the patient potentially affects the required doses of sedatives and may change preparations for anesthesia and recovery.
7. Is the horse receiving any medication? When was the last time the horse was medicated? Some individuals utilize long-acting tranquilizers and other drugs as part of their training regimens. The administration of drugs such as acepromazine and reserpine can affect the required doses of anesthetic agents and the resultant pharmacologic response.

Physical examination

The physical examination is the centerpiece of preanesthetic data collection. The examination should focus on the cardiovascular, respiratory, neurological and musculoskeletal systems.

Examination of the cardiovascular system

The cardiovascular system is easily evaluated by palpating the pulse of a peripheral artery, checking the color of mucous membranes, measuring the capillary refill time, assessing skin turgor, and ausculting the heart. Normal pulse rates in quiet adult horses range from 25 to 45 beats per minute. Interruptions in the regular rhythm (pauses) are not uncommon in fit horses and are usually the result of sinus arrhythmias or second-degree atrioventricular blockade. A brief period of exercise should stimulate an increase in heart rate and resolve the arrhythmia. The most common pathologic arrhythmia in horses is atrial fibrillation.[13] Presumptive diagnosis of atrial fibrillation can be made on physical examination by palpating pulses of unequal strength occurring at irregular intervals and by ausculting variable intensity heart sounds at varying intervals. An electrocardiogram should be obtained if pauses in the pulse rhythm do not respond to exercise or if there are pulses of variable intensity occurring at variable intervals. Heart murmurs can be ausculted in the majority of race horses.[14] Most are systolic murmurs, heard best at the heart base. Murmurs of grade II (out of V) or less are interpreted as innocent flow murmurs if there is no other evidence of heart disease. Murmurs of potential significance include those that result from mitral valve insufficiency, aortic insufficiency or congenital ventricular septal defects; but they comprise less than 0.1% of the population. Additional information can be obtained via electrocardiography and echocardiography.

Transient periods of sinus tachycardia (heart rates greater than 50 beats/min) are not of concern but sustained tachycardia should be interpreted as an indicator of cardiovascular or metabolic disease. Atrial and, less frequently, ventricular premature contractions are observed in horses prior to surgery. Abnormal atrial and ventricular rhythm disturbances are a warning that there may be systemic illness, myocarditis, or associated cardiovascular compromise. Infrequent atrial or ventricular extra systoles (< 5/min when the heart rate is normal) without clinical evidence of cardiovascular compromise are tolerated in horses under general anesthesia. Horses with frequent ventricular premature contractions, paroxysmal ventricular tachycardia, or persistent ventricular tachycardia should not be anesthetized for elective procedures.

Examination of the respiratory system

Examination of the respiratory system is best accomplished in a quiet room or stall and is facilitated by stimulating the horse to breathe deeply. The lung fields over both sides of the thorax should be ausculted. Auscultation of the trachea may be useful in detecting the presence of mucopurulent material. Light squeezing of the trachea in a normal horse does not induce a cough but may produce a cough in a horse with upper respiratory tract infection.

Horses with suspect respiratory disease should receive a further diagnostic workup, potentially including a complete blood count, plasma fibrinogen, tracheal wash and culture, and thoracic ultrasound and radiography. Horses with a history of severe respiratory tract infection may retain large quantities of mucopurulent material in the trachea and have abnormal respiratory sounds in the lung fields upon careful auscultation. Horses with respiratory tract infections should not be anesthetized for elective procedures because the added stress of surgery and general anesthesia predisposes to pneumonia and pleuritis.

Horses with respiratory stridor due to upper respiratory tract obstruction require special evaluation because sedation produces relaxation of the muscles of the upper airway which may worsen the stridor. Many normal horses make upper airway noises during recovery from general anesthesia because of congestion and edema of the nares and nasal turbinates. Horses with preoperative stridor are more likely to do so. Nasal congestion is easily relieved by passing a 12 to 18 mm endotracheal tube into the nares past the site of the obstruction. Additional causes of stridor after anesthesia include dorsal displacement of the soft palate and partial or complete laryngeal paralysis. The soft palate normally displaces dorsally with orotracheal placement of an endotracheal tube. When the endotracheal tube is removed the palate remains displaced until the horse swallows and the palate returns to its normal position below the epiglottis. An endotracheal tube can be used to stimulate swallowing if a horse makes a noise suggestive of dorsal displacement after removal of the endotracheal tube. The degree of obstruction of airflow should be evaluated by assessing the amount of airflow through the nostrils while noting the amount of effort (abdominal movement) required to produce airflow. A temporary tracheostomy may be required prior to

induction or during recovery from anesthesia in horses with severe obstruction.

Examination of the nervous and musculoskeletal systems

The nervous and musculoskeletal systems should be examined to determine if the horse can see, ambulates normally, and bears weight on all four limbs. Horses that are blind in one eye may require special handling during induction and recovery. Slight gait deficits are usually inconsequential, but significant weakness, ataxia or lameness may pose problems during induction to and recovery from anesthesia. Simply walking the horse a short distance and circling it in a small circle provides a sufficient assessment of the horse's stability. Horses that are ataxic or not bearing weight on all four limbs may prove difficult to move while sedated. Thus they should be moved to the area of anesthetic induction prior to administering sedatives.

Preanesthetic hematologic evaluation

The baseline hematologic evaluation of horses prior to anesthesia is dependent on the results of the physical examination but should include determination of the packed cell volume (PCV), total plasma solids, white blood cell count, and plasma fibrinogen. The PCV should be 55% or less to prevent blood sludging and achieve adequate tissue perfusion under anesthesia. Packed cell volumes less than 20% are associated with compromised oxygen delivery. Plasma protein levels below 3.5 g/dL are associated with the formation of peripheral and pulmonary edema because of inadequate plasma oncotic pressure. The hemogram of most horses in our referral hospital suggests mild leukocytosis with neutrophilia and lymphopenia that can be attributed to the effects of excitement and stress associated with transportation, hospitalization or pain. Total white blood cell (WBC) counts greater than 13 000/μL or less than 5500/μL are indications for further evaluation. Elective surgical procedures should be postponed in horses with abnormal WBC counts until the WBC count returns to normal. Plasma fibrinogen levels are used as an index of inflammation but are not specific to any disease. Plasma fibrinogen levels in excess of 300–400 mg/dL are considered abnormal and a reason to delay anesthesia. Preoperative serum chemistry and acid–base evaluations are not necessary unless specifically indicated. Muscle enzyme levels should be measured in horses with a history of rhabdomyolysis.

Preanesthetic medications

Preanesthetic medications in the horse include anticholinergics, tranquilizers/sedatives, and analgesics (Table 59.1).

The administration of the anticholinergic agents atropine and glycopyrrolate is not recommended for routine use prior to anesthesia in horses. Anticholinergics decrease salivation and increase heart rate, but neither excessive salivation nor bradycardia is a frequent problem in the horse. The potential disadvantages (postoperative ileus, tachycardia, and increased myocardial oxygen consumption) are significant; thus anticholinergic administration should be limited to those cases where it is specifically indicated. Common cardiac arrhythmias that respond to anticholinergic agents include atrioventricular conduction disturbances, interference dissociation, and sinus bradycardia (heart rate less than 25 beats/min) with hypotension.

Sedatives and tranquilizers are used to produce a calm, tractable patient by decreasing excitement and unwanted

Table 59.1 Drugs used for standing chemical restraint and as preanesthetics

Drug	Dose and route	Onset of effect	Comments
Acepromazine	0.02–0.06 mg/kg, i.m., i.v.	30 to 40 min i.v., i.m.	Caution in stressed, hypotensive horses
Xylazine	0.5–1.0 mg/kg, i.v. 1.0–2.2 mg/kg, i.m.	3 to 5 min, i.v. 10 to 20 min, i.m.	Ataxia produced with head down posture Begin with low dose and repeat as needed
Detomidine	0.01–0.02 mg/kg, i.v. 0.02–0.04 mg/kg, i.m.	3 to 5 min, i.v. 10 to 20 min, i.m.	Ataxia produced with head down posture Begin with low dose, repeat as needed
Butorphanol	0.01–0.03 mg/kg, i.v.	3 to 5 min	Use in combination with a sedative or tranquilizer
Morphine	0.3–0.5 mg/kg, i.v.	3 to 5 min	Sedate with xylazine or detomidine before administering morphine Potential for excitement

behavior (movement) during induction and recovery. Sedatives and tranquilizers potentiate the action of anesthetic agents, so that the dose of the more potent agent can then be lowered, decreasing the potential for deleterious side effects including hypotension and hypoventilation. Horses that are weight bearing on all four limbs may benefit from intramuscular administration of sedatives because intramuscular administration produces a more prolonged effect than intravenous administration and potentially reduces the magnitude of the deleterious changes in cardiorespiratory function. Some drugs, particularly the phenothiazine tranquilizers (acepromazine), require up to 45 minutes to reach peak effect. Intravenous administration produces a quicker onset of action and an increased intensity of effect, but a shorter duration of effect, than does intramuscular administration. Ataxic or severely lame patients that are non-weight bearing on one limb should be moved to the induction area before administering the agent of choice intravenously.

Phenothiazine tranquilizers are used to produce calming by decreasing locomotor activity, reducing apprehension and increasing tractability. Phenothiazines should be avoided in horses that are severely stressed, have had excessive hemorrhage, or are hypovolemic because the drugs may cause excessive hypotension. Clinical doses usually produce minimal ataxia and weakness. The primary cardiovascular effect produced by phenothiazine tranquilizers is vasodilatation with resultant hypotension. The incidence of clinically significant hypotension following clinical doses of phenothiazines to normal horses is low, and horses that become hypotensive after phenothiazine administration usually respond to intravenous crystalloid administration. The risk of persistent paralysis of the retractor penis muscle should be noted before tranquilization of male horses, and the dose should be carefully limited to the minimum necessary to produce the desired effect.

α_2-Adrenoreceptor agonists produce sedation, muscle relaxation and analgesia when administered intravenously or intramuscularly to horses.[15–17] Horses that have received α_2-agonists assume a 'head-down' or 'sawhorse' stance and may frequently shift their weight from side to side (Fig. 59.1). Arterial blood pressure is initially increased due to drug-induced increases in peripheral vascular resistance. Hypertension may be sustained (20 to 60 minutes), particularly when detomidine is used. Decreases in heart rate, sinus arrhythmia, and first- and second-degree atrioventricular blockade are common. These decreases in heart rate result in significant decreases in cardiac output, often to levels 50% of predrug values. Respiratory rate is usually decreased, but tidal volume increases. Relaxation of the muscles of the upper airway can predispose the horse to stridor. The administration of an α_2-agonist decreases salivation, gastric secretions, and gastrointestinal motility and increases urine volume. Other incidental effects of α_2-agonist administration include increases in intrauterine pressure, hyperglycemia and hypoinsulinemia.

Two α_2-adrenoreceptor agonists are approved for use in horses in the USA. Xylazine, a relatively short-acting α_2-agonist, has a rapid onset (1–3 minutes) and short duration of action (30–60 minutes) after i.v. administration. Xylazine is relatively non-specific, activating both α_2 and α_1 receptors. Detomidine, a more specific α_2-agonist, is approximately 100 times more potent than xylazine and has a duration of action at least twice as long.

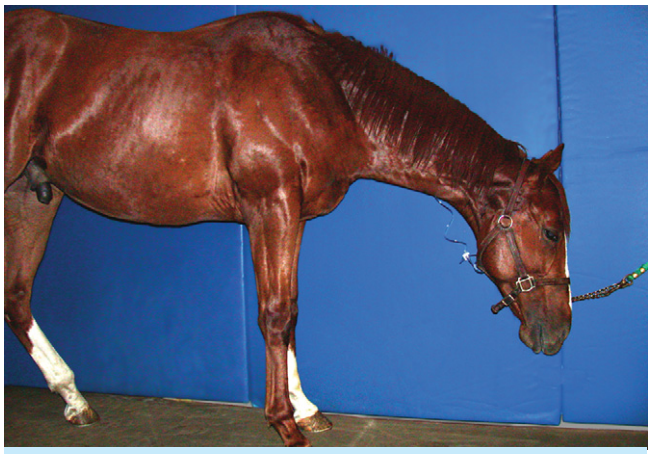

Fig. 59.1
The posture of a horse after the administration of 1.0 mg/kg of xylazine intravenously. Note the ventral position of the head and neck, the relaxed facial muscles, and the unequal distribution of weight on the rear legs.

Sedative-opioid combinations are useful for standing procedures in the horse, producing sedation, analgesia, euphoria and a stuporous 'sawhorse' stance. Butorphanol and morphine are two drugs with opioid activity that have been used in combination with α_2-agonists to produce standing chemical restraint.[18,19] Opioids other than butorphanol are not routinely administered prior to anesthesia but can be used to supplement analgesia intraoperatively.

Many surgical procedures benefit from the administration of antibiotics preoperatively. Antibiotics, particularly sodium or potassium penicillin, should be administered before anesthesia is induced because of their potential to cause hypotension during anesthesia.[20] Aminoglycoside antibiotics, including gentamicin, can cause neuromuscular weakness in some species, but this side effect is uncommon in horses. If antibiotics must be administered intraoperatively, cephalosporins, such as cefazolin, have been shown to produce minimal cardiovascular depression.[17]

Timing of anesthesia and animal preparation

Horses that are transported to the site of anesthesia should be given time to acclimate to the environment. Horses that are injured should be administered first aid, including splinting of the injury, to stabilize their condition. Superior anesthetic and surgical planning is possible if induction is not rushed. The author withholds food for 4 to 6 hours before anesthesia if possible in an attempt to reduce the amount of feed

material in the upper gastrointestinal tract. The mouth should be rinsed prior to induction because foreign material left in the mouth could be pushed into the trachea during orotracheal intubation, leading to upper airway obstruction during or following anesthesia. A large-bore intravenous catheter should be placed in either jugular vein prior to induction of anesthesia. Pre-existing fluid deficits should be corrected prior to anesthesia. During anesthesia, 10 mL/kg/hour of balanced electrolyte solutions should be administered to promote perfusion, replace the lack of fluid intake, and replace insensible losses.

Induction of anesthesia

The smooth, safe and uneventful induction of anesthesia is dependent upon trained personnel, proper premedication of the animal, proper and timely administration of induction agents, appropriate equipment and facilities, and an atmosphere free of unnecessary stimuli that may excite the patient. Indoors, horses should be restrained against a solid wall with their hindquarters in a corner, if possible (Fig. 59.2). One assistant should be positioned at the horse's shoulder and another at the horse's hip. The anesthetist should administer the induction agent and hold the horse's head in a neutral posture until recumbency occurs. Some facilities utilize a 1.5 by 2.0 meter door securely mounted on a wall to facilitate restraint for induction (Fig. 59.3). Horses that must be anesthetized in the open benefit from having a head and tail rope applied before induction. As the horse begins to fall, it can be pulled to the appropriate side. Alternatively, the horse can be made to walk in small circles after the induction drugs are given. The horse will tend to fall toward the outside of the circle as the drugs take effect. The person holding the head should protect the head from sharp blows during the induction period and maintain control at all times.

Fig. 59.2
Correct placement of a horse for induction of anesthesia. The horse is positioned against a wall with its hindquarters in a corner. One attendant pushes on the point of the hip and another on the point of the shoulder. The attendant holding the head lifts the head as the anesthetic drugs take effect.

Fig. 59.3
A padded door, firmly attached to a wall, can be used to control a horse's movement as anesthetic induction occurs.

Many drugs and drug combinations have been used to induce general anesthesia in horses (Table 59.2).[21] Most intravenous anesthetic techniques involve the combined use of dissociative anesthetics (ketamine, tiletamine-zolazepam) or thiobarbiturates (thiopental) and muscle relaxants (guaifenesin, diazepam). Horses that are non-weight bearing on one limb benefit from rapid induction techniques in order to minimize the period of ataxia that occurs as the drugs take effect. The administration of any drug or drug combination regimen designed to produce recumbency should always be preceded by the administration of sufficient doses of sedatives and/or tranquilizers to produce a calm, manageable patient.

Intravenous xylazine followed by intravenous ketamine produces 10 to 15 minutes of general anesthesia.[22] Xylazine-ketamine anesthesia produces recumbency with maintenance of reasonable cardiovascular function and acceptable respiratory depression. Recovery from anesthesia is relatively rapid and uneventful, with the horse rising to its feet 25 to 30 minutes after induction. Characteristically, an apneustic or breath-holding respiratory pattern occurs. The xylazine-ketamine technique has been modified in order to improve the quality of anesthesia. The addition of diazepam and/or butorphanol to xylazine-ketamine improves muscle relaxation and analgesia with minimal cardiorespiratory depression and increases the duration of anesthesia to 20–25 minutes.[23,24] Alternatively, the proprietary combination of tiletamine and zolazepam can be administered after xylazine to produce intravenous anesthesia or to induce anesthesia prior to inhalant anesthesia.[25] Tiletamine-zolazepam is usually administered after sedation with an α_2-agonist and produces a longer duration of anesthesia than diazepam-ketamine. Thirty minutes of anesthesia is produced with the horse returning to standing posture within 60 to 75 minutes. The recovery from anesthesia after tiletamine-zolazepam anesthesia is not as controlled as recoveries

Table 59.2 Drugs used for induction and maintenance of anesthesia in sedate horses

Drug	Dose	Comments
Ketamine	1.5–2.0 mg/kg, i.v.	Horses must be maximally relaxed prior to administration. Relaxation can be produced with xylazine, diazepam, or guaifenesin
Thiopental	4–6 mg/kg, i.v. with guaifenesin, 7–12 mg/kg without	Potential for apnea with administration of large boluses. Use with guaifenesin to allow a reduction in dose
Guaifenesin	50 mg/kg, i.v., to effect	Primarily a muscle relaxant. Do not use alone. Use in sedate horses in combination with ketamine or thiopental
Diazepam	0.06–0.1 mg/kg, i.v.	Primarily a muscle relaxant. Used primarily with ketamine
Tiletamine-zolazepam	0.7–1.0 mg/kg, i.v.	Horse should be fully sedate before administration. Produces 30 minutes of anesthesia with good muscle relaxation. Hypoventilation may occur
'Triple-drip' (mixture of guaifenesin 5%, ketamine 0.1%, and xylazine 0.05%)	2 mL/kg/h	Not used for induction in adult horses. Used to extend xylazine-ketamine or xylazine-diazepam-ketamine anesthesia. Monitor ventilation and the degree of muscle relaxation

from xylazine-ketamine anesthesia because of residual weakness, presumably produced by the zolazepam.

Horses that bear weight on all four limbs benefit from the gradual administration of guaifenesin and guaifenesin drug combinations. Guaifenesin can be rapidly administered in 5% or 10% concentrations until the horse begins to show signs of muscle weakness and ataxia (weaving side to side, knees buckling). When sufficient muscle relaxation is present, ketamine or thiopental is administered to produce recumbency.[23] Guaifenesin combinations can also be used to extend the anesthetic period if inhalant administration is not possible or impractical.[26,27] Guaifenesin (5%) solution can be combined with xylazine (0.5 mg/mL) and ketamine (1–2 mg/mL) to produce a solution that is called 'Triple Drip'. The combination is administered to effect up to a rate of 2 mL/kg of bodyweight/hour producing total intravenous anesthesia (TIVA) with excellent muscle relaxation and suitable analgesia. The quality of recovery is generally good if the anesthetic period is kept to less than one hour. 'Triple Drip' should not be used to produce anesthesia for greater than 90 minutes unless oxygen supplementation and respiratory support are provided.

An endotracheal tube should be placed if the administration of inhalation anesthesia is anticipated or if oxygen supplementation is desired. Twenty to 30 mm (internal diameter) endotracheal tubes should be used in adult horses. A piece of plumber's pipe (5.0 cm in diameter) covered with non-slip tape is a useful bite block (Fig. 59.4). The tube is passed blindly while extending the head dorsally. Successful placement is confirmed by the minimal resistance to advancement when the tube is in the trachea and the passage of air with respiration.

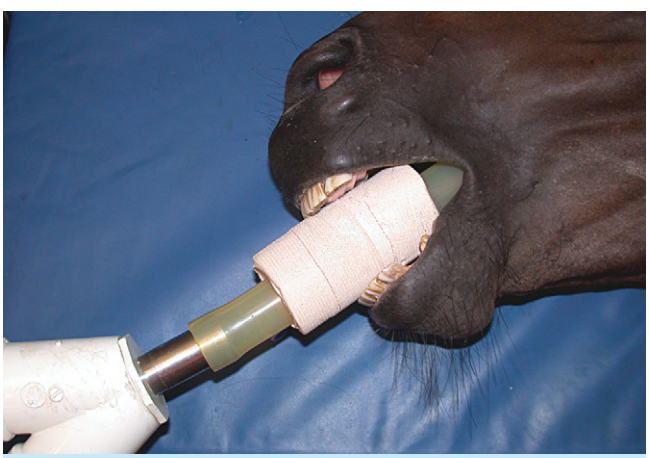

Fig. 59.4
A 10 cm section of plumber's pipe is a useful speculum for endotracheal tube placement. The plastic pipe is covered with adhesive material to reduce slippage.

Padding and positioning

Horses anesthetized and positioned on their side (lateral) or back (dorsal) recumbency are prone to myositis or neurogenic paralysis because of their great weight. Practical steps toward preventing these complications include the maintenance of adequate arterial blood pressure (mean arterial blood pressure greater than 60 mmHg), assuring proper ventilation and oxygenation, minimizing anesthetic duration, and padding and positioning the patient properly. All weight-bearing surfaces of the horse should be padded when the

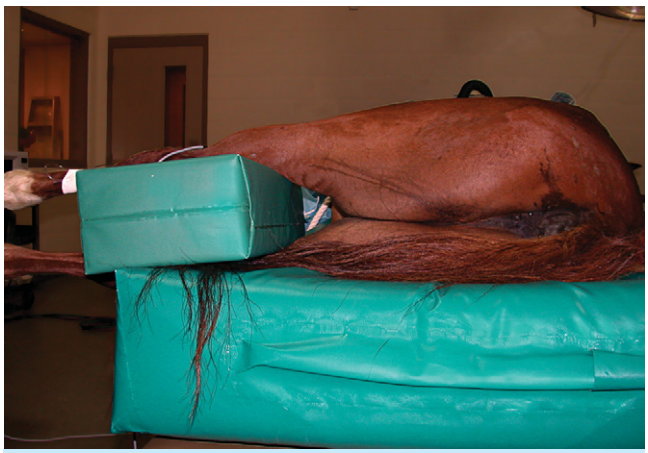

Fig. 59.5
An appropriately padded anesthetized horse in right lateral recumbency. The weight of the left leg is supported by a pad placed between the hocks to reduce compression of the vessels of the right leg.

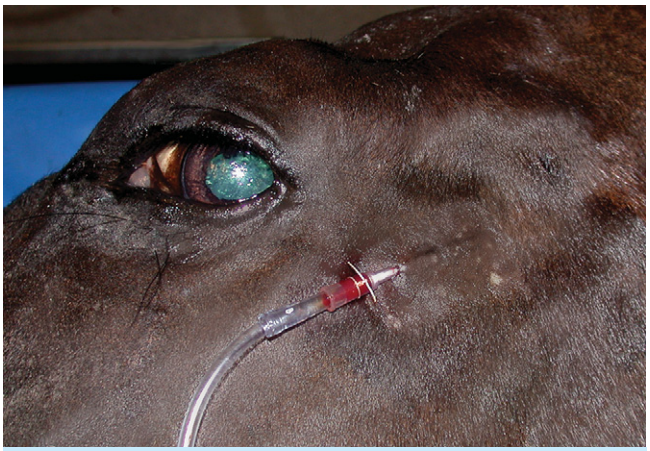

Fig. 59.6
A 20-gauge over-the-needle catheter placed in the transverse facial artery.

horse is recumbent with particular attention paid to bony prominences (Fig. 59.5). A 2 m by 3 m foam rubber pad 20 cm thick works well for horses anesthetized and placed in lateral recumbency. Additional pads should be placed between the rear legs to support the upper leg.

Maintenance of anesthesia

Halothane, isoflurane and sevoflurane are the primary inhalation anesthetics used in the horse. All three drugs can safely be used to anesthetize horses, and the choice is left to personal preference.[28,29] Halothane produces relatively rapid induction to and recovery from anesthesia. Isoflurane and sevoflurane produce more rapid induction and recovery than halothane.[30] There is better maintenance of cardiac output with isoflurane, but arterial blood pressures may be lower than with halothane anesthesia. The cardiovascular profile of sevoflurane is similar to isoflurane. Respiratory depression is greater with isoflurane and sevoflurane than with halothane. Horses anesthetized with isoflurane or sevoflurane may benefit from the administration of a small dose of xylazine (0.1–0.2 mg/kg, i.v.) during recovery from anesthesia.[31]

Monitoring anesthesia

Careful attention is paid to the cardiovascular system, the respiratory system, and ocular reflexes. Evaluations of these systems should be regularly recorded (every 5 minutes). As inhalant anesthesia deepens to surgical planes, the eye rotates medially, the eyelids cease voluntary closure, and tear production decreases. Lateral nystagmus may continue until surgical anesthesia is reached. The palpebral reflex (eyelid closure following brushing of the lids) should decrease as anesthesia deepens, and is generally weak but present during surgical anesthesia. Corneal reflexes (closure of the eyelids in response to pressure on the cornea) should be present at all times during anesthesia. The anal reflex can be used to evaluate the depth of anesthesia if the head is covered; its absence indicates that the animal is too deeply anesthetized.

The heart rate in anesthetized horses normally ranges between 25 and 50 beats/min and does not usually change as the plane of anesthesia deepens or lightens. Anticholinergics should be given to increase rates when less than 25 beats/min. Heart rates in excess of 50 may indicate inadequate planes of anesthesia, hypotension, hypercarbia or hypoxemia. Directly measuring arterial blood pressure and recording the electrocardiogram accomplish more definitive monitoring of the cardiovascular system. The facial, transverse facial, and great metatarsal arteries are all easily palpated and catheterized (Fig. 59.6). Mean arterial blood pressure should range between 60 and 90 mmHg during anesthesia. A mean arterial blood pressure less than 60 mmHg is associated with postanesthetic rhabdomyolysis and the loss of autoregulation of blood flow to vascular beds.[32] Mean arterial blood pressures greater than 90 mmHg are a sign of light anesthetic planes, and movement should be anticipated.

Hypotension is treated by decreasing the delivery of anesthetics (if possible), administering intravenous fluids, and administering vasoactive drugs. If the anesthetic plane is appropriate, the rate of fluid administration should be increased. The choice of fluid is determined by the horse's physical condition, acid–base, and electrolyte status. Hypotension that does not respond to fluid therapy is treated with vasoactive agents such as dobutamine or ephedrine. Dobutamine (1–5 μg/kg/min) is given by infusion and titrated to maintain the desired arterial blood pressure.[33] Signs of dobutamine overdose include tachycardia, hypertension, and supraventricular and ventricular premature arrhythmias. The infusion should be reduced or discontinued if signs of toxicity occur. Ephedrine administration increases arterial blood pressure and cardiac output.[34] Ephedrine (0.05–0.1 mg/kg) is given as an intravenous bolus and

produces effects that persist for 20 to 30 minutes or longer. The administration of calcium solutions may produce increases in arterial blood pressure, particularly if ionized calcium levels are marginal or decreased.

Respiration and oxygenation should be monitored by measuring ventilatory rate and measuring arterial blood gases and pH. Horses that are kept anesthetized for longer than 60 minutes can be expected to hypoventilate. If anesthetic durations of 60 minutes or greater are anticipated, intermittent positive pressure ventilation should be instituted, if possible, as soon as adequate arterial blood pressures are assured. Measurement of the end-tidal concentration of carbon dioxide in the expired airway gas can be used as an indirect assessment of arterial carbon dioxide tension, but the only consistent measurement of adequate ventilation and oxygenation is the measurement of arterial blood gases.[35] If spontaneous ventilation is inadequate, controlled ventilation should be instituted. Initial tidal volumes should be set at 12 to 18 mL/kg. Peak inspiratory pressure should be 20 to 30 cm of water. Respiratory rates should range from 5 to 8 breaths/min.

Horses that are being ventilated correctly ($Paco_2$ of 40 mmHg) occasionally become relatively hypoxemic (Pao_2 less than 100 mmHg) during anesthesia. The cause of the hypoxemia is primarily attributed to mismatches of ventilation and perfusion that occur when horses are placed in lateral or dorsal recumbency. Increasing cardiac output by the administration of fluids and drugs promoting cardiac contractility may help to prevent or reduce arterial hypoxemia. Positive end-expiratory pressure can be used to increase arterial oxygenation but this occurs at the expense of cardiac output because of limited venous return.[36]

The postoperative period

Recovery is the most difficult phase of equine anesthesia to control.[30,37] Optimally, horses should lie quietly for 20 to 35 minutes and regain the standing position in one attempt. Horses may attempt to rise too soon, particularly if sevoflurane or isoflurane are used as maintenance anesthetics. Horses attempting to rise too soon should be sedated with small doses of xylazine (0.2 mg/kg, i.v.). If the horse has not attempted to rise one hour after the end of anesthesia, a handler should enter the recovery stall and stimulate the horse.

The most important feature of any area for recovery of anesthesia is a non-slip flooring surface. Horses exert considerable force as they rise and it is imperative that their feet do not slip as they place them to stand. There are a number of commercial surfaces available. The most consistent surfaces are wrestling or tumbling mats (Fig. 59.7). Three meter by four meter pads, 3 to 4 cm thick, work well. The mats compress as the horse rises, providing secure footing whether wet or dry. The recovery area should be quiet and have lights that can be dimmed. The walls should be padded with secure rings placed 2–3 meters from the floor to facilitate the use of ropes for assisting recovery. Ideally, a ceiling hook should be present for a hoist and sling. Two handlers should remain in the immediate area until the horse is standing. The horse can be helped to its feet by placing a head rope and tail rope (assisted recovery) and running the ropes through rings on opposite sides of the recovery stall (Fig. 59.8). The head and tail ropes are tightened for support as the horse rises to its feet, helping it to balance. More experienced handlers may prefer to remain in the recovery stall with the horse and simply grasp its halter or tail to steady it as it rises. If recovery is to occur out of doors, turf provides excellent footing for recovery and some padding should the horse fall.

Some horses become hypoxemic when they are disconnected from the anesthetic machine for recovery because of the sudden decrease in inspired oxygen concentration. Oxygen can be insufflated during the recovery period with a

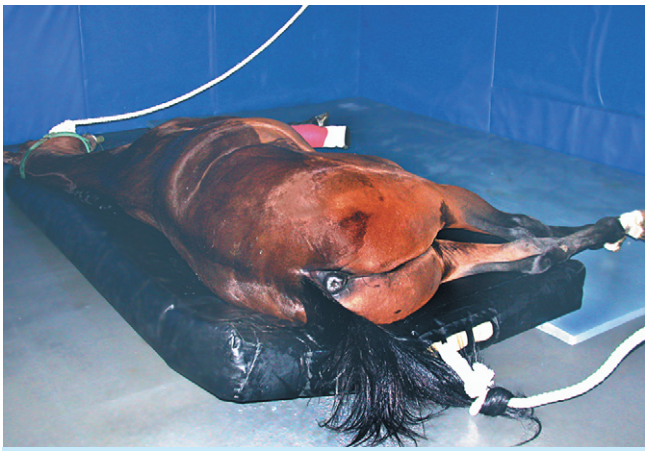

Fig. 59.7
A horse resting on a 15 cm thick foam rubber pad in a recovery stall. A wrestling or tumbling mat is placed to provide good footing when the horse attempts to rise. Cotton ropes run from the halter and the tail to rings affixed to the walls of the recovery stall.

Fig. 59.8
A cotton rope running through a ring affixed to a concrete block wall with expansion bolts. The rope is used to assist and control recovery from anesthesia.

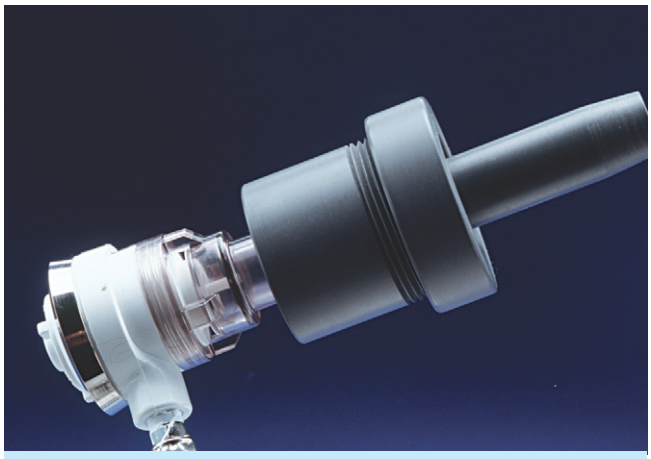

Fig. 59.9
A demand valve is used to ventilate horses in recovery. Depression of the button on the end of the valve causes oxygen to flow. The button is depressed until a normal chest wall excursion is produced. The button is released and exhalation occurs.

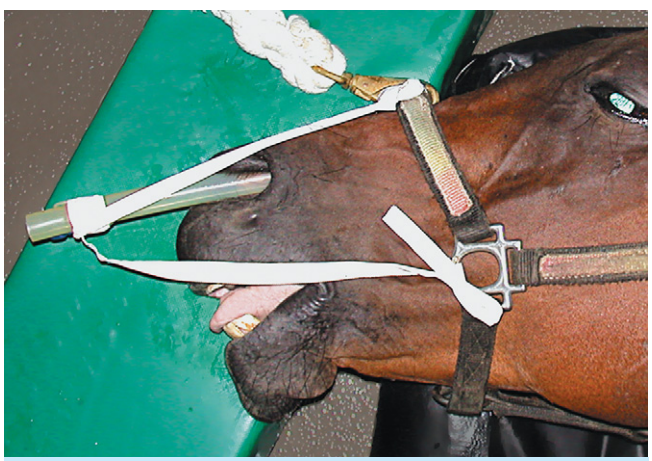

Fig. 59.10
A 14 mm endotracheal tube placed in the ventral nasal meatus to facilitate respiration in the horse recovering from anesthesia. The tube is tied to the halter to ensure it can be retrieved after the horse stands.

nasal oxygen catheter or demand valve.[38] For insufflation, oxygen flow rates should be set at a minimum of 15 L/min to effect a demonstrable change in arterial oxygen tension. More efficient methods of delivering oxygen can be achieved by using a demand valve, which supplies oxygen at high flow rates during the inspiratory phase of respiration (Fig. 59.9). Extubation is performed when the horse begins to swallow and attempts to chew. Prolonged anesthesia in dorsal recumbency can lead to edema of the nasal folds and mucosa of the turbinates. Upper airway obstruction due to edematous nasal folds or turbinates can be relieved by manually holding the nasal cartilages open or by nasotracheal intubation if the obstruction is severe (Fig. 59.10). Rarely, laryngospasm or laryngeal paralysis occurs after the endotracheal tube is removed.

Horses that fail to rise within 90 minutes after the end of anesthesia should be evaluated for possible weakness, rhabdomyolysis or neuropathy. Postoperative weakness can result from lingering drug effects, hypotension, or electrolyte abnormalities (hypokalemia or hypocalcemia). Horses that attempt to stand but are non-weight bearing on one or more limbs should be evaluated for orthopedic injuries, rhabdomyolysis or neuropathy. Distinguishing rhabdomyolysis from neuropathy may be difficult in the horse recovering from anesthesia. Rhabdomyolysis most often affects the gluteal and the quadriceps muscles, whereas neuropathy affects the peroneal nerve supplying the extensors of the rear leg. Large quantities of myoglobin in the urine and the presence of swollen, hardened, affected muscles help differentiate rhabdomyolysis from neuropathy. Other conditions encountered in recovery include femoral and radial nerve palsy and paralysis. The incidence of these conditions is greatly reduced if appropriate padding and positioning are used. Horses that can stand on three legs have a good prognosis for recovery from rhabdomyolysis or neuropathy and generally respond to treatment within 72 hours. Horses that are bilaterally affected and unable to stand have a poorer prognosis.

Emergency sedation and anesthesia of the exhausted horse

Veterinarians and other personnel providing emergency care to horses injured while exercising are often faced with patients that are exhausted, excited, painful, and physically challenged (they may be recumbent or non-weight bearing on one or more limbs). This presentation, coupled with an animal whose evolutionary response to danger is flight, creates the potential for complicated patient management.

Horses that are injured when exercising may be unable to undergo the active 'cool-down' period that is usually incorporated into exercise regimens. This interruption delays the return of hemodynamics and acid–base values to pre-exercise levels.[39] Cardiac output remains increased when horses walk after exercise, leading to more rapid reductions in venous blood lactate concentrations and increases in serum bicarbonate concentration (Fig. 59.11). Most indices return to pre-exercise levels within 60 to 90 minutes whether the horses walk or stand stationary, but increases in rectal temperature persist.

Horses that are injured and cannot ambulate should have an intravenous catheter placed as soon as is practically possible. The early placement of a catheter allows replacement of lost fluids (perspiration, hemorrhage) and facilitates the delivery of sedatives, analgesics and anesthetic agents, if necessary. Injured horses, if agitated, may refuse to drink, thus delaying complete recuperation. The potential for the development of shock is common to most such situations. Volume replacement with balanced electrolyte solutions is of

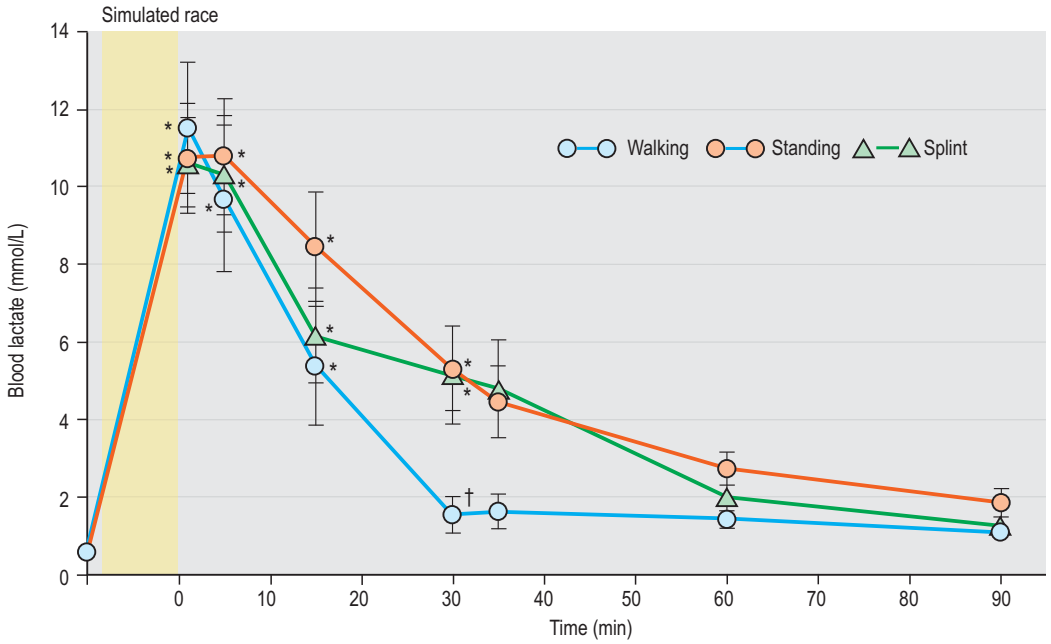

Fig. 59.11
Blood lactate concentrations in horses recuperating from maximal exercise. The data represent mean ± standard error of the mean for six horses. *Indicates significant ($P < 0.05$) differences from baseline values within a trial. † Indicates significant ($P < 0.05$) differences from other groups at a given time. Reprinted with permission from Hubbell JAE, Hinchcliff KW, Muir WW, et al. Cardiorespiratory and metabolic effects of walking, standing, and standing with a splint during the recuperative period from maximal exercise in horses. Am J Vet Res 1997; 58:1007.

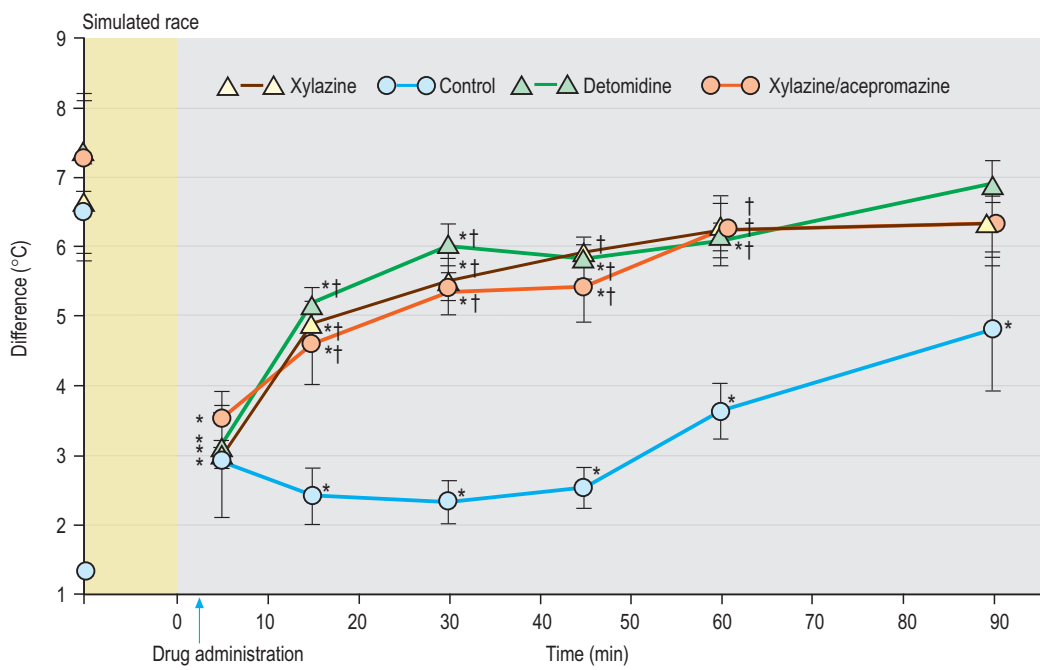

Fig. 59.12
Mean blood temperature versus skin temperature difference for horses given various sedatives or saline solution immediately after maximal exercise on a treadmill. Error bars represent standard error. *Indicates significant ($P < 0.05$) differences from baseline value for that treatment. † Indicates significant ($P < 0.05$) differences from control values (i.e. the value obtained when horses were given saline solution). Reprinted with permission from Hubbell JAE, Hinchcliff KW, Schmall LM, et al. Cardiorespiratory and metabolic effects of xylazine, detomidine, and a combination of xylazine and acepromazine administered after exercise in horses. Am J Vet Res 1999; 60:1276.

benefit regardless of the need for chemical restraint. Other supportive care may include non-steroidal anti-inflammatory drugs, antibiotics and oxygen administration.

The need to provide sedation and analgesia must be carefully assessed. First aid should include immobilization of the injury if possible and cessation of hemorrhage if present. Sedatives and tranquilizers can be safely administered to exhausted horses if indicated.[40] The doses required to produce full effects are approximately twice those needed in horses at rest, but unless the animal is completely uncontrollable, smaller doses should be given and repeated to effect.[41] Xylazine (2.2 mg/kg, i.v.) alone and in combination with acepromazine (0.04 mg/kg) administered to horses immediately after exercise produces heavy sedation with pronounced muscle relaxation sufficient for subsequent induction of anesthesia. Alternatively, detomidine (0.04 mg/kg, i.v.) can be used. The cardiorespiratory depression produced by the administration of these doses was qualitatively similar to that seen when standard doses are administered to horses at rest but does prolong recuperation and exercise-induced increases in body temperature (Fig. 59.12). If less pronounced sedation is desired, standard doses of detomidine (0.01–0.02 mg/kg, i.v.), xylazine (1 mg/kg, i.v.), or a combination of acepromazine (0.02 mg/kg, i.v.) and xylazine (1 mg/kg, i.v.) can be given and the response assessed in 2 to 5 minutes. The need for additional incremental doses is likely. The drugs should be repeated at a rate of one-half the standard dose to effect.

Calming and sedation should be produced before opioids or other analgesic agents are administered. Opioids (morphine, butorphanol, hydromorphone) carry the potential of producing excitement. This effect is most often seen in pain-free animals, but prior administration of a sedative or tranquilizer reduces its likelihood. Butorphanol (0.01–0.02 mg/kg) augments sedation and provides analgesia of short duration. Morphine (0.05–0.1 mg/kg) can provide more profound analgesia. With larger doses horses may head-press and try to move forward. Horses receiving morphine should be carefully monitored for 6 to 8 hours after administration because of the potential for hyperactivity due to residual opioid concentrations. Hyperactivity can be controlled with the administration of small doses of sedatives.

Anesthesia can be safely induced if sufficient sedation is produced.[42] Anesthesia is rarely indicated but can be utilized to facilitate removal of the horse from a public or precarious situation, to prevent further exacerbation of an injury, or to provide an opportunity for further diagnostic tests including radiography. The combinations of diazepam-ketamine or zolazepam-tiletamine cause anesthesia of 20 to 30 minutes' duration when administered to sedate horses. The cardiorespiratory effects of these combinations in exhausted horses are qualitatively similar to those seen when horses at rest are administered the same drugs. The return of exercise-induced increases or decreases in cardiorespiratory and metabolic indices to pre-exercise levels is delayed when short-term anesthesia is performed. Intravenous anesthesia can be safely extended with inhalant agents when indicated.[43] Larger ventilatory volumes may be required to maintain normal arterial partial pressures of carbon dioxide. Exercise-induced changes in metabolic indices such as pH and serum bicarbonate can be returned to normal if intravenous fluids are administered and 'light' anesthetic levels are utilized. Exercise-induced increases in body temperature may persist for the duration of the anesthetic period.

References

1. Short CE, Matthews NS, Tyner CL, et al. Special anesthetic considerations in the racing thoroughbred. Proc 2nd Int Cong Vet Anes 1985; 137.
2. Hall LW. General anesthesia, fundamental considerations. Vet Clin North Am Equine Pract 1981; 1:3–15.
3. Art T, Lekeux P. Training-induced modifications in cardiorespiratory and ventilatory measurements in Thoroughbred horses. Equine Vet J 1993; 25:532–536.
4. Koterba AM, Kosch PC, Beech J, et al. Breathing strategy of the adult horse (*Equus caballus*) at rest. J Appl Physiol 1988; 64:337–346.
5. Foreman JH, Bayly WM, Grant BD, Gollnick PD. Standardized exercise test and daily heart rate responses of Thoroughbreds undergoing convention race training and detraining. Am J Vet Res 1990; 51:914–920.
6. Snow DH, Mackenzie G. Some metabolic effects of maximal exercise in the horse and adaptations with training. Equine Vet J 1977; 9:134–140.
7. McKeever KH, Schurg WA, Jarrett SH, et al. Exercise-training induced hypervolemia in the horse. Med Sci Sports Exerc 1987; 19:21.
8. Kriz NG, Hodgson D, Rose R. Changes in cardiac dimensions and indices of cardiac function during deconditioning in horses. Am J Vet Res 2000; 61:1553–1560.
9. Snow DH, Valberg SJ. Muscle anatomy, physiology, and adaptations to exercise and training. In: Hodgson D, Rose R, eds. The athletic horse: principles and practice of equine sports medicine. Philadelphia: WB Saunders; 1994:145–179.
10. Lavoie JP, Pascoe JR, Kurpershoek CJ. Effects of xylazine on ventilation in horses. Am J Vet Res 1992; 53: 916–920.
11. Lavoie JP, Pascoe JR, Kurpershoek CJ. Effect of head and neck position on respiratory mechanics in horses sedated with xylazine. Am J Vet Res 1992; 53:1652–1657.
12. MacLeay JM, Sorum SA, Valberg SJ, et al. Epidemiological analysis of factors influencing exertional rhabdomyolysis in Thoroughbreds. Am J Vet Res 1999; 60:1562–1566.
13. Bonagura JD. Clinical evaluation and management of heart disease. Equine Vet Educ 1990; 2:31–37.
14. Kriz NG, Hodgson DR, Rose RJ. Prevalence and clinical importance of heart murmurs in racehorses. J Am Vet Med Assoc 2000; 216:1441–1445.
15. Hoffman PE. Clinical evaluation of xylazine as a chemical restraining agent, sedative, and analgesic in horses. J Am Vet Med Assoc 1974; 164:42–45.
16. Muir WW, Skarda RT, Sheehan W. Hemodynamic and respiratory effects of a xylazine-acepromazine drug combination in horses. Am J Vet Res 1979; 40:1518–1522.
17. Wagner AE, Muir WW, Hinchcliff KW. Cardiovascular effects of xylazine and detomidine in horses. Am J Vet Res 1991; 52:651–657.

18. Robertson JT, Muir WW. A new analgesic drug combination in the horse. Am J Vet Res 1983; 44:1667–1669.
19. Dyson DH, Pascoe PJ, Viel L, et al. Comparison of detomidine hydrochloride, xylazine, and xylazine plus morphine in horses: a double blind study. Equine Vet Sci 1987; 7:211–215.
20. Hubbell JAE, Muir WW, Robertson JT, Sams RA. Cardiovascular effects of intravenous sodium penicillin, sodium cefazolin, and sodium citrate in awake and anesthetized horses. Vet Surg 1987; 16:245–250.
21. Matthews NS, Hartsfield SM, Cornick JL, et al. A comparison of injectable anesthetic regimens in horses. Vet Surg 1991; 20:268–273.
22. Muir WW, Skarda RT, Milne DW. Evaluation of xylazine and ketamine hydrochloride for anesthesia in horses. Am J Vet Res 1977; 38:195–201.
23. Butera TS, Moore JN, Garner HE, et al. Diazepam-xylazine-ketamine combination for short-term anesthesia in the horse. Vet Med Small Anim Clin 1978; 73:490–499.
24. Brock N, Hildebrand SV. A comparison of xylazine-diazepam-ketamine and xylazine-guaifenesin-ketamine in equine anesthesia. Vet Surg 1990; 19:468–474.
25. Hubbell JAE, Bednarski RM, Muir WW. Xylazine and tiletamine-zolazepam anesthesia in horses. Am J Vet Res 1989; 50:737–746.
26. Greene SA, Thurmon JC, Tranquilli WJ, et al. Cardiopulmonary effects of continuous intravenous infusion of guaifenesin, ketamine, and xylazine in ponies. Am J Vet Res 1986; 47:2364–2367.
27. McCarty JE, Trim CM, Ferguson D. Prolongation of anesthesia with xylazine, ketamine, and guaifenesin in horses: 64 cases (1986–1989). J Am Vet Med Assoc 1990; 197:1646–1650.
28. Grosenbaugh DA, Muir WW. Cardiorespiratory effects of sevoflurane, isoflurane, and halothane anesthesia in horses. Am J Vet Res 1998; 59:101–106.
29. Steffey EP, Howland D. Comparison of circulatory and respiratory effects of isoflurane and halothane anesthesia in horses. Am J Vet Res 1980; 41:821–825.
30. Whitehair KJ, Steffey EP, Willits NH, et al. Recovery of horses from inhalation anesthesia. Am J Vet Res 1993; 54:1693–1702.
31. Matthews NS, Hartsfield SM, Mercer D, et al. Recovery from sevoflurane anesthesia in horses: comparison to isoflurane and effect of postmedication with xylazine. Vet Surg 1998; 27:480–485.
32. Grandy JL, Steffey EP, Hodgson DS, et al. Arterial hypotension and the development of postanesthetic myopathy in halothane-anesthetized horses. Am J Vet Res 1987; 48:192–197.
33. Swanson CR, Muir WW, Bednarski RM, et al. Hemodynamic responses in halothane-anesthetized horses given infusions of dopamine or dobutamine. Am J Vet Res 1985; 46:365–370.
34. Grandy JL, Hodgson DS, Dunlop CI, et al. Cardiopulmonary effects of ephedrine in halothane-anesthetized horses. J Vet Pharmacol Ther 1989; 12:389–396.
35. Cribb PH. Capnographic monitoring during anesthesia with controlled ventilation in the horse. Vet Surg 1988; 17:48–52.
36. Wilson DV, Soma LR. Cardiopulmonary effects of positive end-expiratory pressure in anesthetized, mechanically ventilated ponies. Am J Vet Res 1990; 51:734–739.
37. Hubbell JAE. Recovery from anaesthesia in horses. Equine Vet Educ 1999; 11:160–167.
38. Mason DE, Muir WW, Wade A. Arterial blood gas tensions in the horse during recovery from anesthesia. J Am Vet Med Assoc 1987; 190:989–994.
39. Hubbell JAE, Hinchcliff KW, Muir WW, et al. Cardiorespiratory and metabolic effects of walking, standing, and standing with a splint during the recuperative period from maximal exercise in horses. Am J Vet Res 1997; 58:1003–1009.
40. Hubbell JAE, Hinchcliff KW, Schmall LM, et al. Cardiorespiratory and metabolic effects of xylazine, detomidine, and a combination of xylazine and acepromazine administered after exercise in horses. Am J Vet Res 1999; 60:1271–1279.
41. Hubbell JAE, Hinchcliff KW, Schmall LM. Sedative administration to horses immediately after maximal exercise: determination of drug and dose. Proc Am Assoc Equine Pract 1997; 43:279–284.
42. Hubbell JAE, Hinchcliff KW, Schmall LM, et al. Anesthetic, cardiorespiratory, and metabolic effects of four intravenous anesthetic regimens induced in horses immediately after maximal exercise. Am J Vet Res 2000; 61:1545–1552.
43. Rankin DC, Greene SA, Keegan RD, et al. Anesthesia of horses with a combination of detomidine, zolazepam, tiletamine, and isoflurane immediately after strenuous treadmill exercise. Am J Vet Res 1999; 60:743–748.

CHAPTER 60

Emergency procedures and first aid

Joanne Hardy

The most commonly encountered emergencies in the athletic horse involve the musculoskeletal system. These include fractures, luxations, lacerations, puncture wounds, infection, and exertional rhabdomyolysis. Other injuries include head and ocular injuries. Although most of these conditions cannot be treated in the field, accurate identification and provision of appropriate emergency treatment are essential for a successful outcome.

Fractures and luxations

- A thorough physical examination is warranted for any athletic horse injury.
- Completion of physical examination can be complicated by the severity of the injury, and other factors such as anxiety, exhaustion, dehydration, and owner/trainer anxiety.
- The goals of initial coaptation of fractures are to relieve anxiety; prevent further injury; and allow safe transportation for additional evaluation.
- Emergency coaptation of unstable limbs should be performed before radiographic evaluation or transportation to a surgical facility.
- Appropriate transportation of the injured horse is important.

Initial assessment

History

Fractures or luxations should be suspected if a loud crack is heard, there is acute non-weight-bearing lameness, the limb is misaligned, or the limb is visibly unstable.

Physical examination

Physical examination of the injured horse should be completed in the best possible setting to avoid further injury to the horse, or to bystanders. Help should be obtained to facilitate crowd control. A knowledgeable handler should be identified to help with horse restraint. While the veterinarian is examining the horse, the person responsible for making decisions on the patient should be sought, and emergency transportation (ideally, an equine ambulance) should be organized.

If the horse is recumbent, examination should be completed before attempting to stand the horse. If the horse is standing, examination should be completed before attempting to move the horse. Sedation and a twitch can be used to help restraint. For sedation, an α_2-agonist such as xylazine, or xylazine and acepromazine can be used. If sedation is needed immediately after maximal exercise, up to double the standard dosage regimen may be required to achieve effective sedation.[1] Butorphanol or detomidine should be reserved for horses that are not controlled with xylazine. It is important to remember that α_2-agonists will often cause the horse to lean forward, which may increase the weight on an injured forelimb and decrease the ability to manipulate the limb. Therefore the minimal effective dose should be used. In addition, heavy sedation will prolong the exercise-induced increase in body temperature, which may be significant in hot humid environment. Active cooling by washing with cold water is an effective method of facilitating heat dissipation.[2] If the horse is recumbent and there is concern for a serious injury, general anesthesia should be induced and maintained until further assessment is made. General anesthesia can be safely induced in horses following maximal exercise using sedation with a combination of xylazine and acepromazine, followed by induction of

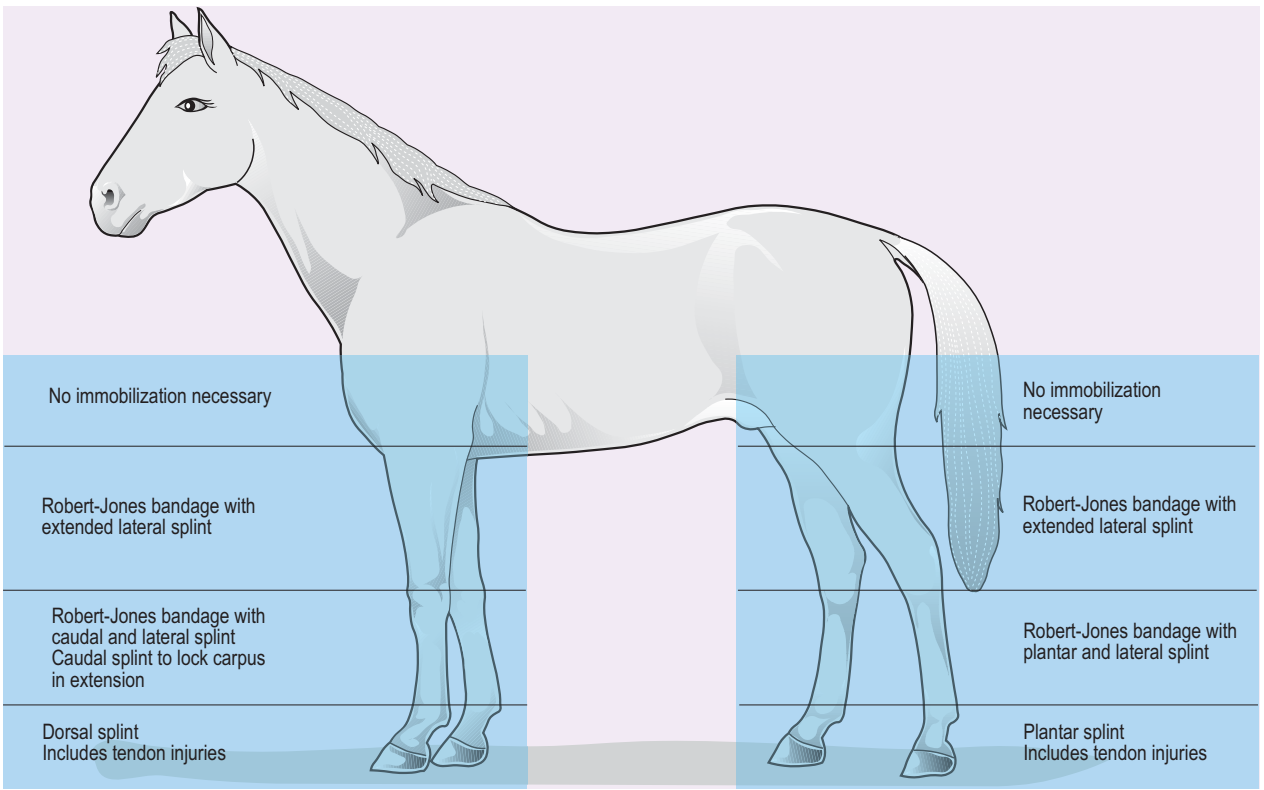

Fig. 60.1
Classification of the level injury system used to understand methods of external coaptation. (After Bramlage LR. First aid and transportation of fracture patients. In: Nixon, AJ, ed. Equine fracture repair. Philadelphia: WB Saunders; 1996:38, with permission.)

anesthesia with ketamine and diazepam or tiletamine-zolazepam. The combination of guaifenesin and thiopenthal produces more hypotension and is less desirable.[3]

Once restraint is achieved, a brief assessment of circulatory status should be made, by evaluating heart rate, mucous membrane color, capillary refill time, and pulse quality. Identification of a heart rate of greater than 80 beats per minute accompanied by a delayed capillary refill time and poor peripheral pulse quality indicates the need for intravenous fluid support.

Once the general status of the patient has been assessed, location and assessment of the injury follows. It is useful to divide the limbs into four levels, which will help define the method of coaptation (Fig. 60.1).[4] Note that flexor tendon injuries located at the level of the metacarpus/metatarsus are considered level 1 injuries.

The presence of a fracture can be determined by instability, crepitus, or abnormal motion. Luxations can be suspected when there is abnormal lateral to medial motion at the level of a joint, and can be confirmed with stress radiographs.

Special examination

Radiographic examination is indicated to confirm the presence of a fracture or luxation. If radiographic equipment is unavailable on site, external coaptation should be applied as if a fracture or luxation exists and the horse transported to a referral facility for further examination.

It is important also to remember that incomplete (hairline) fractures of the radius, tibia and other bones can be difficult to demonstrate radiographically, particularly in field conditions. Therefore, in the presence of severe lameness with pain localized to a long bone, external coaptation should be completed before transportation, to avoid catastrophic displacement of a fracture.

Laboratory examination

Laboratory determinations of biochemistry profile indices are more commonly available even in field situations. If available, parameters of hydration and electrolyte balance are useful to dictate fluid volume and type.

Emergency treatment

Therapeutic aims

- Relieve anxiety.
- Immobilize fracture or luxation for transportation.
- Prevent further damage.
- Provide safe transportation.

Therapy

The principles of emergency coaptation include:

- appropriate wound care before application of external coaptation
- provision of adequate padding to prevent skin abrasions
- immobilization of the joint below and above the area of injury
- prevention of latero-medial and cranio-caudal motion
- never ending a splint in the middle of a long bone segment, or at the end of a fracture line.

Bandage and splint application

Any wound should be carefully cleaned and debrided. An antiseptic ointment can be applied and held in place with conforming gauze. Cotton padding is applied to the entire length of the segment to be immobilized, and held in place with gauze followed by non-stretch bandage material. The bandage should be snug, to avoid loosening with packing of the cotton material. The splint(s) is(are) then applied and held in place, ideally with fiberglass casting tape. This is particularly useful if there is a luxation, as these can be difficult to keep stabilized. If unavailable, heavy tape can be used. It is important to make sure the splints are well padded to avoid the development of sores.

Materials needed for emergency coaptation of fractures or luxations:

Cotton padding
Conforming gauze
Non-elastic bandage
Tape
Casting tape
Splints: PVC pipe material or 2 inch × 4 inch boards of different lenghts

Immobilization of level I injuries Level 1 injuries include phalangeal fractures, fetlock, pastern or coffin joint luxations, and severance of one or more flexor tendons. Although technically a level 1 injury, extensor tendon lacerations require a different mode of splint application and will be presented separately. Forelimb and hindlimb immobilization differ slightly, because of the presence of the reciprocal apparatus in the hindlimb.

Forelimb In forelimb injuries, immobilization is best accomplished by aligning the cannon bone with the phalanges, to establish a straight column (Fig. 60.2). The horse will bear weight on its toe. To accomplish this goal, the forelimb is held above the carpus, bandaged, and the splint is applied on the cranial aspect of the distal limb, extending from the toe to the carpus. If there is latero-medial instability, a lateral splint can also be applied.

Hindlimb In the hindlimb, the reciprocal apparatus prevents extension of the distal limb if the animal is non-weight bearing. Therefore the limb is best immobilized by applying the splint on the caudal aspect of the limb, from the toe to the point of the hock (Fig. 60.3). Again, if there is latero-medial instability, a lateral splint should also be placed.

Use of the Kimzey apparatus (Kimzey Leg Saver, Kimzey Metal Products, Woodland, CA; www.kimzeymetalproducts.com).

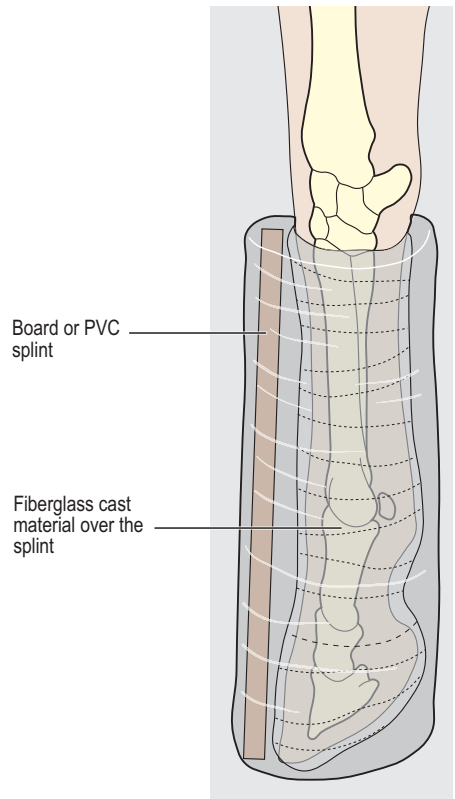

Fig. 60.2 Application of a splint for level 1 injury of the forelimb.

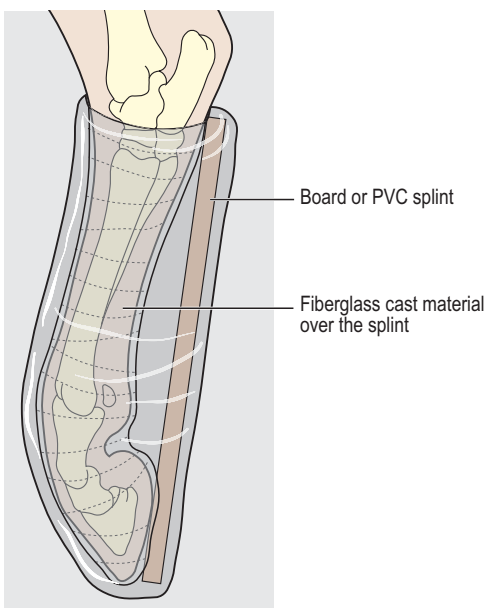

Fig. 60.3 Application of a splint for level 1 injury in a hindlimb.

A commercially available splint is available for level 1 injuries (Fig. 60.4). The advantages of this splint are that it is readily available, easy to apply and is effective in achieving immobilization. Two configurations are available: one with a slightly forward angled bar (for the forelimb) and one with a backward angle with the curve at the level of the fetlock (for the hindlimb). In the author's experience, the forward angle configuration is more effective for either fore- or hindlimb injuries. The hindlimb splint has a heel piece to facilitate

Fig. 60.4
Illustration of the Kimzey Leg Saver (reproduced by permission, John W. Kimzey, Kimzey Metal Products, CA).

weight bearing. Alternatively, a heel piece can be welded onto the splint to increase weight-bearing surface area. Non-slip tape should be placed on the foot plate to make it less slippery, particularly on cement floors.

Extensor tendon injuries With complete severance of both extensor tendons of the forelimb or hindlimb, the horse will knuckle over, which can cause injury to the dorsal aspect of the fetlock and further disruption of the wound. In this instance, external coaptation is needed to prevent knuckling over at the fetlock. A splint is applied to the cranial aspect of the fore- or hindlimb, with the hoof flat on the ground.

Immobilization of level 2 injuries Examples of level 2 injuries include cannon bone fractures, wounds of the carpus or hock, olecranon fractures and radial nerve paralysis. Forelimb and hindlimb immobilization will again be discussed separately, because the angle of the hock requires a different splint configuration.

Forelimb In level 2 injuries, two splints are needed, applied at a 90° angle, with one splint lateral and one splint caudal. The splints need to extend from the hoof to the elbow (Fig. 60.5). For olecranon fractures and radial nerve paralysis, the goal of immobilization is to prevent tendon contracture and injury to the dorsal aspect of the limb. Only a caudal splint is needed for these types of injuries.

Hindlimb As in the forelimb, two splints are needed, one applied laterally and the other applied caudally, from the hoof to the stifle. The angle of the hock makes it difficult to apply a caudal splint. Therefore the caudal splint can end at the point

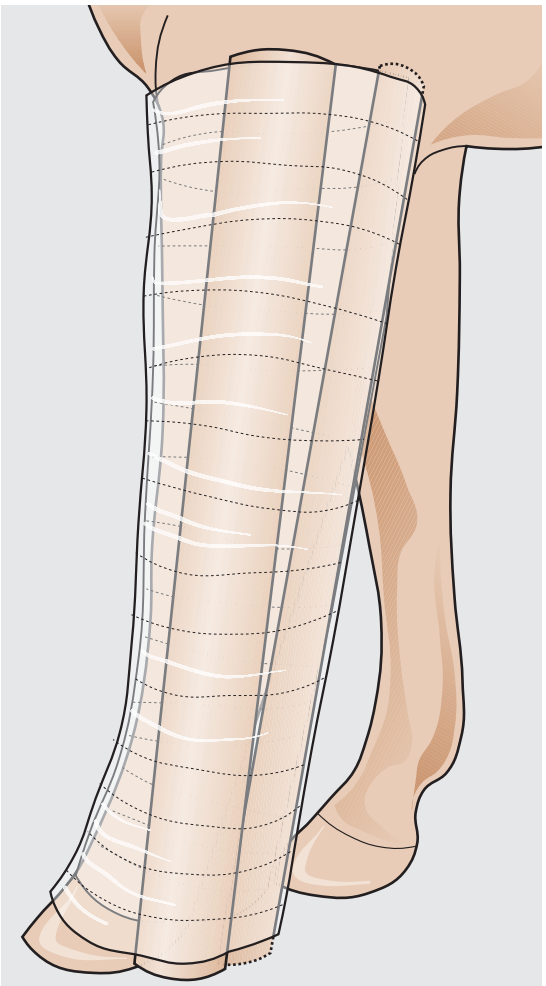

Fig. 60.5
Application of splints for level 2 injury to the forelimb.

of the hock, rather than at the stifle (Fig. 60.6). Alternatively, if possible, a splint can be molded to the hock so it can be applied.

Immobilization of level 3 injuries Level 3 injuries include fractures of the radius or tibia. With fracture, the flexor muscles become abductors, resulting in displacement and comminution of the medial aspect of the limb. The medial aspect of both the radius and ulna does not include a muscle mass to help prevent penetration of the skin by fractured bone. Therefore the goal of external coaptation is to prevent abduction of the limb.

Forelimb The splint is applied to the lateral aspect of the limb, and must extend from the hoof to the withers (Fig. 60.7). The tip of the splint can be taped around the chest for further stability.

Hindlimb The splint is applied to the lateral aspect of the limb, extending from the hoof to the hip (Fig. 60.8).

Immobilization of level 4 injuries Level 4 injuries include fractures of the scapula, humerus, femur or pelvis. External coaptation is not recommended for these injuries as these areas are not amenable to bandaging. Reliance on the hematoma and swelling around the injury for immobilization is needed. A bandage should not be applied to the distal limb,

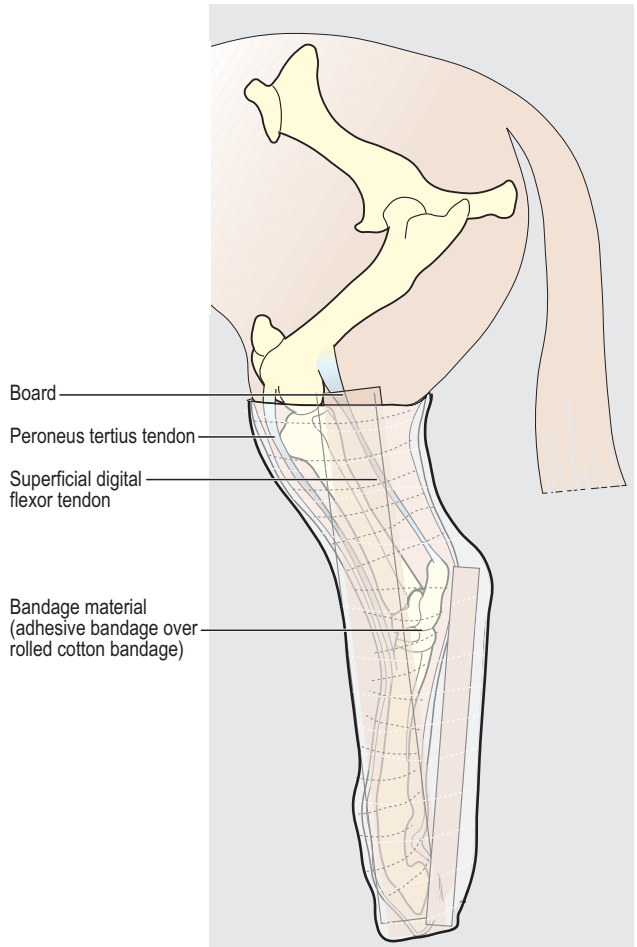

Fig. 60.6
Application of a splint for level 2 injury in a hindlimb.

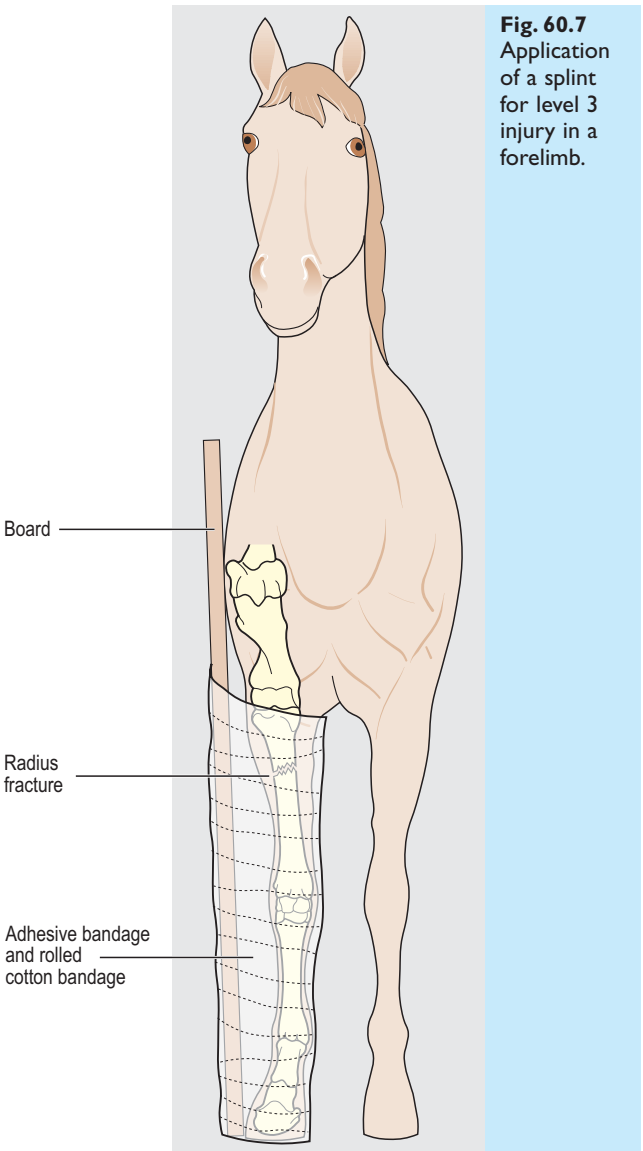

Fig. 60.7
Application of a splint for level 3 injury in a forelimb.

as it will make it more awkward to move, and may increase motion at the fracture site. If a fractured pelvis is present, the need for transportation should be discussed, as moving of the fracture segments can result in lacerations of major vessels. General anesthesia for pelvic fracture should be delayed for 3 to 4 weeks, to avoid fatal hemorrhage.

Guidelines for safe transportation

Before loading an injured horse, proper functioning of the vehicle should be assured. The horse should be stabilized, and the injury immobilized as best as possible before loading. All relevant paperwork (medical records, insurance information, contact numbers and map to referral facility) should be gathered, and the referral facility contacted.

The injured horse will need to negotiate loading and unloading a trailer with a potentially cumbersome splint applied to the injured leg. A low ramp will facilitate this process. While in the trailer, the horse may lean on the wall and partitions to help reduce the load on the injured leg. It will be easier for the horse to travel with partitions in place rather than loose in a makeshift stall. A sling can be placed under the horse's abdomen to help the horse take weight off the injured limb. Many trailers today have standing stalls at 45° angles (slant load trailer), which helps horses balance during transport. If a regular straight-load trailer is used, the horse should face backward for a forelimb injury, and forward for a rearlimb injury, to help cushion sudden stops. Finally, providing hay will help relieve anxiety, and frequent stops should be made to check on the status of the horse and provide drinking water. If significant cardiovascular compromise exists intravenous fluids can be administered while in transit.

If the horse is deemed severely injured and needs to remain recumbent, it can be pulled onto the trailer using a large tarp or blanket. The horse should be kept sedated during transport, to avoid injuries. A head protector (Equine head protector, Jupiter Veterinary Products, Harrisburgh, PA) or bandage can be used to protect the eye and head from self-induced trauma. Bandages should be applied to the lower limbs, also to avoid trauma caused by paddling.

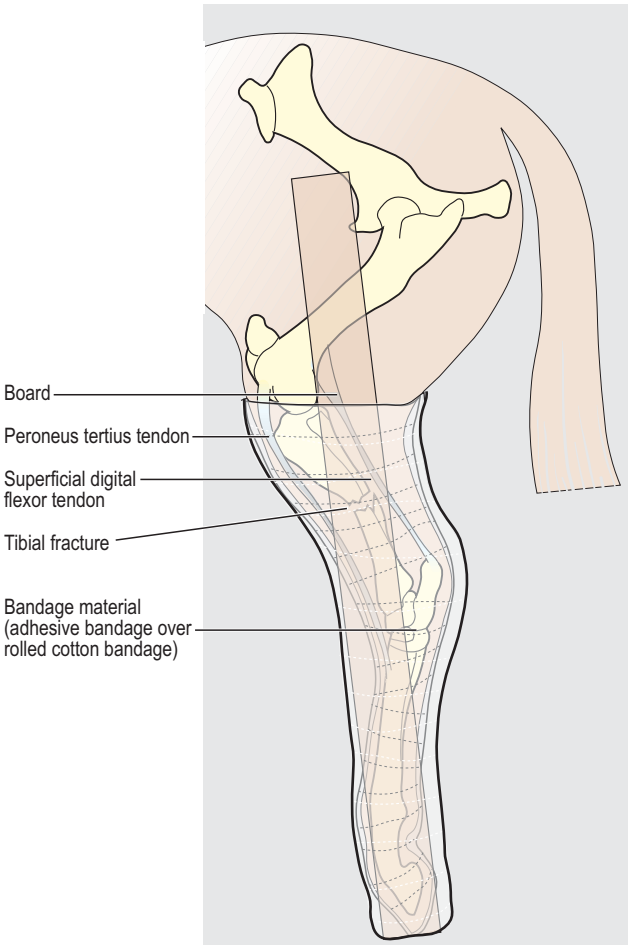

Fig. 60.8
Application of a splint for a level 3 injury in a hindlimb.

Wounds and lacerations

- First step: identification of all involved structures.
- Control of hemorrhage.
- Determine need for referral based on the presence of:
  tendon injury
  penetration of synovial structure
  extensive degloving injury
  severe blood loss.
- Provide tetanus prophylaxis, analgesia, and appropriate antibiotic therapy.
- In severe blood loss, provide cardiovascular support.

Assessment of wounds and lacerations

As with any condition, a general physical examination should be briefly completed before addressing the primary problem. If the wound is located on a limb, the presence and degree of lameness should be noted. The presence and severity of lameness is an important sign of a potentially more serious injury.

The wound is then evaluated for the following findings.

Location

Wounds in the following locations should be explored in detail for injury to important underlying structures:

- wounds over joints or tendon sheaths
- wounds over tendons, particularly flexor tendons
- wounds that have bone exposed, or that are down to bone.

Hemorrhage

The presence of severe hemorrhage may require hemorrhage control before further wound assessment is possible. Severe hemorrhage is best controlled using a pressure bandage applied directly over the bleeding area. Attempts to find the bleeding vessels are usually not successful.

Wound configuration

Certain wound configurations may lead to significant damage to blood supply to the skin and subcutaneous tissues and will result in sloughing. Examples include an inverted 'V' configuration, or significant bruising or trauma to adjacent tissue.

Penetration of a body cavity

Wounds over the chest or abdomen have the potential for penetrating injuries to important organs. In the case of thoracic wounds, development of an open or closed pneumothorax can lead to severe respiratory distress. Any horse with chest trauma and respiratory distress should be evaluated for the presence of pneumothorax.

Determination of synovial structure involvement

The potential involvement of a synovial structure should be *immediately* determined. To evaluate penetration of a synovial structure the following steps can be taken:

- The horse is restrained and sedated as needed.
- A site of entry of the joint or tendon sheath remote from the wound is chosen.
- The site is clipped and prepared aseptically.
- Using sterile technique, saline or a balanced electrolyte solution is injected into the synovial structure, using an amount sufficient to achieve distension. The amount can vary from a few milliliters in the case of a distal tarsal joint injury to 100 mL or more for the femoro-patellar joint (Fig. 60.9). It is also important to assess all possible joint compartments. The wound is observed for leakage of the injectate.

Determination of tendon involvement

Extensor tendon injury of the distal limbs will result in inability to appropriately place the hoof on the ground, resulting in

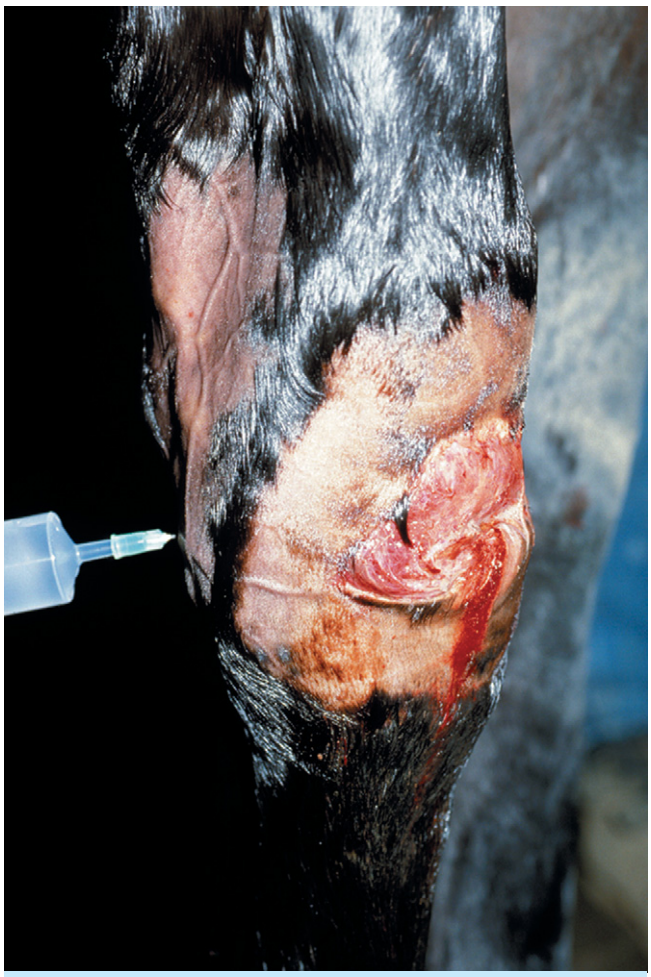

Fig. 60.9
Injection of the middle carpal joint showing communication of the joint with a wound.

the horse knuckling over. For this to occur, both tendons will have to be involved in proximal metacarpal/tarsal injuries.

Flexor tendon injuries will result in hyperextension of the fetlock (superficial digital flexor), lifting up of the toe (deep digital flexor) (Fig. 60.10) or complete dropping of the fetlock to the ground (severance of the suspensory ligament). In order to observe this the horse must bear weight on the limb at least transiently. Importantly, in the case of complete suspensory breakdown, there can be severe stretching of digital vessels, which can lead to thrombosis and avascular injury to the hoof. In complete breakdown injury, it is therefore critical to support the fetlock and not allow weight bearing until further stabilization can be performed.

Emergency treatment of limb wounds and lacerations

Wound care

The goal of initial wound care is to decontaminate the wound as much as possible, and prevent further contamination during transportation. Lavage with saline and sharp debridement of gross contaminants are used to accomplish this goal. Local antiseptics or antibiotics can be then packed in the wound to further decontaminate it.

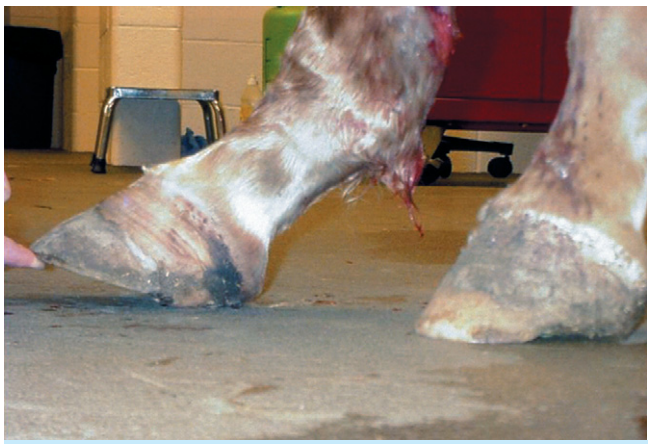

Fig. 60.10
Hyperextension of the coffin joint in a horse with a completely severed deep digital flexor tendon.

Limb immobilization Immobilization of the limb will be needed if there is injury to a supporting structure (bone tendon) or significant instability (luxation). Refer to the above section for a description of the appropriate method of immobilization.

Emergency treatment of wounds involving the chest or abdominal cavity

Pneumothorax An open chest wound (Fig. 60.11) can result in the development of pneumothorax. Pneumothorax will cause respiratory distress manifested by a restrictive pattern of breathing. On auscultation, there will be absence of sound in the dorsal lung fields. Because of the incomplete mediastinum in horses, a unilateral chest wound can lead to bilateral pneumothorax.

An open pneumothorax is managed by providing a temporary seal over the chest wound. This is accomplished by bandaging the wound and applying an impervious airtight layer of a material such as plastic (Fig. 60.12). The chest is then evacuated by inserting a 14-gauge catheter using aseptic technique in the dorsal aspect of the 12th intercostal space, and aspirating the air out of the chest. The use of a three-way stopcock will facilitate this procedure.

Penetrating abdominal wounds Penetrating abdominal wounds are serious and potentially fatal injuries. They can lead to penetration of a viscus, or development of peritonitis. If a penetrating wound is suspected, the wound should be cleaned, explored for the presence of a foreign body, and debrided. An abdominocentesis can be performed to detect fecal contamination indicative of a ruptured viscus. However, abdominocentesis may not be diagnostic in this early stage of peritoneal contamination, as indicators of peritonitis take several hours to develop. The wound can be bandaged, and broad-spectrum systemic antibiotics initiated. In the presence of a large wound, or if abdominal musculature is involved, the abdomen can be

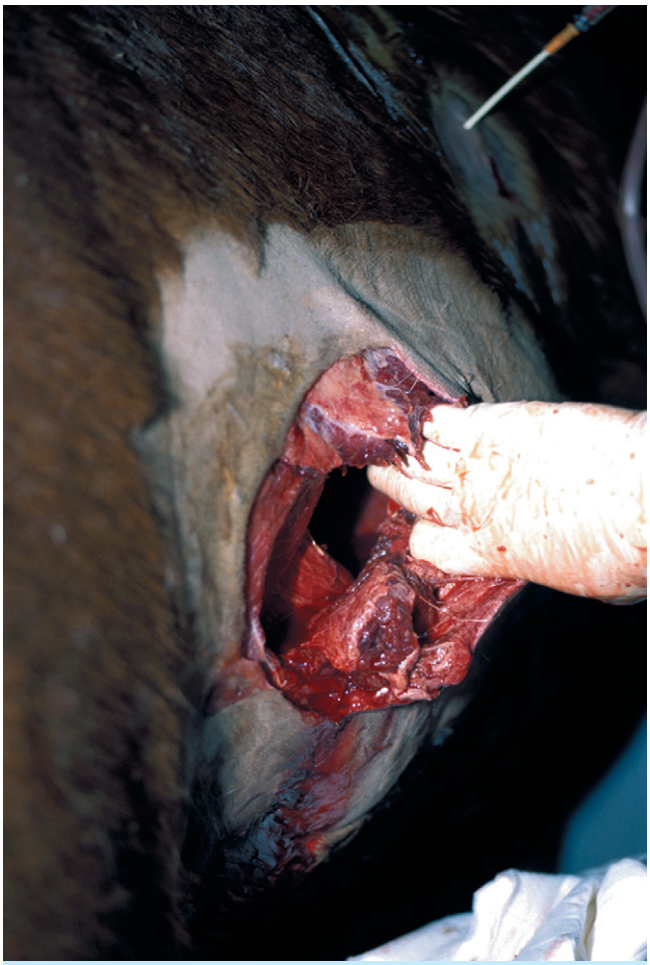

Fig. 60.11
Open chest injury and pneumothorax in a horse. Note the placement of a 14-gauge catheter at the 12th intercostal space dorsally to evacuate air from the chest.

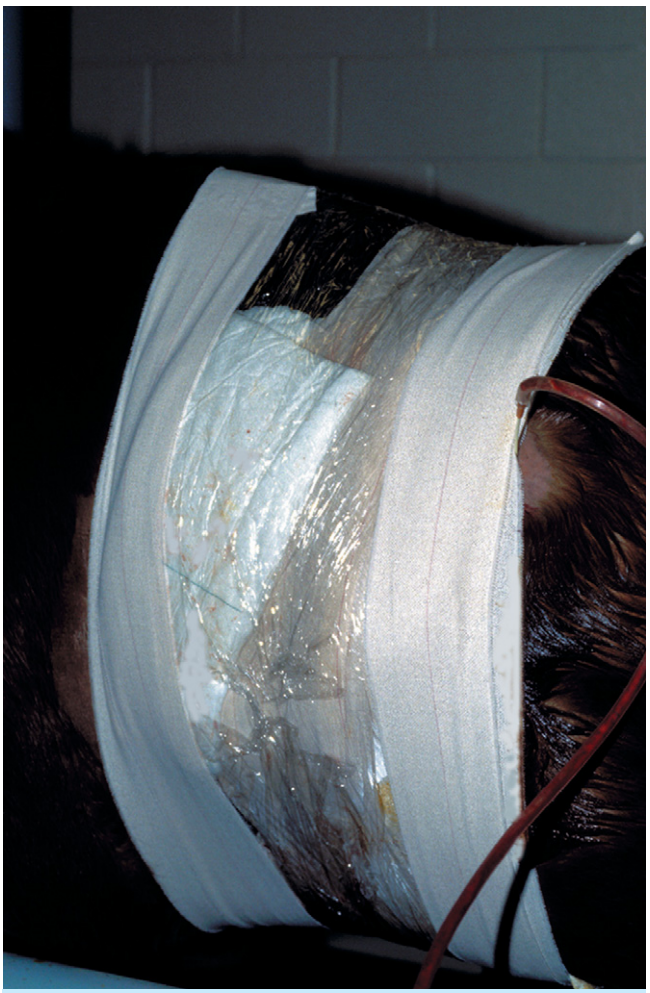

Fig. 60.12
Application of an airtight bandage to a horse with open pneumothorax.

supported (Equus Sta-Put equine abdominal support, Equus Therapeutics, Inc, Afton, VA).

Head injuries

Head injuries can result in severe central nervous system damage. Central nervous system (CNS) injury can be primary where contusions, lacerations and hemorrhage cause the acute damage, or secondary, when subsequent edema, reperfusion injury and necrosis result in worsening of the injury. Therapy for head injury is aimed at minimizing secondary CNS damage.

The causes of head injury in athletic horses include direct trauma from a fall, a blow to the head or falling over backwards onto the poll region. The associated injuries include basisphenoid fractures and avulsion of the ventral straight muscles of the head.

Basisphenoid fractures

The location of this injury can result in acute optic nerve damage, and cerebral signs. Temporary blindness can result. The diagnosis is made by radiography (Fig. 60.13), and treatment is targeted towards minimizing secondary brain damage, and supportive care.

Rectus and longus capitis muscle rupture

This injury occurs most commonly from falling over backwards. The muscles attach to the base of the cranium, and with injury hematoma, and even avulsion fractures of the muscular insertion, can result. Because of the location of these muscles within the guttural pouch septum, hematomas can rupture into one of the guttural pouches, resulting in epistaxis. This epistaxis can be severe, and may require blood transfusion.

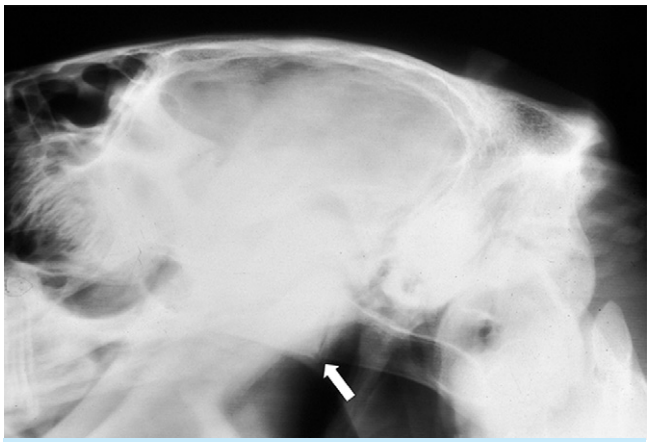

Fig. 60.13
Lateral projection of the head of a horse with a basisphenoid fracture (arrow).

The diagnosis of this injury is made by endoscopy, where an epistaxis of guttural pouch origin is identified, in conjunction with a large hematoma in the guttural pouch septum. Radiographs are useful to demonstrate an avulsion fracture accompanied by a soft tissue opacity overlying the guttural pouches (Fig. 60.14).

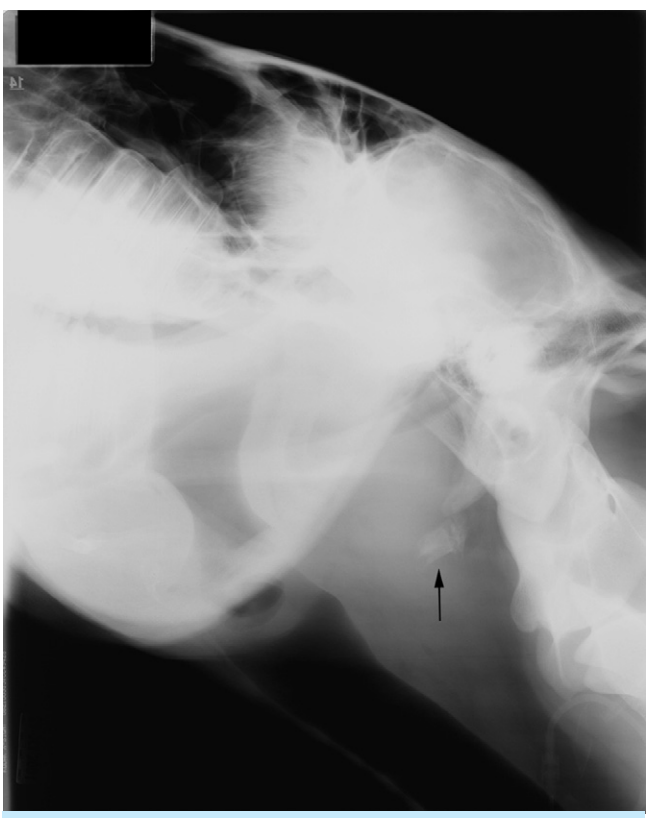

Fig. 60.14
Lateral projection of the head of a horse with avulsion of the longus capitis muscle. Note the avulsion fractures located at the attachment of the longus capitis to the basisphenoid bone (arrow).

Treatment is supportive, with anti-inflammatory drugs and edema-reducing agents.

Treatment of acute head injuries

Horses with head injury can be severely ataxic, and need to be handled and moved with extreme caution. If the horse is down, a short-term general anesthesia is best used to move the horse to a referral facility for further evaluation.

Non-steroidal anti-inflammatory drugs (NSAIDs) are used to minimize inflammation. Although controversial, corticosteroids may be indicated if used in the immediate phase of injury. DMSO is often used to minimize secondary edema. Magnesium has recently been proposed as another therapeutic agent for acute head injury.

Ocular injuries

Ocular injuries encountered in the athletic horse are traumatic in origin, and include periocular lacerations, corneal lacerations or foreign body penetrating injury, or direct blow to the eye with retinal detachment.

Evaluation of acute ocular injury includes evaluation of the different structures of the eye, as well as evaluation of cranial nerve function. Eyelids, conjunctiva, cornea, lens and fundic examinations can be performed to assess the degree of damage (Fig. 60.15). Vision can be assessed by the menace

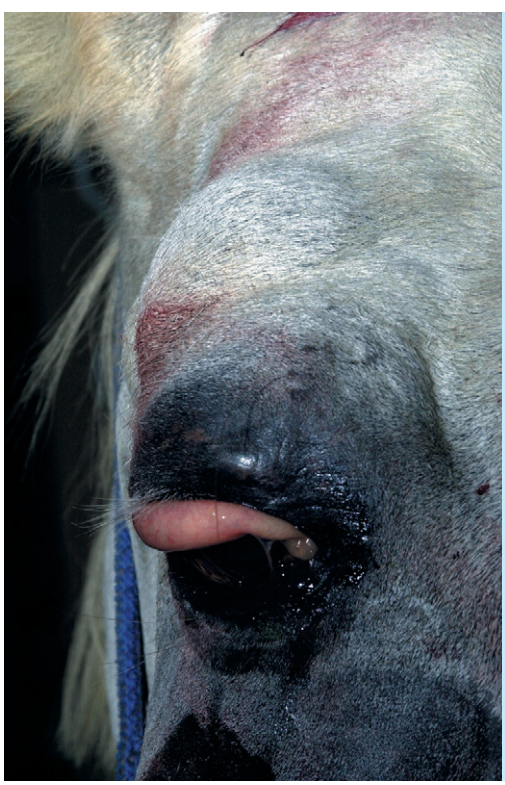

Fig. 60.15
Horse with severe chemosis resulting from contact with an irritant.

response, supplemented with obstacle course testing. Oculomotor, trochlear and abducent nerve function are assessed by the position of the eye, and pupillary light responses. Facial nerve and sympathetic innervation to the eye are assessed by eyelid tone, and position of the eyelashes.

Treatment of acute ocular injuries includes minimizing pain and inflammation, preventing infection, and preventing further injuries. If penetration by a foreign body is suspected, rapid surgical intervention is indicated to prevent further injury.

Anti-inflammatory drugs that are used to minimize pain and inflammation associated with ocular injuries include NSAIDs, DMSO, and topical osmotic agents. Pain from pupillary spasm can be minimized by dilating the pupil with atropine. Direct sunlight should be minimized by protecting the eye. Acute injuries can be associated with ulceration and secondary bacterial invasion. A broad-spectrum topical antibiotic can be used to prevent secondary infection of an ulcer.

Horses that are acutely blind will not negotiate their environment well. Further injury should be prevented by protecting the blind eye (Eye Saver, Jupiter Veterinary Products, Harrisburgh, PA), and by carefully handling the horse.

Acute rhabdomyolysis

Recognition

History and presenting complaint

Acute rhabdomyolysis (tying up) is a generalized inflammation of skeletal muscles. Predisposing factors include genetics, intense exercise, exercise following a period of confinement, dietary practices, particularly the feeding of a high percentage of carbohydrate in the diet, general anesthesia, and sex (higher prevalence in females).

Physical examination

The manifestations of acute rhabdomyolysis (AR) will vary from mild stiffness to recumbency. The most common signs include a stiff gait with reluctance to move, tachycardia, tachypnea, focal or generalized sweating, hardness of large muscle groups such as the glutei, quadriceps and triceps, and muscle fasciculations. The urine will be dark to black as a result of myoglobinuria. Occasionally, particularly if the episode follows exertion, there will also be signs of endotoxemia (injected mucous membranes, poor peripheral pulse). Ileus as manifested by absence of auscultable motility, presence of nasogastric reflux, and palpable small intestinal distension, can also be present, particularly if hypocalcemia is present.

Laboratory findings in AR include elevation of plasma muscle enzymes: early (within 6 hours) creatine kinase (CK) often reaching 50 000 to 100 000 units/dL followed by a later rise in aspartate aminotransferase (AST). Azotemia may be present, and may result from dehydration or from primary renal damage (acute tubular necrosis resulting from pigmenturia). Common electrolyte abnormalities include ionized hypocalcemia, and a metabolic alkalosis.

Treatment

Therapeutic aims

- Pain control.
- Muscle relaxation.
- Fluid support:
  – correction of electrolyte abnormalities
  – prevention of acute renal failure.

Therapy

Acute rhabdomyolysis can be a very painful condition. Adequate fluid replacement should be ensured to prevent renal toxicity of some of these drugs. Drugs used for pain control include flunixin meglumine, phenylbutazone, and ketoprofen. In severe cases, morphine can be added to the therapeutic regimen. If practical, lidocaine (lignocaine) can be given as a constant rate infusion for additional pain relief.

Muscle relaxants are often added to therapy, particularly when the large muscle groups are hard and painful. Methocarbamol, dantrolene, and guaifenesin are recommended, although efficacy is uncertain.

Acepromazine, a peripheral vasodilator, has been recommended to improve muscle blood flow.

Fluid therapy is an essential part of the treatment of acute rhabdomyolysis. Renal tubular necrosis and subsequent renal failure can result from the combination of dehydration, pigmenturia, and nephrotoxicity of NSAIDs. Balanced electrolyte solutions are preferred. Calcium supplementation is indicated as low ionized calcium concentration is often present.

Emergency fluid therapy in the athletic horse

Injuries with blood loss, or horses suffering from exhaustion, acute rhabdomyolysis or overheating, are conditions that require emergency fluid replacement as part of the management of these conditions. This section will discuss the basics of fluid therapy in shock states with emphasis on fluids used for resuscitation. Mention will be made of emergency treatment of the horse with an HYPP (hyperkalemic periodic paralysis) event.

Designing a fluid therapy regimen

Fluids can be administered for maintenance purposes, when fluid intake is physically not possible, or for replacement purposes when excessive losses have been incurred and/or

ongoing losses are anticipated. In the athletic horse, replacement therapy is the mainstay of fluid therapy and will be discussed here. The first section will discuss the mathematics for fluid administration in horses, and the next section will outline the materials commercially available to achieve this goal.

Designing a replacement fluid therapy regimen requires the clinician to answer the following questions:

- What volume of fluids is required?
- What type of fluid is required?
- What route of administration is available/optimal?
- What will be the rate of administration?

Calculating the volume of fluid to give

The volume of fluid to give on a daily basis can be calculated using the following equation:

Total volume to give in the next 24 hours (in liters) =
maintenance (60 mL/kg bodyweight/day)
+
estimate of dehydration (% of bodyweight)
+
ongoing losses

Maintenance volumes will be equivalent to approximately 1 liter of fluid per hour for an adult horse.

An estimate of dehydration can be made by using clinical and, if available, laboratory parameters, as outlined in Table 60.1. These numbers will be weighed in relation to the horse's clinical condition. For example, a nervous horse may have a transiently high heart rate in response to excitement, and a high hematocrit because of splenic contraction. The clinician will therefore have to use judgment in the interpretation of each parameter.

Ongoing losses can be the most difficult estimation, as losses through the gastrointestinal tract are difficult to measure. The equine gastrointestinal tract secretes and reabsorbs the equivalent of the extracellular volume (approximately 30% of bodyweight) on a daily basis. If ileus is present, the amount of reflux can be quantitated. If the large colon is not reabsorbing water, as in diarrhea, significant losses can occur. With severe diarrhea, approximately 50% of extracellular fluids can be lost on a daily basis.

The clinician must be aware that this calculation is a crude estimate, and volumes are then adjusted based on objective responses to fluid administration such as heart rate, pulse quality, capillary refill time, urine production, hematocrit, total protein, and creatinine. These monitoring parameters will need to be repeated as often as dictated by the horse's clinical condition. With a horse in severe shock, monitoring cardiovascular parameters may need to be continuous, or at least every 15 minutes until an improvement is noted. In a horse with severe ongoing fluid losses, cardiovascular parameters should be monitored at least every 4 hours, and laboratory parameters as frequently as four times a day until stabilized. Following these evaluations, an adjustment in the estimate of fluid requirements can be made.

Table 60.1 Physical and laboratory parameters used to estimate the percentage of dehydration in horses

% Dehydration	Heart rate (beats/min)	CRT (s)	PCV/TP (%/g/L)	Creatinine (mg/dL)
6	40–60	2	40/7	1.5–2
8	61–80	3	45/7.5	2–3
10	81–100	4	50/8	3–4
12	> 100	> 4	> 50/> 8	> 4

Deciding the type of fluids to give

Fluids available for administration in horses are of two categories: *crystalloids* are fluids containing substances that freely cross the capillary membrane; these include balanced electrolyte solutions, saline solutions, and dextrose solutions; and *colloids*, which are made up of fluids that are retained in the vascular space for a certain number of hours, because of their larger molecular size; these include plasma, albumin solutions, dextrans, and hydroxyethylstarch. Crystalloids are most commonly used for replacement fluid therapy in the athletic horse, whereas colloids are reserved for resuscitation purposes.

Crystalloids There are two basic types of crystalloid available for horses: *balanced electrolyte solutions* (BES), which consist of electrolyte solutions in concentrations similar to plasma; and *saline solutions*, which contain only sodium chloride. Although considered a crystalloid, dextrose solutions are rarely used alone. Table 60.2 outlines the different composition of crystalloid commercially available for horses.

The decision to choose BES or saline is based, if available, on a serum chemistry profile. Saline is chosen if the sodium concentration is less than 125 meq/L, or the potassium is greater than 5.9 meq/L. Otherwise, a BES is used. If unavailable, a BES is safe, unless HYPP is suspected, in which case saline should be used. Several portable point-of-care monitoring devices that can measure blood gas and electrolytes are now available (IRMA Blood Analysis System, Diametrics Medical Inc. St Paul, MN. www.diametrics.com, I-Stat Portable Clinical Analyzer, I-Stat Corporation, East Windsor, NJ. www.istat.com).

Colloids The addition of colloids to a fluid therapy regimen serves two purposes: addressing the problem of edema formation in hypoproteinemic states; or sustaining the intravascular circulating volume. Selected products containing targeting antibodies are also available for the treatment or prevention of endotoxemia, *Rhodoccocus equi* pneumonia, and clostridial diseases. These products will not be discussed in this section. Colloidal solutions are available in two forms: natural or synthetic. Natural colloids are plasma, serum products or albumin. Table 60.3 summarizes the characteristics of each product. In general, plasma is selected when an increase in oncotic pressure is needed, but in addition, coagulation factors or specific anticoagulants such as antithrombin III are required by the disease

Table 60.2 Composition of crystalloids commonly used for fluid therapy in horses

Product	Approximate pH	mOsmol/L	Na (meq/L)	K (meq/L)	Ca (meq/L)	Mg (meq/L)	Cl (meq/L)	Buffer (meq/L)
Lactated Ringer's	6.5	273	130	4	3		109	Lactate 28
PlasmaLyte A	7.4	294	140	5		3	98	Acetate 27 Gluconate 23
PlasmaLyte 148	7.4	294	140	5		3	98	Acetate 27 Gluconate 23
PlasmaLyte 148	5.5	294	140	5		3	98	Acetate 27 Gluconate 23
5% Dextrose	4	252						
0.9% NaCl	5	308	154				154	
7% NaCl		2400	1196				1196	
5% $NaHCO_3$	8	1190	595				595	
1.3% $NaHCO_3$		308	154				1541	

process. Albumin solutions are not commonly used, as the intravascular half-life of albumin in states of compromised vascular permeability is short, and this solution does not have the added benefits of plasma. Synthetic colloids commonly used in horses include dextran 70 and hydroxyethylstarch (HES). These products are used to increase plasma oncotic pressure, and their effect is best evaluated either by clinical response (decreased edema) or by increased oncotic pressure (measured by colloid osmometry).[5,6] A refractometer cannot be used to monitor the effect of synthetic colloid administration.

Table 60.4 Fluid properties and dosages used for resuscitation in the horse

Fluid	Properties	Dosages
Lactated Ringer's	Crystalloid	Shock: 60 mL/kg
Hypertonic saline	Crystalloid	4 mL/kg rapidly; follow with isotonic fluids
Hetastarch	Synthetic colloid	4 mL/kg rapidly; do not exceed 10 mL/kg

Products used for resuscitation

The goal of fluid therapy in shock states is to rapidly expand circulating blood volume to improve perfusion and oxygen delivery. Isotonic crystalloids can serve this purpose, but must be administered at a rate of 60 to 80 mL/kg in the first hour (approximately one blood volume), for beneficial effects. Hypertonic solutions can be used to rapidly expand circulating volume by redistributing extravascular fluids into the vascular space. Because of redistribution, the duration of effect of hypertonic solutions in horses is short. Colloid solutions can be used to sustain the effect of hypertonic crystalloid solutions to several hours. For resuscitation, a combination of hypertonic saline and hetastarch would have the most beneficial and sustained effects. Table 60.4 lists the properties and dosages of fluids commonly used for resuscitation in the horse.

Table 60.3 Composition of colloids commonly used for fluid therapy in horses

	Characteristics of colloid fluids			
Characteristics	*5% albumin*	*Dextran 40*	*Dextran 70*	*Hetastarch*
Molecular weight (Da)				
weight average	69 000	40 000	70 000	450 000
number-average	69 000	25 000	39 000	70 000
range		10 000–80 000	15 000–160 000	10 000–3 400 000
Solvent		0.9% saline or 5% dextrose	0.9% saline or 5% dextrose	0.9% saline or BES
Concentration (%)	5	10	6	6
Half-life	14–16 days	2.5 h	6 h	25 h
Extravascular percentage (after 24 h)		22	33	39
Overall survival in blood		44 h	4–6 weeks	17–26 weeks
Colloid oncotic pressure (mmHg)	20	40	N/A	30

Table 60.5 Selected traumatic injuries, recommended treatment and prognosis in adult horses

Injury	Recommended treatment	Prognosis
Coffin bone fracture	Corrective shoeing or internal fixation	Extra-articular: good Articular: guarded
P2 fracture	Pastern arthrodesis	Good to guarded
P1 fracture	Internal fixation	Non-displaced: good Displaced or comminuted: guarded
Sesamoid fracture		
Apical	Surgical: extraction	Good
Midbody	Surgical: internal fixation	Guarded
Basilar	Medical or surgical	Guarded to poor
Comminuted/biaxial	Medical or surgical	Poor
Sagittal	Medical or surgical	Poor
Cannon bone fracture	Internal fixation	Guarded to poor depending on degree of comminution
Carpal fracture	Arthroscopic removal or internal fixation	Good for small fracture guarded for large fracture poor if carpal instability
Radius fracture	Hairline: stall rest Displaced: internal fixation	Hairline, non-displaced: good if no displacement occurs Displaced: grave
Olecranon fracture	Non-articular: stall rest Articular: internal fixation	Good unless extreme comminution or open
Humeral fracture	If > 200 kg, stall rest If < 200 kg, internal fixation	Guarded. Risk for contralateral laminitis if stall rest. Implant failure rate high with internal fixation
Scapular fracture		
Supraglenoid tubercle	Non-displaced: medical Displaced: surgical	Guarded
Body/neck	Surgical	Poor
Hock fractures		
Calcaneus	Large fragment: internal fixation Small or comminuted fractures: medical	Guarded Guarded
Tibial fracture	Hairline: stall rest Displaced: internal fixation	Hairline, non-displaced: good if no displacement occurs Displaced: grave
Femoral fracture	If > 200 kg, stall rest If < 200 kg, internal fixation	Guarded. Risk for contralateral laminitis if stall rest. Implant failure rate high with internal fixation
Patellar fracture	Fragmentation: arthroscopic removal Sagittal or comminuted fracture: internal fixation	Guarded to good Guarded
Luxations: hock, fetlock	Reduction and external immobilization	Good for light exercise if no articular injury

Materials for fluid therapy

The flow rate of fluids through an administration system is directly proportional to the diameter of the line and inversely proportional to the viscosity of the fluid and the length of the line. For routine use, 14-gauge catheters made of Teflon or polyurethane are used in adults. When gravity flow is used, a rate of 2 to 3 liters per hour can be achieved when fluids are approximately 10 feet higher than the jugular vein. For more rapid flow 10- or 12-gauge catheters with large-bore connecting sets can be used, but it should be remembered that 10-gauge catheters are more thrombogenic. Finally, both jugular veins can be cannulated for increased fluid administration and a pressure bag system or a pump can increase the rate of fluid flow. Peristaltic pumps can cause endothelial damage and increase the risk of thrombosis.

Materials needed for high-volume fluid therapy in field situations in horses:

Catheters
- 12- or 14-gauge, cm
- Large bore extension set

Administration set
- Coiled set
- Pressure bag

Fluids
- Balanced electrolyte solutions, 5 liters

Epidemiology

Injuries occurring at equine athletic events are best documented in the Thoroughbred racing industry. Fatal musculoskeletal injuries are the most significant cause of death in horses during training or racing activities. In these horses, the injury is so severe as to warrant euthanasia, usually within 2 days of the injury. Forelimb sesamoid bone fracture, suspensory ligament rupture or third metacarpal fracture represent the most common training or racing-related injuries in Thoroughbred race horses. Other fatal musculoskeletal injuries include carpal fractures, fractures of the scapula, tibia or pelvis, and first phalangeal fractures.[7] The influence of training intensity on the prevalence of injury is variable. In California, horses with intense racing schedules (35 furlongs of race in 2 months) were at greater risk of fatal musculoskeletal injury.[8] In contrast, Kentucky horses with injuries had less cumulative high-speed exercise in the months preceding the injury.[9] In one study, horses with toe grabs were at increased risk for fatal musculoskeletal injury, specifically suspensory apparatus failure or condylar fractures.[10] In one study, pre-race examination findings, particularly abnormalities of the suspensory ligament, were highly associated with an increased risk of injury during racing.[11] Table 60.5 describes the current recommended treatment, and prognosis of common injuries in the athletic horse.

References

1. Hubbell JA, Hinchcliff KW, Muir WW, et al. Cardiorespiratory and metabolic effects of walking, standing, and standing with a splint during the recuperative period from maximal exercise in horses. Am J Vet Res 1997; 58(9):1003–1009.
2. Kohn CW, Hinchcliff KW, McKeever KH. Evaluation of washing with cold water to facilitate heat dissipation in horses exercised in hot, humid conditions. Am J Vet Res 1999; 60(3):299–305.
3. Hubbell JA, Hinchcliff KW, Schmall LM, et al. Anesthetic, cardiorespiratory, and metabolic effects of four intravenous anesthetic regimens induced in horses immediately after maximal exercise. Am J Vet Res 2000; 61(12):1545–1552.
4. Bramlage L. Current concept of emergency first aid treatment and transportation of equine fracture patients. Compend Contin Educ Pract Vet 1983; 5:S564–S574.
5. Jones PA, Tomasic M, Gentry PA. Oncotic, hemodilutional, and hemostatic effects of isotonic saline and hydroxyethyl starch solutions in clinically normal ponies. Am J Vet Res 1997; 58(5):541–548.
6. Jones PA, Bain FT, Byars TD, et al. Effect of hydroxyethyl starch infusion on colloid oncotic pressure in hypoproteinemic horses. J Am Vet Med Assoc 2001; 218(7):1130–1135.
7. Estberg L, Stover SM, Gardner IA, et al. Fatal musculoskeletal injuries incurred during racing and training in thoroughbreds. J Am Vet Med Assoc 1996; 208(1):92–96.
8. Estberg L, Stover SM, Gardner IA, et al. Relationship between race start characteristics and risk of catastrophic injury in thoroughbreds: 78 cases (1992). J Am Vet Med Assoc 1998; 212(4):544–549.
9. Cohen ND, Berry SM, Peloso JG, et al. Association of high-speed exercise with racing injury in thoroughbreds. J Am Vet Med Assoc 2000; 216(8):1273–1278.
10. Kane AJ, Stover SM, Gardner IA, et al. Horseshoe characteristics as possible risk factors for fatal musculoskeletal injury of thoroughbred racehorses. Am J Vet Res 1996; 57(8):1147–1152.
11. Cohen ND, Mundy GD, Peloso JG, et al. Results of physical inspection before races and race-related characteristics and their association with musculoskeletal injuries in Thoroughbreds during races. J Am Vet Med Assoc 1999; 215(5):654–661.

CHAPTER 61

Reproductive management

Nigel R. Perkins

Reproductive management of equine athletes has traditionally focused on control or prevention of reproductive behavior to minimize any adverse effects on performance. Although this area remains of interest to owners, trainers and riders of competition animals, recent advances in reproductive techniques provide opportunities for breeding horses during their competitive careers.

Control of reproductive behavior in horses

Male and female athletic horses commonly train and compete together. Day-to-day management under such conditions is often facilitated if sex-steroid-induced sexual or aggressive behavior is suppressed.

Suppression or prevention of estrus in mares

The presence of an estral female in close proximity to other horses may be disruptive and present risk of injury to horses or people. Some female horses become more difficult to handle in estrus, and there is anecdotal evidence linking variation in athletic performance to stages of the estrous cycle in horses.[1] There is a lack of evidence demonstrating an association between stage of cycle and behavior-associated interference with training or athletic performance.

Mares presented for estrus-associated changes in behavior or athletic performance should be examined prior to any treatment. A detailed history should be collected including times of onset of behavioral change, and duration, to determine if the pattern is consistent with normal reproductive cyclicity. Examination should include the following procedures:

- general physical examination with particular consideration to ruling out other causes of a change in performance (musculoskeletal pain or disease involving another body system)
- observation of mare behavior when exposed to an intact stallion
- transrectal palpation and ultrasound examination of the genital tract at a time when the mare is showing behavior suggestive of estrus
- measurement of blood concentrations of reproductive hormones such as progesterone, estrogen, testosterone and possibly inhibin
- potential repetition of the examination to correlate changes in behavior with findings of clinical and laboratory procedures.

Diagnostic confirmation requires observation of clinical signs consistent with estrus behavior, changes in the genital tract that are consistent with estrus,[2] and low circulating progesterone concentration. Response to test treatment of the mare with altrenogest, a progesterone analogue, may be a useful diagnostic aid. Improvement in mare behavior when estrus signs are suppressed using a known effective product adds confidence in a diagnosis of estrus-associated behavioral change. Absence of ovarian follicular development and low or undetectable levels of circulating progesterone or estradiol may indicate a lack of association between behavior and ovarian activity. The presence of constant estrus-like or aggressive behavior may be observed during spring transition, functional ovarian neoplasia and in some cases of behavioral psychosis. Pathologic conditions that account for behavioral change should be treated specifically. Mares without detectable lesions of the genital tract and where behavioral change can be attributed to estrous cyclicity may be considered as candidates for one or more of the treatment options outlined below.

Pharmacologic suppression of estrus

An ideal estrus control product should be highly effective at suppressing signs of estrus, easily administered, rapidly absorbed, require infrequent dosing, and be safe for both animals and people.[3] It should have no residual effect on fertility, allowing treated animals to begin a breeding career following withdrawal of treatment.[3] There should ideally be no restriction on use of the product by rules controlling athletic horse events.

A number of products used for estrus control are not registered for use in horses. Care must be taken when administering products to animals that are not registered for that species. In addition to rules regulating administration of drugs to horses during competition, attention should be paid to drug residues in those countries where horses are classed as 'food-producing' animals.

The mare is seasonally polyestrous. During winter most mares are in a reproductively quiescent state with small inactive ovaries in response to reduced pituitary secretion of follicle-stimulating hormone (FSH), and luteinizing hormone (LH), and reduced secretion of hypothalamic gonadotrophin-releasing hormone (GnRH).[4,5] Increasing hours of daylight after the winter solstice result in an increase in production and secretion of GnRH, with a resultant increase in production and release of pituitary gonadotrophins.[4,6] FSH dominates the initial rise in gonadotrophin secretion in late winter and early spring, stimulating the development of ovarian follicular waves that do not result in ovulation.[4] This endocrine environment results in spring transition, with large, anovulatory follicles, and irregular expression of estrus behavior. Spring transition may persist for several weeks, ending with the first ovulation of the breeding season. Once the first ovulation occurs mares usually enter a regular ovulatory cycle for the remainder of the ovulatory season.

During the ovulatory season the estrous cycle is characterized by a relatively constant diestrus lasting 14 to 15 days and dominated by the corpus luteum, and a more variable estrus dominated by the developing ovulatory follicle. Estrus length is variable both between and within mares, ranging from 5 to 9 days.[7] In spring estrus tends to be longer and more variable in length while in late summer it becomes shorter and less variable. The combination of rising estradiol and low progesterone concentrations seen during estrus is responsible for expression of estrus behavior. Progesterone concentration in peripheral blood rises within 24 to 36 hours after ovulation and is largely responsible for cessation of estrus behavior.[7]

The hypothalamic–pituitary–ovarian (HPO) axis controls ovarian function and expression of reproductive behavior, and offers a range of control points at which intervention may allow suppression of either estrus alone or both estrus and ovulation.

Progestagens The two most commonly used progestagens in mares are natural progesterone and altrenogest (Regumate, Intervet, Millsboro, Delaware, USA).

Daily intramuscular injection of 150 mg or more progesterone in oil will suppress behavioral signs of estrus within days even if started in early estrus. Estrus suppression was also achieved in mares treated with 50 or 100 mg per day if treatment started during diestrus while the same doses failed to suppress estrus behavior if treatment was begun on the first day of estrus.[8] The requirement for ongoing daily injections makes long-term use of this product impractical. Controlled release implants containing progesterone and estradiol have a longer duration of action, and may offer some promise for estrus suppression.[9]

Altrenogest (Regumate) is generally used at the recommended dose rate (0.044 mg/kg by mouth, once daily), for estrus suppression. Continued expression of estrus behavior has been reported in mares being treated with altrenogest and may be due to incorrect dosing, failure to administer the product effectively, errors in estrus detection, treatment during estrus and individual mare variability in response to the product.[10] There are unsubstantiated reports of mares being maintained on lower daily doses of altrenogest for estrus suppression (NR Perkins, unpublished data, 1993).

Little work has been done on assessment of effects of long-term estrus suppression. Mares treated with altrenogest for 88 days showed effective suppression of estrus, no evidence of adverse effects, and normal fertility when bred following resumption of cyclicity.[11] Progestagen therapy has been shown to enhance uterine infection in mares exposed to intrauterine bacteria and in mares with a history of uterine infection, and this may represent a potential adverse effect of long-term treatment for estrus suppression in some mares.[12]

Progestagens have only moderate control over follicular development in the mare, and luteal ovulations are relatively common in mares receiving progestagens, compared with other domestic species.[13] Corpora lutea resulting from ovulation during progestagen treatment may have a prolonged lifespan due to failure of the normal luteolytic mechanism.[13,14] During the ovulatory season mares can be expected to show estrus within 3 to 5 days and ovulate within 9 to 11 days after the end of progestagen therapy.[15]

A wide range of other progestagens has been administered to mares for suppression of estrus with little or no supporting data concerning efficacy or safety.

Intravaginal progestagen-releasing devices have been used for estrus synchronization[16] and appear to offer little value as a means of estrus suppression for any length of time due to the lack of safety data following repeated or long-term vaginal insertion of such devices.

Melengestrol acetate (MGA), chlormadinone acetate (CAP), and norgestomet (Synchromate-B), are all effective at suppressing estrus in cattle and have been used in mares. MGA is effective in cattle at a dose of 0.4 mg/day but appears to be ineffective in mares even when used at doses as high as 20 mg/mare/day.[17] The limited evidence available for both CAP,[17] and norgestomet[18] indicates they are similarly ineffective at inhibiting estrus behavior in mares.

Anecdotal reports have also supported the use of steroid-containing implants registered for use in cattle, as a means of suppressing estrus in mares. Administration of Synovex-S implants to mares, each containing 200 mg progesterone and 20 mg estradiol benzoate, did not result in increased peripheral blood progesterone concentration, did not inhibit

expression of behavioral estrus, and did not prevent ovulation, even when mares received a dose equivalent to 10 times the bovine dose.[19]

Proligestone and medroxyprogesterone acetate (MPA) are synthetic progestagens with prolonged activity registered in some countries for estrus suppression in dogs and cats. There is anecdotal evidence indicating that intramuscular administration of 1500 to 2500 mg proligestone, or 250 to 500 mg MPA, to a mare during diestrus may suppress behavioral signs of estrus for up to 2 to 3 months. The author is not aware of scientific evidence to support this claim.

A number of synthetic progestagens have been shown to be ineffective at maintaining pregnancy in ovariectomized mares, including hydroxyprogesterone caproate and hexanoate, medroxyprogesterone acetate, norgestomet, and megestrol acetate.[20,21] Although not a primary objective of these studies, the authors observed that treatments appeared ineffective at inhibiting signs of estrus and follicular development.

Caution is urged when considering the use of non-registered products in mares for estrus suppression. In most cases scientific assessment of such products has dismissed anecdotal claims of efficacy, and there is little or no information available on safety.

Anabolic steroids Administration of anabolic steroids to mares commonly results in a dose-dependent reduction in ovarian size and cessation of estrous cyclicity, with a gradual return to normal cyclicity occurring after the end of treatment.[22] Anabolic steroids also commonly result in masculinization of behavior and appearance with behavioral changes persisting for several months after cessation of chronic steroid treatment.[22–24] Reduced fertility has been reported experimentally in mares treated with anabolic steroids,[24] although Bourke reported no long-term effect on fertility in brood mares that received anabolic steroid treatment during their racing careers.[25]

Anabolic steroids are more commonly administered to performance horses because of beliefs regarding their influence on physical or performance attributes. Drug detection systems associated with penalties for detection of anabolic steroids or their metabolites currently limit the use of these drugs in most countries.

GnRH immunization

Immunization of females with a GnRH analogue resulted in cessation of estrous cycles in many species including horses.[26–29] Immunization of fillies resulted in an increase in circulating anti-GnRH antibodies, and suppression of gonadal function and sexual behavior for up to 25 to 30 weeks.[28,29] This approach offers promise in the management of undesirable reproductive behavior in athletic horses. Limited data indicate that animals resume cycling and have normal fertility after treatment,[29] though there is little information on the effects of long-term or repeated immunization. Further studies on such effects are required before this methodology can be considered for use by equine athletes in which the option of a future breeding career is desired.

Intrauterine glass balls

Placement of a glass ball in the uterine body one day after ovulation may be effective at suppressing estrus in mares.[30] A single, sterilized, 35 mm glass ball (www.glassmarbles.com) was manually passed through the cervical lumen and into the uterine body on the day following detected ovulation. Five of 12 (42%) treated mares showed prolonged luteal function for a mean of 89 days (range 76 to 109 days), following insertion of the ball.[30] Prolonged luteal function was associated with elevated endogenous progesterone concentration and suppression of behavioral estrus. There appeared to be no evidence of uterine damage in response to the treatment. It is suggested that treated mares be examined to ensure that endometritis does not develop, particularly in the period soon after placement of the ball. This approach may offer a non-pharmacologic alternative for estrus suppression that is effective for reasonable time periods in some mares.

Ovariectomy

Bilateral ovariectomy is occasionally performed in performance mares to prevent estrus and pregnancy, or improve behavior though it is not consistently effective at inducing either outcome.[31] The author routinely advises that clients considering bilateral ovariectomy as a behavioral management aid should initially treat the mare with altrenogest for several weeks. If the mare's behavior improves on altrenogest treatment, then ovariectomy may be expected to result in a similar level of behavioral improvement. If the mare's behavior does not improve on altrenogest then there is an increased risk that ovariectomy will not result in any improvement in behavior.

Bilateral ovariectomy may be performed in the standing sedated mare or through ventral midline or paramedian approaches in the anesthetized recumbent mare.[31] Laparoscopic techniques for ovariectomy have been described recently and may be associated with reduced complications and more rapid recovery.[32]

Control of reproductive behavior in the stallion

Effective control of reproductive behavior in stallions during a performance career can be achieved in most cases using training techniques.[33] Castration or pharmacologic treatment are sometimes considered in horses that are poorly responsive to training alone.[33,34] Interventions should always be combined with training and handling when attempting to modify male sexual or aggressive behavior.

Surgical castration

Castration of male horses is commonly performed to prevent breeding and as a method of behavior modification.[35] Castration may be performed in the standing sedated horse using local anesthesia or in the recumbent horse under general anesthesia.[36] A number of sources provide

information on options for anesthesia and restraint.[35–38] The choice of method and type of restraint are influenced by a large number of factors including: owner and veterinary preference and experience, horse behavior, physical location of the testicles, available equipment and the facilities or surgical environment.[35]

Castration may be performed at any age.[35] There appear to be little scientific data on which to base a recommendation regarding timing of castration. Normal animals are commonly castrated between weaning and 3 years of age. Reasons for delaying castration in animals that do not have a potential breeding career are poorly defined and may include allowing the animal to benefit physically from endogenous testosterone production. Children experience a pubertal growth spurt associated with a rise in circulating sex steroid concentrations.[39] It is not clear whether horses are subject to the same rapid growth phase and limited studies in male dogs have not consistently identified a pubertal growth spurt.[40] In male dogs prepubertal castration delays physeal closure and results in increased long bone length.[40] The clinical significance of this change on musculoskeletal development and function remains unclear. There is a need for research to investigate the impact of age at castration on male horse growth and performance. It is suggested that castration of non-breeding animals may be better performed prior to weaning though advantages appear to be primarily associated with ease of surgery, shortened recovery time and reduced risk of complications either during or after the procedure.[35] Conversely, delaying castration until after puberty may have a beneficial effect on musculoskeletal development. There does appear to be little benefit in delaying castration until a horse is more than 2 years of age except in animals that may be subsequently used as sires in a breeding program.

Castration is effective in modifying male behavior though geldings can continue to display aggression and male sexual behavioral traits including erection, teasing, mounting and copulation.[37] No difference was observed in sexual and aggressive behavior between geldings castrated when less than 2 years of age, and geldings castrated when greater than 3 years of age.[41] These findings indicate that sexual and aggressive behavior in male horses is only partially dependent on the presence of circulating sex steroids. Training and behavior modification may be more effective in geldings than in stallions and this may explain much of the perceived difference in behavior between geldings and intact males.[33]

Pharmacologic modification of male behavior

Administration of progestagens is the most commonly used pharmacologic method for modifying male horse behavior.[42] There is little information concerning mechanism of action, safety, or efficacy in the horse. Progestagens have been shown to decrease the occurrence of male sexual behavior in castrated male monkeys even when circulating plasma testosterone levels were maintained within the range of intact males by testosterone implants.[43] This suggests that the behavioral effect of progestagens is not dependent on reduction in plasma concentration of testosterone concentration, even though progestagen administration in intact animals may also result in suppression of plasma concentrations of LH and testosterone. The behavioral effect of progestagens is mediated by a reduction in uptake of either androgens or estradiol within areas of the brain known to influence male sexual behavior, and both estradiol and androgen levels in the brain influence male behavior.[44] Anecdotal evidence indicates that progestagen administration to male horses results in suppression of sexual and aggressive behavior as well as a general calming effect.[42,45] Progestagen therapy may be combined with training in an attempt to modify unsuitable behavior in male horses.[45]

Treatment of stallions with 0.044 mg/kg altrenogest per day for 30 days had no effect on sperm production or measures of sperm quality.[46] Most behavioral parameters did not change though time to mount and ejaculate was increased in altrenogest treated stallions after the completion of treatment, returning to pre-treatment values by 60 days after cessation of treatment. Reductions in circulating concentrations of LH, testosterone, inhibin and estrogen conjugates were also detected in treated animals at the end of the treatment period, returning to pre-treatment levels within 30 days of cessation of treatment. In a similar experiment stallions treated with 0.088 mg/kg altrenogest per day for 8 weeks, showed reduced scrotal circumference and sperm production, and increased sperm abnormalities.[47] Treated animals also showed reduced male sexual and aggressive behavior, and reduction in serum testosterone concentration. These studies suggest that altrenogest does have an impact on reproductive parameters, and that longer treatment periods may be necessary to obtain measurable changes in male behavior. The effects of altrenogest on behavior and fertility in stallions appear to be reversible.

It is possible that certain progestagens may affect both behavior and fertility while other products may have little or no effect on fertility. Evidence in monkeys indicates that both medroxyprogesterone acetate and progesterone are effective at reducing male behavior, while they have different effects on circulating testosterone levels. Animals treated with medroxyprogesterone acetate showed reduced plasma concentrations of LH and testosterone while animals treated with progesterone did not.[44] Further work is needed to investigate the effects of progestagens on behavior and fertility in stallions.

Tranquilizers such as phenothiazine derivatives and reserpine have been used in the past in stallions as aids for behavior modification.[42] They are no longer recommended for use in male horses because of the small but important risk of adverse sequelae including penile paralysis, paraphimosis and psychotic behavior.[42]

Immunomodulation of male fertility and behavior

Immunization of male horses against GnRH results in reduction in circulating testosterone concentration, testicle size,

and sperm numbers. Young colts also show reductions in male sexual behavior and aggression though behavioral effects are less noticeable in mature animals.[28,48,49] Treatment effects appear to be fully reversible over time.

GnRH vaccination may offer an alternative treatment modality for controlling reproductive behavior and fertility in male horses during their athletic career. However, more research is required, particularly on the possible adverse effects of long-term or repeated treatment, before this approach can be recommended.

Combining breeding and athletic careers

Developments in assisted reproductive technologies have allowed increased flexibility in managing the breeding careers of mares and stallions while still performing as athletes.

Stallion

Advances in techniques for producing and managing chilled and frozen semen, improved pregnancy and foaling rates, and increased market demand for such services, have seen a progressive increase in the proportion of mares bred using chilled or frozen semen artificial insemination (AI) in all breeds except Thoroughbreds. Semen may be collected from stallions for processing throughout the year, including during periods of training or competition. Training techniques providing clear distinction between performing and breeding may help to ensure that periodic breeding opportunities do not disrupt a stallion's training performance or general behavior.[33]

Individual stallion semen quality is one of the most important factors influencing the success of artificial insemination programs and a breeding soundness examination should be performed on any stallion being considered as a semen donor in an AI program. Detailed description of procedures and techniques involved in breeding soundness examination of stallions may be found elsewhere as well as discussion of factors influencing semen production and quality.[50–54]

It is particularly important to be aware of individual variability in fertility of thawed–frozen stallion semen, even in stallions that have excellent fertility when bred naturally or using fresh AI.[55] Results of laboratory analysis of either fresh or thawed–frozen stallion semen are poorly predictive of pregnancy rates in mares bred with thawed–frozen semen from the same stallion and test mating of a small number of mares remains a useful method of determining whether a particular stallion has fertile, thawed–frozen semen. Continued developments are expected in techniques for freezing and thawing semen, and laboratory assessment of the potential fertility of thawed–frozen semen.

Mare

Developments in assisted reproductive technology have had a dramatic impact on breeding options available to mares during an athletic career.

Natural breeding

Mares are occasionally bred while still competing, perhaps in an attempt to gain some benefit from the calming effect of endogenous progesterone secretion that occurs during pregnancy.[45] There is little information on the effect of different exercise levels in mares on fertility, pregnancy development, or risk of pregnancy loss. The first two-thirds of pregnancy in the mare are characterized by little or no increase in nutrient requirements[56] or bodyweight over the non-pregnant state. Animals that tolerate the stresses and demands of training and competing are likely to have minimal risks associated with continuation of an athletic career during the first few months of pregnancy. Exercise-associated risks to pregnancy appear to be mediated through effects such as reduction of uterine blood flow due to redistribution of blood to the musculoskeletal system, reduction of available glucose due to increased muscle metabolism, and exercise-induced temperature rise.[57] There appears to be no information in horses on the effects of pregnancy on performance. Studies in women report a progressive decline in all aspects of athletic performance during pregnancy.[58] It seems plausible to expect a similar effect in horses.

Embryo transfer

Use and availability of embryo transfer (ET) has increased tremendously over the past decade, particularly with development of techniques for short-term storage and shipment of embryos. Embryos can now be shipped from the site of collection to a centralized facility for transfer to recipients or long-term storage, removing the necessity for recipient mares to be maintained at the same site as donors.[59] ET techniques have changed little over the last decade and are well described.[59–63] ET use in performance mares can allow multiple foals to be produced from mares while they continue to train and compete.[64] In seasonal sports such as polo, mares may move from intensive athletic performance to being embryo donors, depending on the time of year.[60,65] The lack of a reliable, commercially viable method for superovulating donor mares continues to be a major limitation on embryo recovery rates.[66] Reported pregnancy rates following transfer of thawed–frozen equine embryos have been disappointing and preference is given to transfer of fresh or chilled embryos to avoid the necessity of freezing, though this is expected to change as techniques are refined.[59]

Other assisted reproductive techniques

Commercial in vitro fertilization (IVF) and embryo production is now being offered for cattle industries in several countries. Similar procedures have been performed in mares

and selected facilities offer these techniques on a commercial basis.[67] Oocytes are generally collected by transvaginal ultrasound-guided follicular aspiration, from either immature or mature follicles. Oocyte maturation may be combined with intracytoplasmic sperm injection (ICSI) to circumvent the requirement for sperm capacitation and even for sperm motility.[68–70] Oocyte transfer procedures have also resulted in pregnant recipients.[70, 71]

The use of ICSI or low-volume insemination with sexed semen provides the added option of obtaining sex-selected offspring from performance mares during their competitive career.[72] Other assisted reproductive techniques that may offer potential in future equine breeding programs include freezing of oocytes, cloning and production of transgenic animals.[66]

Until recently many breed registries that allowed assisted reproductive techniques such as embryo transfer allowed only one foal per mare per year to be registered. In mid 2002, legal action in Texas resulted in the American Quarterhorse Society overturning this restriction and removing all numerical restrictions on the number of foals that may be eligible for registration in any one year. This action has ramifications for other breed registries that may be considering, or already have, restrictions on the number of foals that may be registered in one year.

Management of performance horses to optimize future reproductive potential

In most cases little consideration is given to the reproductive potential of performance horses until they are reaching the end of their performance career. This is expected to change in the future. Management of performance horses will involve increasing attention to both short- and long-term impacts on fertility of disorders, management procedures and treatments. In some instances this may result in changes in management or treatment because of a possible adverse impact on fertility.

Many female horses for example are subjected to a Caslick's (vulvoplasty) procedure during their performance career because of a belief that pneumovagina during periods of intense physical exertion may interfere with performance. In some cases the vulval lips are sutured further ventrally than the general Caslick recommendation of 1 cm below the ischial arch. It is possible that an overzealous Caslick may interfere with normal ventrocaudal urine flow during urination with urine splashing cranially into the anterior vagina. This may lead to chronic urine-induced inflammation involving the vagina, cervix and uterus. The author has observed maiden mares at stud with a very low Caslick in place and severe degenerative changes in the uterine epithelium on examination of endometrial biopsy.

In stallions, improper application of a stallion ring to prevent erections during a performance career may result in penile scarring and interference with the long-term ability to obtain a normal erection.

Some treatments administered to horses during their performance careers may also have long-term adverse effects on future fertility. Anabolic steroids, anti-cancer drugs and GnRH vaccines are examples of treatments that may have a long-term effect on fertility. Anabolic steroids can cause cessation of estrous cyclicity in females and reduce testis size, sperm production and sperm quality in stallions.[22,73–75] Limited data in horses appear to indicate that effects are generally reversible following cessation of treatment.[25,76] The long-term effect of administering combinations of different steroids, or using dose rates or treatment frequencies that differ from manufacturer guidelines, remains unknown. Evidence from chronic misuse of anabolic steroids by human athletes indicates that there may be serious and long-term effects on fertility and general health.[77]

Management of performance horses during their performance career will need to be modified to pay more attention to breeding potential. Drugs that may have adverse effects on fertility and cyclicity should be avoided in animals that are to be used for breeding purposes during their performance career. In addition every effort should be made to avoid administering drugs associated with any risk of adverse effects in pregnant animals. There is little specific information on safety of products during pregnancy in horses. Information is predominantly extrapolated from studies in laboratory animals and reports from human medicine. Lists of common drugs used in veterinary medicine have been produced with comments on their safety during pregnancy.[78] Effects of administration of harmful drugs during pregnancy depend on the action of the drug, dose and duration of exposure, and stage of pregnancy. Possible effects include pregnancy loss, induction of fetal malformations, alteration of normal fetal development, abnormal parturition and reduced fetal viability.[78]

References

1. Jorgensen J, Vivrette S, Correa M, Mansmann R. Significance of the estrous cycle on athletic performance in mares. Proc Am Assoc Equine Pract 1996; 42:98–100.
2. Carleton C. Clinical examination of the non-pregnant female reproductive tract. In: Youngquist R, ed. Current therapy in large animal reproduction. Philadelphia, PA: WB Saunders; 1997:79–95.
3. Shille V. Suppression or prevention of estrus in racing and sporting dogs. In: Bloomberg M, Dee J, Taylor R, eds. Canine sports medicine and surgery. Philadelphia, PA: WB Saunders; 1998:309–312.
4. Hart P, Squires E, Imel K, Nett T. Seasonal variation in hypothalamic content of gonadotropin-releasing hormone (GnRH), pituitary receptors for GnRH, and pituitary content of luteinizing hormone and follicle stimulating hormone in the mare. Biol Reprod 1984; 30:1055–1062.

5. Sharp D. Vernal transition. In: McKinnon A, Voss J, eds. Equine reproduction. Philadelphia, PA: Lea and Febiger, 1993:133–144.
6. Sharp D, Grubaugh W. Use of push–pull perfusion techniques in studies of gonadotrophin-releasing hormone secretion in mares. J Reprod Fertil 1987; Suppl 35:289–296.
7. Ginther O. Reproductive biology of the mare: basic and applied aspects, 2nd edn. Cross Plains, WI: Equiservices; 1992.
8. Loy R, Swan S. Effects of exogenous progestogens on reproductive phenomena in mares. J Anim Sci 1966; 25:821–826.
9. Jasko D, Farlin M, Hutchinson H, et al. Progesterone and estradiol in biodegradable microspheres for control of estrus and ovulation in mares. Theriogenology 1993; 40:465–478.
10. Lofstedt R. Control of the estrous cycle in the mare. Vet Clin North Am Equine Pract 1988; 4:177–196.
11. Squires E, Shideler R, Voss J, Webel S. Clinical applications of progestins in mares. Comp Contin Educ 1983; 5:S16–S22.
12. Colbern G, Voss J, Squires E, et al. Development of a model to study endometritis in mares. J Equine Vet Sci 1987; 7:73–76.
13. Lofstedt R, Patel J. Evaluation of the ability of altrenogest to control the equine estrous cycle. J Am Vet Med Assoc 1989; 194:361–364.
14. Daels P, McCue P, DeMoraes M, Hughes J. Persistence of the luteal phase following ovulation during altrenogest treatment in mares. Theriogenology 1996; 46:799–811.
15. Squires E. Use of progestins in open and pregnant mares. Anim Reprod Sci 1993; 33:183–193.
16. Driancourt M, Palmer E. Seasonal and individual effects on ovarian and endocrine responses of mares to a synchronization treatment with progestagen impregnated vaginal sponges. J Reprod Fertil 1982; Suppl 32:283–291.
17. Neely D. Progesterone/progestin therapy in the broodmare. Proc Am Assoc Equine Pract 1988; 33:203–218.
18. Wiepz G, Squires E, Chapman P. Effects of norgestomet, altrenogest and/or estradiol on follicular and hormonal characteristics of late transitional mares. Theriogenology 1988; 30:181.
19. McCue P, Lemons S, Squires E, Vanderwall D. Efficacy of progesterone/estradiol implants for suppression of estrus in the mare. Proc Am Assoc Equine Pract 1996; 42:195–196.
20. McKinnon A, Lescun T, Walker J, et al. The inability of some synthetic progestagens to maintain pregnancy in the mare. Equine Vet J 2000; 32:83–85.
21. McKinnon A, Del Marmol Figueroa S, Nobelius A, et al. Failure of hydroxyprogesterone caproate to maintain pregnancy in ovariectomised mares. Equine Vet J 1993; 25:158–160.
22. Skelton K, Dowsett K, McMeniman N. Ovarian activity in fillies treated with anabolic steroids prior to the onset of puberty. J Reprod Fertil 1991; Suppl 44:351–356.
23. Maher J, Squires E, Voss J, et al. Effect of anabolic steroids on reproductive function of young mares. J Am Vet Med Assoc 1983; 183:519–524.
24. Squires E, Voss J, Maher J, et al. Fertility of young mares after long term anabolic steroid treatment. J Am Vet Med Assoc 1986; 186:583–587.
25. Bourke J. Anabolic steroids and fertility in Thoroughbred mares. J Reprod Fertil 1982; Suppl 32:623–624.
26. D'Occhio M. Immunological suppression of reproductive function in male and female mammals. Anim Reprod Sci 1993; 33:345–372.
27. Ladd A, Tsong Y, Walfield A, Thau R. Development of an antifertility vaccine for pets based on active immunization against luteinizing hormone releasing hormone. Biol Reprod 1994; 51:1076–1083.
28. Dowsett K, Tshewang U, Knott L, et al. Immunocastration of colts and immunospaying of fillies. Immunol Cell Biol 1993; 71:501–508.
29. Tshewang U, Dowsett K, Knott L, Trigg T. Preliminary study of ovarian activity in fillies treated with a GnRH vaccine. Aust Vet J 1997; 75:663–667.
30. Nie G, Johnson K, Braden T, Wenzel J. Use of a glass ball to suppress behavioral estrus in mares. Proc Am Assoc Equine Pract 2001; 47:246–248.
31. Moll H, Slone D. Surgery of the ovaries. In: Wolfe D, Moll H, eds. Large animal urogenital surgery, 2nd edn. Baltimore, MD: Williams and Wilkins; 1999:137–141.
32. Ragle C. Laparoscopic ovariectomy. In: Wolfe D, Moll H, eds. Large animal urogenital surgery, 2nd edn. Baltimore, MD: Williams and Wilkins; 1999:143–146.
33. McDonnell S. Stallion sexual behavior. In: Samper J, ed. Equine breeding management and artificial insemination. Philadelphia, PA: WB Saunders; 2000:53–61.
34. Stout T. Immunocastration of horses: a tool for behavioural modification? 2002; Available at http://www.vetscite.org/cgi-bin/pw.exe/Issue4/000047/000047.htm. (Accessed 20 October 2002).
35. Pleasant R. Castration of the normal horse. In: Wolfe D, Moll H, eds. Large animal urogenital surgery, 2nd edn. Baltimore, MD: Williams and Wilkins; 1999:23–31.
36. Searle D, Dart A, Dart C, Hodgson D. Equine castration: a review of anatomy, approaches, techniques and complications in normal, cryptorchid and monorchid horses. Aust Vet J 1999; 77:428–434.
37. Trotter G. Castration. In: McKinnon A, Voss J, eds. Equine reproduction. Philadelphia, PA: Lea and Febiger; 1993:907–914.
38. Geiser D. Chemical restraint and analgesia in the horse. Vet Clin North Am Equine Pract 1990; 6:495–512.
39. Cutler G, Cassorla F, Ross J, et al. Pubertal growth: physiology and pathophysiology. Recent Prog Horm Res 1986; 42:443–470.
40. Salmeri K, Bloomberg M, Scruggs S, Shille V. Gonadectomy in immature dogs: Effects on skeletal, physical, and behavioral development. J Am Vet Med Assoc 1991; 198:1193–1203.
41. Line S, Hart B, Sanders L. Effect of prepubertal versus post pubertal castration on sexual and aggressive behavior in male horses. J Am Vet Med Assoc 1985; 186:249–251.
42. McDonnell S. Pharmacologic manipulation of sexual behavior. In: McKinnon A, Voss J, eds. Equine reproduction. Philadelphia, PA: Lea and Febiger, 1993:825–830.
43. Zumpe D, Clancy A, Bonsall R, Michael R. Behavioral responses to Depo-Provera, Fadrazole, and estradiol in castrated, testosterone treated cynomolgus monkeys (*Macaca fascicularis*): the involvement of progestin receptors. Physiol Behav 1996; 60:531–540.
44. Zumpe D, Clancy A, Michael R. Progesterone decreases mating and estradiol uptake in preoptic areas of male monkeys. Physiol Behav 2001; 74:603–612.
45. Roberts S, Beaver B. The use of progestins for aggressive and hypersexual horses. In: Robinson N, ed. Current therapy in equine medicine, 2nd edn. Philadelphia, PA: WB Saunders; 1987:129–131.
46. Miller C, Varner D, Blanchard T, et al. Effects of altrenogest on behavior and reproductive function in stallions. Proc Am Assoc Equine Pract 1997; 43:197–198.
47. Brady H, Johnson N, Whisnant C, et al. Effects of oral altrenogest on testicular parameters, steroidal profiles, and seminal characteristics in young stallions. Proc Am Assoc Equine Pract 1997; 43:195–196.
48. Dowsett K, Knott L, Tshewang U, et al. Suppression of testicular function using two dose rates of a water soluble

gonadotrophin releasing hormone (GnRH) vaccine in colts. Aust Vet J 1996; 74:228–235.
49. Malmgren L, Andresen O, Dalin A. Effect of GnRH immunisation on hormonal levels, sexual behaviour, semen quality and testicular morphology in mature stallions. Equine Vet J 2001; 33:75–83.
50. Pickett B. Factors affecting sperm production and output. In: McKinnon A, Voss J, eds. Equine reproduction. Philadelphia, PA: Lea and Febiger; 1993:689–704.
51. Pickett B. Collection and evaluation of stallion semen for artificial insemination. In: McKinnon A, Voss J, eds. Equine reproduction. Philadelphia, PA: WB Saunders; 1993:705–714.
52. Love C. Examination of the male reproductive tract: Evaluation of potential breeding soundness. In: Youngquist R, ed. Current therapy in large animal theriogenology. Philadelphia, PA: WB Saunders; 1997:12–15.
53. Hurtgen J. Semen collection in stallions. In: Samper J, ed. Equine breeding management and artificial insemination. Philadelphia, PA: WB Saunders; 2000:81–90.
54. Magistrini M. Semen evaluation. In: Samper J, ed. Equine breeding management and artificial insemination. Philadelphia, PA: WB Saunders; 2000:91–108.
55. Samper J. Artificial insemination. In: Samper J, ed. Equine breeding management and artificial insemination. Philadelphia, PA: WB Saunders; 2000:109–131.
56. Kohnke J, Kelleher F, Trevor-Jones P. Feeding horses in Australia. Kingston, ACT: Rural Industries Research and Development Corporation, 1999.
57. Riemann M, Kanstrup Hansen I. Effects on the foetus of exercise in pregnancy. Scand J Med Sci Sports 2000; 10:12–19.
58. Clapp J, Little K. Effect of recreational exercise on pregnancy weight gain and subcutaneous fat deposition. Med Sci Sports Exerc 1995; 27:170–177.
59. Squires E, McCue PM, Vanderwall D. The current status of equine embryo transfer. Theriogenology 1999; 51:91–104.
60. Aguilar J, Woods G. Embryo transfer in horses: Indications, techniques and expected outcomes. In: Youngquist R, ed. Current therapy in large animal theriogenology. Philadelphia, PA: WB Saunders; 1997:208–213.
61. Foss R, Wirth N, Schiltz P, Jones J. Nonsurgical embryo transfer in a private practice (1998). Proc Am Assoc Equine Pract 1999; 45:210–212.
62. Fleury J, Alvarega M. Effects of collection day on embryo recovery and pregnancy rates in a nonsurgical equine embryo transfer program. Theriogenology 1999; 51:261.
63. Carnevale E, Ramirez R, Squires E, et al. Factors affecting pregnancy rates and early embryonic death after equine embryo transfer. Theriogenology 2000; 54:965–979.
64. Woods G, Steiner J. Embryo transfers from mares in athletic competition. Cornell Vet 1986; 76:149–155.
65. Pashen R, Lascombes F, Darrow M. The application of embryo transfer to polo ponies in Argentina. Equine Vet J 1993; Suppl 15:119–120.
66. Squires E. Future equine reproductive technologies. In: Samper J, ed. Equine breeding management and artificial insemination. Philadelphia, PA: WB Saunders; 2000:283–292.
67. Palmer E, Bezard J, Magastrini M, Duchamp G. In vitro fertilization in the horse: A retrospective study. J Reprod Fertil 1991; Suppl 44:375–384.
68. Dell'Aquila M, Cho Y, Minoia P, et al. Intracytoplasmic sperm injection (ICSI) versus conventional IVF on abattoir derived and in vitro-matured equine oocytes. Theriogenology 1997; 47:1139–1156.
69. McKinnon A, Lacham-Kaplan O, Trounson A. Pregnancies produced from fertile and infertile stallions by intracytoplasmic sperm injection (ICSI) of single frozen/thawed spermatozoa into in-vitro matured mare oocytes. Proceedings of the 7th International Symposium on Equine Reproduction 1998; 137 abs.
70. Carnevale E, Maclellan L, Coutinho da Silva M, et al. Comparison of culture and insemination techniques for equine oocyte transfer. Theriogenology 2000; 54:981–987.
71. Carnevale E, Alvarenga M, Squires E. Use of oocyte transfer in a commercial breeding program to obtain pregnancies from mares with reproductive pathologies. Proc Am Assoc Equine Pract 1999; 45:200–202.
72. Lindsey A, Morris L, Allen W, et al. Hysteroscopic insemination of mares with low numbers of nonsorted or flow sorted spermatozoa. Equine Vet J 2002; 34:128–132.
73. Squires E, Todter G, Berndtson W, et al. Effects of anabolic steroids on reproductive capacity in young stallions. J Anim Sci 1982; 54:576–582.
74. Blanchard T. Some effects of anabolic steroids – especially on stallions. Compend Contin Educ Pract 1985; 7:S372–S380.
75. Garcia M, Ganjam V, Blanchard T, et al. The effects of stanozolol and boldenone undecyclenate on plasma testosterone and gonadotrophins and on testis histology in pony stallions. Theriogenology 1987; 28:109–119.
76. Snow D. Anabolic steroids. Vet Clin North Am Equine Pract 1993; 9:563–577.
77. Parssinen M, Seppala T. Steroid use and long term health risks in former athletes. Sports Med 2002; 32:83–94.
78. Papich M. Pharmacological considerations during pregnancy in small animals. Proceedings of the Annual Meeting of the Society for Theriogenology 1990; 224–235.

CHAPTER 62

Examination of the equine athlete prior to purchase

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- Aim and philosophy of the prepurchase examination.
- General approach and examination procedure.
- Special considerations and ancillary tests.
- Examination of different types of equine athlete.

A rigorous and thorough examination of the athletic horse by a veterinarian who understands and is familiar with the sporting endeavors of a particular athlete is a challenging and potentially troublesome task. With practice and diligence it can be a very rewarding professional and financial experience. In order to conduct such examinations proficiently, knowledge of the types of injuries and diseases affecting athletic horses and which may shorten or cause problems in a career should be understood. In this chapter the aim and philosophy of the prepurchase examination, general approach and examination procedure used, the use of special examination techniques and the differences in examination approach between various athletes will be discussed. The prepurchase examination of horses intended for breeding will not be discussed but has been reviewed elsewhere.[1,2]

Aim and philosophy

The selling and buying of athletic horses is essential for a vibrant and profitable equine industry. Breeders of horses strive to produce well-grown athletic individuals from superior blood lines in the hope of selling a product that will be successful on the racetrack, cross-country course or in the dressage arena. Horses are sold privately or at public auction sales. High-quality animals command high dollar prices from thousands to millions. Purchasers of high-quality animals want to ensure that their investment has a good chance of providing a successful return. Purchasers decide on the breeding, type and quality of the horse they desire and seek from the veterinarian an assurance that what they are about to buy does not have any problems currently or in the future that will inhibit the investment from performing up to expectation.

The ultimate decision on the purchase of any horse resides with the purchaser. As part of the decision-making process the veterinarian provides information to the purchaser on the health status of the horse. Successful athletes are seldom injury free and older athletes in particular have invariably suffered some 'wear and tear'. In the case of young unbroken athletes, a variety of congenital and acquired defects, which may interfere with an athletic career, might be present. For these reasons it should be understood by the purchaser that the veterinarian essentially conducts a *risk assessment* for the purchaser.

The aim of the examination of the equine athlete prior to purchase is to first identify, and second assess, the relative significance of factors of a veterinary nature, which at the time of examination might impair athletic performance in the occupation for which the horse is intended.[3] In addition, conditions that have the *potential* for impairment of athletic performance in the future should also be identified and an opinion of their significance made in light of the horse's intended use.[3–5]

The way in which the opinion of the examining veterinarian is presented to the purchaser has become very controversial. Unfortunately, it is a frequent perception by the purchaser that a veterinarian's examination prior to purchase provides a warranty that the prospective animal is free of all impediments currently and in the future and that such an examination in some way guarantees a risk-free purchase. This perception has been perpetuated to some extent by the use of the terms 'sound', 'suitable' or 'serviceable', all of which when used in the context of a prepurchase

examination imply a degree of warranty. Using these terms when giving an opinion may leave the examining veterinarian legally vulnerable if the horse should prove to be unusable by the purchaser and they are not recommended.[6] Another reason why it is unwise to use such terminology is that in many instances a complete examination of the horse to be purchased is not possible. Providing an opinion on suitability or serviceability based on an incomplete examination is fraught with difficulties.

The veterinarian should confine his or her opinion to the functional significance of relevant examination findings.[7] A decision to purchase the horse or a decision on the suitability or serviceability of a horse for a specific intended purpose is a business judgment that is the sole responsibility of the purchaser and is made on the basis of a variety of factors, only one of which is the report provided by the examining veterinarian.[6,7]

It is common to find some clinical problems in athletic horses. Rather than take the easy road of advising against purchase where problems are recognized it is better to provide the purchaser with a balanced assessment of risk. Probably the most practical method is to assign a measure of likelihood or percentage chance that an abnormality or clinical finding will impair athletic performance.[4,8] In forming such an opinion the veterinarian draws on her or his own experience, the experience of others and the scientific literature. For example, recent evidence suggests that the presence of dorsal medial intercarpal disease identified on presale radiographs of the carpus of Thoroughbred yearlings is associated with a 20% chance of an affected horse not starting a race.[9]

It should be noted that the way in which the veterinary opinion is presented to the purchaser differs around the world. The variation often reflects the results of court decisions in cases of dispute and the establishment of legal precedent.[6] For example, the British Equine Veterinary Association recommends that the opinion given on examination for purchase be that a horse is 'suitable or unsuitable' for the purpose for which it is intended.[3] The equine industry accepts this method and the British legal system recognizes it as reasonable.[10]

Requirements for the prepurchase examination

In order to perform a successful prepurchase examination a number of requirements should be met and include the following:[10]

- Clear communication with the purchaser or purchaser's agent, vendor or vendor's agent before, during and after the examination. This communication should be both verbal and in writing. The limitations of the veterinary examination should be discussed with the purchaser together with an explanation of how the examination findings will be reported. The results of the examination are privileged and confidential and are the property of the purchaser.
- If the vendor is a client of the veterinarian (current or past) this represents a potential conflict of interest. All parties should be consulted and if the examination is to go ahead this agreement should be made in writing.
- Written confirmation of what portions of the examination the purchaser requires (see buyer's statement in Appendix at the end of this chapter). The requirement of additional ancillary tests should be indicated. Where regular examination procedures are unable to be performed (e.g. horse is not broken to lead) this should be detailed in the written report furnished to the purchaser. Other than for young stock, the horse should be in full athletic work and it is unwise to perform examinations on animals not in regular work because previous lameness or back problems may not be apparent.[8] These issues should be discussed carefully with the purchaser or purchaser's agent.
- A vendor's statement (see Appendix) should be completed in writing prior to examination of the horse.
- It is ideal although often not possible to have the vendor and purchaser present during the examination. A methodical and thorough examination process is required which includes examination before and after strenuous activity, preferably similar to that performed by the horse in its chosen occupation. Adequate personnel and conditions throughout this procedure are necessary.
- A thorough knowledge of the intended use of the horse.
- The veterinarian should have the skill necessary to differentiate normal and abnormal variations in physical and gait evaluations and be able to relate these to the horse's intended use so that an assessment on current and future performance can be made.
- Precise and detailed recording of examination findings.
- Be able to advise on the necessity of ancillary diagnostics and perform these or refer on for specialist examination.
- If the horse is to be insured or is being purchased for resale these issues should be discussed thoroughly with the purchaser. While some conditions identified during the examination will be acceptable risks for a certain intended use they may cause problems if the horse is to be insured or resold. For example, a distal intermediate ridge osteochondral fragment not resulting in clinical signs may be a low risk for purchase in a Thoroughbred yearling that is to be trained and raced by the buyer. If the purchaser, however, intends to condition the horse and sell it in a '2 year old in training sale' such a radiographic finding might deter a future purchaser. In addition, an insurance exclusion could be put in place on such a horse if the purchaser opted to surgically remove this fragment prior to further sale.

Examination procedure

Veterinarians use a variety of protocols for examination of the athletic horse prior to purchase.[6–8,11,12] Some veterinary societies recommend a standardized procedure that should be

used by their members.[7,8,11] By following such methods a degree of protection is afforded the veterinarian in case of litigation and a standard method reduces the chances of missing problems. However, other veterinary associations such as the American Association of Equine Practitioners have not produced an official step-by-step protocol because of the legal ramifications that may arise if a veterinarian did not strictly adhere to the policy. In addition, by not using a standard protocol veterinarians are free to adopt their own methods of examination.

One method used by the authors, and one that has been well accepted in Australia, New Zealand and Great Britain, is based on a five-stage procedure and this is described below.

Stage 1. Preliminary examination

An accurate description of the horse is required. A vendor's statement should be completed. The current state of work should be noted and the resting examination conducted. This part of the examination is usually performed within the horse's stall or stable having been at rest for at least 30 min. Access to a dark area is useful for examination of the eyes. A nose to tail examination should be conducted and the hands passed over every part of the body. Each foot should be picked up, examined and a hoof tester applied. The limb joints are checked for effusion and flexed to detect pain or limitation of movement. The palmar/plantar flexor tendons, ligaments and soft tissues are evaluated for swelling, heat and pain. The accompanying checklist (see Appendix) should be followed precisely so that no part is overlooked. With experience the veterinarian develops an automatic inspection procedure. The horse is then brought out of the stable and inspected thoroughly from all sides. Conformation is evaluated with the horse standing on a level surface. At this stage if any obvious defect is present which would impair the function of the animal the examination is stopped with the consent of the purchaser. The premature termination of the examination and the reason is explained in the report.

Stage 2. Examination during walking, trotting, turning and backing

A competent attendant should handle the horse. The horse is walked 20 m away from the examiner and then back. The horse should be viewed from the front, back and sides. The horse is then trotted for 30–40 m and trotted back and then trotted in a circle both ways. The horse should be turned one way and then the other in tight circles and then backed a few paces. Coordination and proprioception are carefully assessed and to test for hindlimb strength a 'tail pull test' is used. Following this a full series of flexion tests as outlined in the guidelines are performed. The significance and interpretation of flexion tests are controversial. Force applied, duration of application, age and work history can all influence the outcome of these manipulations. Flexion tests should not be interpreted in isolation. Positive flexion tests without concurrent lameness or other clinical abnormalities may have little clinical significance.[13] In our hands flexion tests have proved useful to detect signs of disease. The radiograph in Fig. 62.1 shows a subchondral cyst-like lesion in the proximal phalanx of a 2-year-old unbroken Paint gelding that had been paddock rested for 12 months. A repeatable response to forced flexion and lameness following this was the only sign evident. Joint effusion was not present.

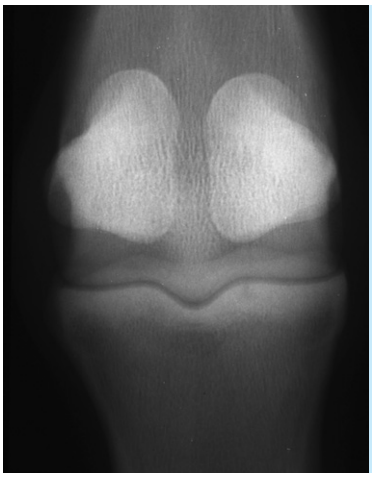


Fig. 62.1 Dorsopalmar view of the right front fetlock of a 2-year-old Paint gelding. Note the small subchondral lucency communicating with the fetlock joint in the medial proximal aspect of the first phalanx. A positive distal limb flexion test was present in this horse.

The clinician should develop a consistent and repeatable technique and this is probably the best way of achieving reproducible results. If during this examination signs of lameness are present the examination may be terminated. Sometimes the purchaser wishes to continue with the examination – this is ill advised – but if the purchaser or vendor wishes to know the source of the lameness, the format, cost and person responsible for payment of this extra examination needs to be clarified.

Stage 3. Examination during and immediately after strenuous exercise

Within the confines of the animal's age, condition, training, fitness and only after the vendor's consent, exercise of sufficient intensity and duration should be performed so as to:

- induce rapid deep breathing so that unusual breathing sounds can be heard
- tire the animal so that strains and injuries and other exercise-related problems (e.g. epistaxis) may be revealed after a period of rest
- increase the action of the heart so that exercise-related cardiac abnormalities may be detected, e.g. atrial fibrillation.[7]

Examples of such exercise for the race horse include a sufficient warm-up followed by a gallop for 400–600 m. The examiner should position himself or herself close to the horse to observe and listen to the breathing pattern. A normal horse has only a single respiratory sound heard on expiration. When an inspiratory sound is heard this typically is due to impaired arytenoid function (e.g. laryngeal neuropathy).

Upper respiratory tract obstruction that results in loud inspiratory and expiratory sounds can be caused by conditions such as intermittent epiglottic entrapment, arytenoid chondritis or pharyngeal collapse. Excessive production of airway secretions and alar fold collapse are other possibilities. The horse should be pulled up as quickly as is safe and the breathing pattern closely observed to detect sounds of dorsal displacement of the soft palate, inspiratory noises typical of laryngeal neuropathy, abnormal nasal discharge and signs of respiratory distress. The horse should then have an endoscopic evaluation. Untrained animals, those too young or unable to be ridden should be lunged and the duration and intensity of exercise recorded.

Stage 4. Examination during the period after exercise

The animal should be allowed to 'cool down' quietly over a period such that respiratory and heart rates return to normal. A crude assessment of fitness and respiratory function can be made by evaluating heart and respiratory rate over this period. This period allows for any injuries or musculoskeletal problems to 'stiffen up' (e.g. degenerative changes within the fetlock joints).

Stage 5. The final examination during walking, trotting, turning and backing

The horse is examined as in stage 2 paying careful attention to any signs of lameness. Lunging in the circle both ways for a few rounds is also advised. Hoof tester and flexion tests may be repeated if signs of lameness are present.

Avoiding problems in the prepurchase examination

Examination of claims made against veterinary surgeons relating to the prepurchase examination show they are of two broad types.[14] In the first instance the veterinarian is accused of not detecting an abnormality that subsequently becomes a problem. This most commonly relates to lameness occurring soon after purchase. A careful and thorough examination procedure should help reduce the chances of inadvertently making such errors. Testing for drug administration may also act as a deterrent to the use of agents that may hide lameness problems or help confirm the presence of such agents at the time of examination.

In the second instance the complaint is that the purchaser was not informed of a condition or abnormality (e.g. sarcoid) that could become a problem. To avoid this situation good communication before, during and after the examination with the purchaser is necessary. Most importantly the limitations of the examination procedure must be carefully discussed. Having a clear understanding of the expectations and intentions of the purchaser with respect to the future use and training of the horse is critical.

Another frequent problem is dissatisfaction expressed by the vendor. This may be that the veterinarian improperly discriminated against the horse in question by providing the purchaser with incorrect opinions regarding the significance of the clinical findings of the examination. Such examples include the diagnosis of lameness, response to flexion tests, significance of conformational defects and opinion on the significance of radiological findings. It must be remembered that the vendor is of course trying to *sell* the horse and a balanced opinion regarding any defect or abnormality present is naturally tainted by some bias.

Notwithstanding this, it behooves the examining veterinarian to confine his/her opinion to fact, which is supported by experience and knowledge of the scientific literature. A second opinion from a respected colleague may be very useful. Because opinions between veterinarians differ it is best to confine any opinion given in terms of the degree of risk that any defect or abnormality may have currently or in the future on athletic performance. It is recommended that the veterinarian does not express his or her opinions relating to the outcome of the examination procedure to the vendor.

Special considerations and ancillary tests

Conformation assessment

The assessment of conformation is a very important part of the prepurchase examination. Many veterinarians believe that conformation, or more specifically, deficiencies in conformation, play a significant role in the maintenance of athletic soundness and contribute to the ability of elite performers. For example, it is well known that some conformational faults predispose athletic horses to injuries and lameness.[15–19] In addition, many astute observers of horses believe that the way horses are 'put together' has a major effect on how successful they are in various disciplines.[16,19] Unfortunately, objective scientific data to support these commonly held opinions is limited. Moreover, very talented individuals appear to compensate for deficiencies in conformation. It is probably true to say, however, that marked discrepancies from what is considered optimal conformation result in injuries that limit athletic performance. Limitations in the short term, especially in gifted individuals, can be overcome, but in the long term recurrent injury and lameness is more likely. Issues relating to the conformation assessment of various athletic horses are discussed below under the examination of each athlete. The reader is directed to more extensive recent reviews on the subject.[15–19]

Laboratory evaluation

Although a variety of laboratory evaluations may be useful as ancillary aids during the prepurchase examination,[20,21] drug testing and those tests required for insurance purposes or certification of disease status when horses are transported between states or countries are the most common. Blood tests such as evaluation of the hemogram, plasma fibrinogen and

serum chemistry are not routinely performed but would be indicated to determine if observed clinical symptoms were significant, e.g. nasal discharge, cough, elevated rectal temperature or submandibular lymph node enlargement. The vendor's permission should be sought and, to avoid confusion with the interpretation of results, blood should be collected prior to exercise.

Because equine athletes are frequently medicated and because unscrupulous vendors might use drugs to mask musculoskeletal pain, many purchasers now request drug testing. Drug testing is thought to provide insurance against 'foul play' but the purchaser should be advised carefully as to the limitations associated with such testing. For instance, the range of drugs tested by some laboratories may be limited (e.g. only testing of non-steroidal anti-inflammatory agents), testing is expensive, results are not immediate, some drugs are difficult to detect (e.g. some intra-articularly injected agents) or are no longer traceable but still exert a pharmacologic effect. Therefore, a negative test is not always commensurate with an animal that has not been medicated. Blood is usually the fluid sampled but in fact urine, although more time-consuming to collect, is the preferred sample because many drug metabolites are concentrated in urine and many agents can be detected for extended intervals in urine.

It is probably always wise to take a blood sample at the time of examination.[20] The simple act of collecting the sample, especially if the vendor is advised in advance, can have a deterrent effect. If the purchaser does not want the sample tested it should be kept for at least 2 weeks in case they change their mind. If testing is requested the samples should be packaged appropriately and dispatched by courier immediately. Regardless of when the sample is tested the process must be transparent and the vendor and purchaser should have an opportunity to witness collection and each party should acknowledge this by signature on any paperwork and on the tubes of collected blood. In some countries (e.g. Britain) a standardized collection process is used.[8]

The Coggins test for equine infectious anaemia (EIA) needs to be performed on horses that will travel interstate. For those horses imported into the USA and which might compete internationally, tests for piroplasmosis, dourine, glanders and EIA should be performed. When breeding stock are examined, tests for equine viral arteritis and contagious endometritis may be required.[8,20] In each case the client should be warned about the cost of such tests and the delays that testing might incur. Horses would ideally not be purchased until the results of such tests were known.

Examination of the cardiovascular system

During the clinical examination before and after exercise the cardiovascular system should be carefully examined. Chapter 32 discusses the evaluation of the cardiovascular system in detail. Principally the examiner determines if there is evidence of overt cardiac disease (elevated resting heart rate, elevated resting respiratory rate, distended jugular veins, dependent edema and exercise intolerance) cardiac murmurs or cardiac arrhythmias. Second it is important to differentiate between physiologic cardiac murmurs and arrhythmias and those that are pathologic. Where there is doubt an electrocardiographic examination and an echocardiographic examination may be required. It is advisable to seek specialist opinion in these areas. The following points should be kept in mind:[22]

- Physiologic murmurs (flow murmurs) are usually localized, of low intensity (grade 1 and 2), short in duration and sometimes musical. They are usually early to mid systolic, early diastolic or presystolic.
- Pathologic murmurs are often (but not always) louder, radiating and holo-pansystolic (mitral and tricuspid valve regurgitation) or holodiastolic (aortic valve regurgitation).
- Mild localized regurgitant murmurs may be associated with a low risk for athletic performance. Echocardiography is best.
- Sinus arrhythmia, sinus block and second-degree atrioventricular block are relatively common and of no clinical significance.
- Atrial fibrillation and premature beats (atrial premature complexes, ventricular premature complexes) are usually not acceptable in athletic animals. Exercise or 24-hour electrocardiographic examinations may be required to determine clinical significance.

Imaging and the prepurchase examination

The most common ancillary diagnostic aid used to evaluate the musculoskeletal system in the prepurchase examination is radiography. Radiography was performed in 49% of all prepurchase evalutions in one review[23] and this was more likely if the examination was performed at a clinic. The principal indications or reasons for prepurchase radiography include:[24]

- Clinical examination findings indicating an abnormality that requires quantification/clarification (e.g. fetlock joint effusion with pain on flexion).
- Intended use of horse (e.g. dressage competitor versus low-level pleasure horse).
- In young unbroken horses or in horses unable to be rigorously exercised, or athletic horses that have been rested, survey radiographs may help identify clinically silent or quiescent lesions which may cause future problems when training starts or is recommenced.
- Client's instructions. Clients may instruct the examining veterinarian to perform a radiographic examination. The reasons for this can be many and include the desire to sell the horse in the future, previous bad experiences or because of advice from others.[24]
- A standard set of radiographs is required as part of the examination of Thoroughbred horses being exported for racing to some countries (e.g. Hong Kong and Macau).
- Purchase price.

The routine use of radiography in the prepurchase examination can be problematic. Opinions differ as to the reliability of radiographs to be of predictive value for future athletic

soundness.[24] Some veterinarians believe that radiography should be avoided if it will not influence the opinion given on clinical grounds. The added expense and the possibility that radiographs will only 'confuse the picture' especially if questionable changes are identified should also be considered. Regardless of these issues, radiographic lesions or changes can only be properly interpreted when combined with examination findings and clinical history. Radiographs by themselves may be meaningless. In addition, high-quality images with sufficient views are required.[25] The minimum number of radiographic views required to examine a specific anatomical site during prepurchase radiography are presented in Table 62.1.[24,25] The radiographs must be permanently marked with the name or number of the horse, date, name of the veterinarian or veterinary hospital and identification of the leg examined. A method for recognizing which oblique view has been taken (e.g. always placing markers on the lateral aspect of the film) is necessary. The radiographs belong to the veterinarian and are part of the animal's medical record and need to be kept for the period determined

Table 62.1 Minimum recommended radiographic views for prepurchase radiography

Distal phalanx	
Lateromedial	LM
Dorsoproximal – palmaro (plantaro) distal oblique	Upright pedal or D45° Pr-Pa (PL) Di O
Dorsopalmar (plantar)	DPa (PL)
Navicular bone	
Lateromedial	LM
Dorsoproximal – palmaro (plantaro) distal oblique	Upright pedal or D60° Pr-Pa (PL) DiO
Palmaro (plantaro) proximal – palmaro (plantaro) distal oblique	Pa45° Pr-Pa (PL) Di O
Pastern	
Specific views of the pastern can be taken. The horse should stand squarely on wooden blocks. However, for survey purposes the pastern is often included in views of the foot or the fetlock	
Lateromedial	LM
Dorsopalmar (plantar)	DPa (PL)
Dorsolateral – palmaro (plantaro) medial oblique	D45°L- Pa (PL) MO
Dorsomedial – palmaro (plantaro) lateral oblique	D45°M- Pa (PL) LO
Fetlock	
Lateromedial or flexed lateromedial	LM
Dorsoproximal palmaro (plantaro) distal oblique	D30° Pr- Pa (PL) Di O
Dorsoproximal lateral – palmaro (plantaro) distomedial oblique[a]	D5° or 10°Pr45°L- Pa (PL) Di MO
Dorsoproximal medial – palmaro (plantaro) distal lateral oblique[a]	D5° or 10°Pr45°M- Pa (PL) Di LO
Metacarpus/metatarsus	
Lateromedial	LM
Dorsopalmar (plantar) palmaro (plantaro)	DPa (PL)
Dorsolateral – palmaro (plantaro) medial obilque	D45°L- Pa (PL) MO
Dorsomedial – palmaro (plantaro) lateral oblique	D45°M- Pa (PL) LO
Carpus	
Lateromedial	LM
Flexed lateromedial	Flexed LM
Dorsopalmar	DPa
Dorsolateral – palmaromedial oblique	D30° or 45° L – Pa MO
Dorsomedial – palmarolateral oblique	D30° M – Pa LO
Flexed dorsoproximal – dorsodistal oblique	Flexed D 30° Pr – DdiO (skyline of C3)
Tarsus	
Lateromedial	LM
Dorsoplantar	DPL
Dorsolateral – plantaromedial oblique	D45° L – PL MO
Dorsomedial – plantarolateral oblique	D55° M – PL LO
Stifle	
Lateromedial	LM
Caudocranial	Cd Cr or
Caudolateral – craniomedial oblique	Cd 30° L – Cr MO

[a] By angling the X-ray beam distally by 5° in the front fetlocks and 10° in the hind fetlocks the palmar or plantar aspect of the proximal phalanx can be clearly visualized to identify bone fragments at this site.

Table 62.2 Estimate of risk that various observed radiological changes result in reduced athletic performance[a,b]

Region	Radiological diagnosis
Distal phalanx	■ **Laminitis**[26] – high. ■ **Pedal osteitis complex/concussive trauma**[26] – moderate – manageable. ■ **Hoof imbalance** – low to moderate – manageable. ■ **Degenerative joint disease (DJD) distal interphalangeal joint**[26] – high. ■ **P3 Osseous cyst like lesions**[26] – if communicate with joint risk is high. Upright pedal or D45° Pr-Pa (PL) DiO required. ■ **Ossification of hoof cartilages**[26] – low. ■ **Mineralized opacities adjacent to extensor process of P3**[24,26] – low, usually insignificant. ■ **Round smooth densities adjacent to palmar processes** – low, secondary centers of ossification or old fracture.[26,27]
Navicular bone	**Navicular syndrome** – controversial since radiological changes can be similar in sound and lame horses. Those most likely to be significant include:[24–26] ■ Increased number of enlarged synovial fossae. ■ Medullary sclerosis/loss in corticomedullary definition. ■ Medullary lucency. ■ Flexor cortex erosions/new bone formation. ■ The above changes in combination with clinical findings are indicative of navicular disease/syndrome which represents a high risk for impairment in future athletic performance.
Pastern	■ **DJD** – generally risk is high. Proximal P2 osteophytes may be incidental in Warmbloods.[8] ■ **Osseous cyst-like lesions (distal P1 or proximal P2)** – risk is high if communicate with proximal interphalangeal joint (especially if medial or lateral of midline) and if accompanying evidence of DJD, low if isolated from joint. Centrally located cyst-like lesions in the distal aspect of P1 in yearling Thoroughbreds appear to have a low risk for future lameness. ■ **Osteochondral fragments palmar/plantar eminence of proximal P2** – risk is low–moderate.[28]
Fetlock	■ **DJD**[26] – Generally risk is moderate–high in any performance horse. If supracondylar lysis and osteophyte formation on the sesamoid bones are present, risk is high. Reduced risk if only slight modeling, correlate with age, occupation and clinical findings. ■ **Palmar/plantar proximal P1 fragments** – origin may be proximal sesamoid bones or P1, can be articular or non-articular and could be avulsion fragments or OCD. Risk is considered low and articular fragments can be removed arthroscopically with a good prognosis. Little effect on ability to start a race (presale findings in Thoroughbred yearlings[9]) and little effect on racing performance in Standardbreds.[29] ■ **Ununited proximoplantar tuberosity** – suggested clinical significance 12.5%[30] when recognized in young animals. May heal back to parent bone in young animals. Correlate with exam findings. Evidence of periosteal proliferation, calcification of distal sesamoidean ligaments and articular involvement increases risk. ■ **Proximal dorsal P1 fragments** – possibly developmental in yearlings but most likely traumatic in adults. Risk is low if other signs of DJD are absent. Correlate with age, occupation and exam findings. Prognosis following arthroscopic removal is very good.[9,25,26] ■ **OCD** – distal MC3/MT3 and distal 2/3 of MC3/Mt3 sagittal ridge[9] – risk is variable. Large defects, those with fragments and those showing subchondral bone changes represent a moderate–high risk. Follow-up on yearling Thoroughbreds and Standardbreds showed these changes to have little effect on starting a race (Thoroughbred) or on racing career (Standardbred) – amenable to surgery with a reasonable prognosis.[9,25] ■ **Osseous cyst-like lesions of Mc3/Mt3 and proximal P1** – risk is high if communicate with articular surface. Some cysts, however, can be incidental findings.[25]
Proximal sesamoid bones	■ **Sesamoiditis**[26] – conflicting opinion and research evidence on risk. Proposed etiology varies between occupations.[26,31–34] Radiological changes include osteophytes, enthesophytes, osteolysis and enlarged vascular channels. If multiple changes ultrasound of suspensory apparatus is warranted. Correlate with age, occupation, conformation (e.g. upright pasterns), exercise history and exam findings. Increased numbers of enlarged, irregular vascular channels especially if enthesophytes are present represent an increased risk.[9,34] Check for DJD of fetlock joint. Presale radiography of Thoroughbred yearlings showed > 50% of proximal sesamoid bones had irregular vascular channels but this did not affect the ability of horses to start a race when 2 or 3 years old.[9] Young Standardbreds with sesamoid changes showed improvement over time and earnings as 3- and 4-year-old horses were not different to those horses without sesamoid changes.[33] ■ **Fractures**[32] – sesamoid fractures identified on presale radiographs of yearling Thoroughbreds did not appear to influence the ability to start a race at 2 or 3 years of age.[9] These fractures (some of which may be separate centers of ossification), often occur when the horse is a foal and healing can result in a complete bony union.[32] An elongated or malshaped sesamoid bone can result if the fracture was displaced. Ability to start a race was not affected by these changes.[9] Hindlimb apical sesamoid fractures in particular appear to be low risk.[9] Fracture size, position and evidence of other changes should be evaluated in young horses to estimate risk. In mature horses sesamoid fractures are often clinically significant and careful evaluation of the suspensory apparatus and fetlock joint is required.

Table 62.2–cont'd.

Region	Radiological diagnosis
Metacarpus/ metatarsus	■ **Exostoses/splints**[26] – active splints represent a short-term moderate–high risk for impaired athletic performance. Palmar soft tissues may require ultrasonography. ■ **Proximal MT3/MC3 sclerosis**[26] – may alert clinician to conduct an ultrasound of the proximal suspensory ligament but the presence of this change alone may have little clinical significance.
Carpus	■ **DJD**[26] – generally risk is moderate–high for any performance horse. Mild changes, including mild articular osteophyte production, especially in the radiocarpal joint, have reduced risk. Assess with respect to age, conformation, occupation, work history and intended use. Smooth/mature non-articular enthesous bone formation on dorsal carpal bones – low risk.[24] Some third carpal bone sclerosis in race horses is expected. Significant focal lucency and marked loss of trabecular pattern – high risk. Presale radiography of yearling Thoroughbred race horses showed the presence of dorsal medial intercarpal disease reduced the chance of starting a race at age 2 or 3 by 20%.[9] ■ **Osseous cyst-like lesions** – can affect any of the carpal bones, usually incidental findings.[24] Osseous cyst-like lesions of the radial carpal bone or distal radius may cause lameness – correlate with clinical signs.
Tarsus	■ **DJD (tarso-metatarsal and distal intertarsal joints)**[26] – generally risk is moderate – high for any performance horse. Assessment of risk can be difficult based on radiographs alone because correlation between radiographic findings and lameness is poor. Therefore, clinical examination, age, occupation and exercise history is important. Smooth mineralized enthetic osteophytes on the dorsoproximal aspect of MT3 may be incidental findings without other articular changes – risk is low.[25] Thoroughbred yearlings with evidence of osteophyte or enthesophyte formation at the distal intertarsal or tarso-metatarsal joint margins were significantly less likely to start as 2- or 3-year-olds (difference was 7%).[9] The presence of periarticular osteophytes dorsomedially in Icelandic Ponies had a 53% predictive value for lameness.[35] ■ **OCD**[26] – generally risk for affecting athletic performance is considered low–moderate but site, size, subchondral bone changes and other joint changes should be considered. Studies in conservatively treated Standardbred race horses that were evaluated as young horses show racing performance to be similar to unaffected horses.[29,36] Other studies show mild reductions in earnings and numbers of starts (especially in 2-year-olds).[37,38] Small or well-attached fragments are low risk but effusion and lameness may result (unpredictably) when workload increases.[24] Evidence of OCD of the tarsus had little effect on the ability of a Thoroughbred yearling to start as a 2- or 3-year-old.[9] Success rates following arthroscopic surgery are good (75–80%).[39] ■ **Wedged, third and/or central tarsal bones** – represents a moderate–high risk for reduced athletic performance and may predispose to fractures.[40]
Stifle	■ **OCD (osteochondritis dissecans)**[26] – most horses show clinical signs within the first 2 years of life. However, clinical signs can manifest at any age. In addition, radiographic changes may correlate poorly with intra-articular pathology. Therefore, clinical examination findings are most important and should be assessed together with site, size, subchondral bone change, presence of concurrent DJD, age, occupation and exercise history to assess risk. Mild changes (flattening, irregularity) without effusion – low risk. Larger lesions have higher risk. Prognosis for successful athletic performance following stifle arthroscopy is approximately 64%.[39] ■ **Subchondral cystic lesions (SCL)** – although some SCLs may be asymptomatic, all SCLs of the stifle (medial femoral condyle, proximal tibia) have a moderate to high risk for affecting future athletic performance. Communication with the articular surface increases the risk. In addition, surgical therapy (arthroscopic debridement) only carries a 56–74% success rate for successful athletic performance.[41] Shallow concavities of the distal medial femoral condyle without underlying subchondral changes on the articular surface are generally insignificant.[24] ■ **DJD**[26] – risk is high and treatment only palliative.

[a] All conditions should be assessed in light of the clinical examination. Only rarely do radiographic lesions by themselves allow a complete assessment of risk. Assessment of risk has been generalized for each condition. However, each horse should be evaluated as an individual.
[b] Cited references describe aspects of the radiographic, radiological or clinical features of each condition.

by the statute of limitations for the state or locality in which the veterinarian lives.

What are we looking for on prepurchase radiographs that may result in a reduced capacity to perform as an athlete? When viewing radiographs during the prepurchase examination a thorough examination of each film is performed.[26] Significant radiographic abnormalities associated with the appendicular skeleton of the horse have been reviewed.[26] Any abnormalities should be described in terms of size, shape, position, density and relationship to adjacent structures. With respect to the athlete, however, there are a number of recognized conditions or anomalies observed on radiographs that carry a degree of risk for reduced athletic performance (Table 62.2).[24–26] The examiner should look carefully for the presence of developmental orthopedic disease (age, breed and joint specific), osteoarthritis or evidence of 'wear and tear', fracture and bone modeling. In young untrained animals developmental orthopedic disease must be conscientiously ruled-out. In animals that have performed, especially older animals, osteoarthritis and 'wear and tear' injuries are important.

Limitations and problems associated with prepurchase radiographs Radiographic evaluation in the prepurchase environment has a number of limitations and these should be discussed with the purchaser. Routine radiographic views may not detect all lesions, apparently normal radiographs do

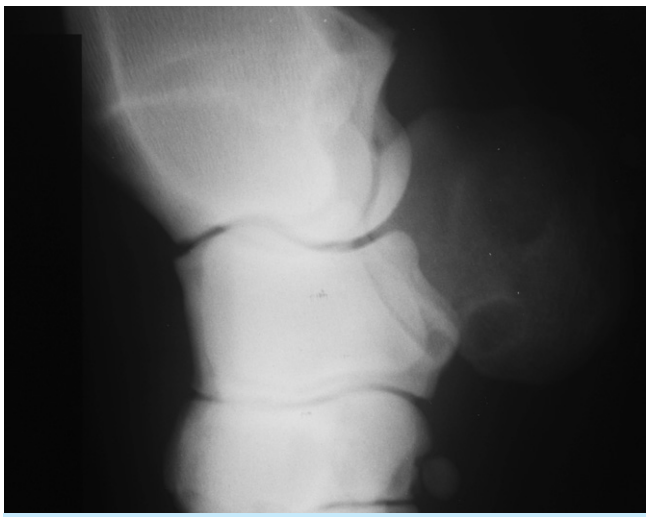


Fig. 62.2
Lateral to medial view of the left carpus of a 4-year-old dressage horse. Note the two, large, circular lucencies present in the accessory carpal bone. No clinical signs were associated with these findings.

not always exclude pathological processes (e.g. developing lesions may not be detected) and apparently abnormal findings may not have current or future clinical relevance. For example, Fig. 62.2 shows a radiograph of a lateral to medial view of the left carpus of a 4-year-old dressage horse. There are two, large, well-circumscribed lucencies in the accessory carpal bone. These are unlikely to be of clinical significance and the horse did not show any pain to palpation of the accessory carpal bone or lameness after carpal flexion. Another example of an obvious radiological lesion that is not necessarily clinically significant is shown in Fig. 62.3. An old apical fracture of the medial proximal sesamoid bone in the right hind leg of this 2-year-old Thoroughbred race horse is present. The horse was purchased at a public auction sale as a yearling and has shown no lameness or clinical signs associated with this joint. The best way of deciding on current clinical significance of a radiographic change is to match it carefully with the physical examination. This is why a rigorous five-stage examination is useful.

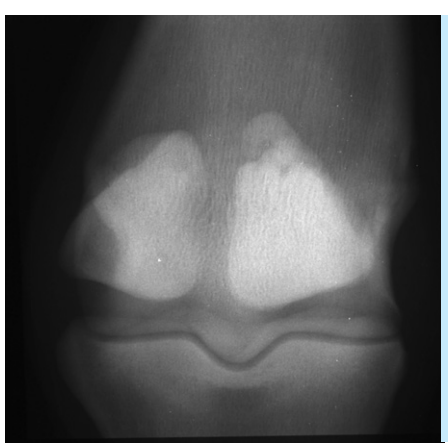


Fig. 62.3
Dorsoplantar view of the right hind fetlock of a 2-year-old Thoroughbred race horse. Note the old apical fracture of the medial proximal sesamoid bone. No clinical signs were associated with this finding.

More challenging is predicting the likelihood that radiographic changes will become a clinical problem when dealing with a young unproven animal that has not yet been subjected to training. This difficulty is compounded by the paucity of objective information relating radiographic changes with future athletic performance. The combination of physical examination, conformation analysis, intended use and published information is used to provide the prospective purchaser with an opinion on the level of risk a particular radiographic change might pose. For example, the radiograph in Fig. 62.4 shows an osteochondral fragment typical of osteochondritis dissecans (OCD) associated with the distal aspect of the medial malleolus in the tarsus of a 4-year-old Warmblood dressage horse that has had 6 months of basic training. Given the age of the horse, the fact there was no lameness on clinical examination, no effusion and no response to a hock flexion test, the client was advised that the OCD was not currently a clinical problem and the risk for future problems was considered low (less than 25%). Surgical removal carried a predicted success rate of approximately 80% if a problem developed. In contrast, Fig. 62.5 shows a dorsomedial-palmarolateral oblique radiographic view of the right front fetlock in a 2-year-old Thoroughbred race horse examined prior to purchase and export to Hong Kong. The medial proximal sesamoid bone shows evidence of moderate sesamoiditis with a focal lucency within the abaxial part of the bone. The palmar border of the sesamoid is irregular. This horse had a positive distal limb flexion test and was painful to focal pressure applied to the sesamoid bone. The risk for future lameness related to these findings was considered moderate to high.

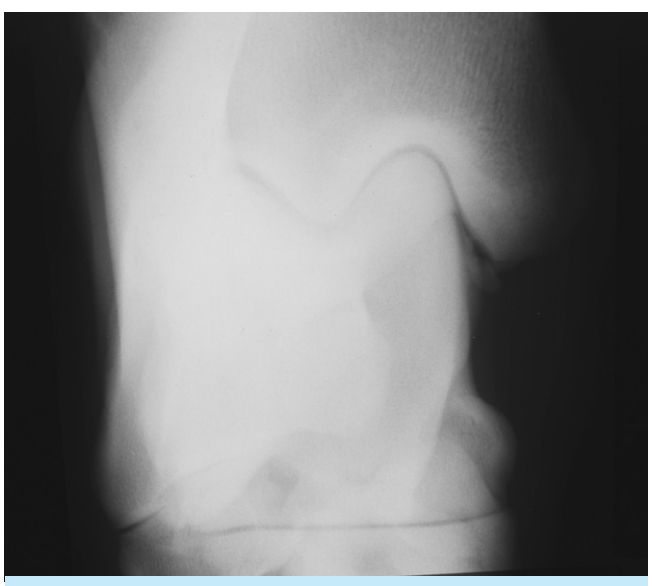


Fig. 62.4
Dorsoplantar view of the right hock of a 4-year-old dressage horse. Note the osteochondral fragment associated with the distal medial malleolus. This is typical of osteochondritis dissecans. There was no tarsocural joint effusion and a hock flexion test was negative.

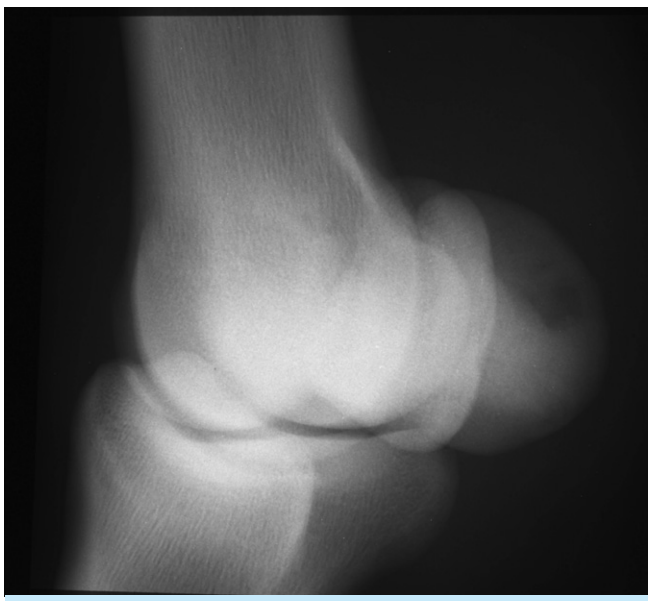


Fig. 62.5
Dorsomedial–palmarolateral oblique view of the right front fetlock of a 2-year-old Thoroughbred race horse. Note the abnormal lucency in the abaxial part of the proximal medial sesamoid bone. The palmar border of the bone is also irregular. This change is typical of sesamoiditis and carries a moderate–high risk for future lameness problems. Pain could be elicited on deep palpation of this bone.

By giving purchasers an assessment of risk, rather than a 'pass or fail' opinion, the veterinarian can help facilitate a successful sale. However, the acceptance of risk by the purchaser can be variable and depending on the experience of the purchaser there is also a variable level of tolerance to faults or problems a horse may have. It may be advisable to seek more than one opinion on radiographic changes or send the films for review to a radiologist or surgeon.

Other imaging modalities

While not routine, ultrasonographic evaluation of the soft tissue structures distal to the carpus and hock has been performed with increasing frequency as part of the prepurchase examination in recent years. Common use of ultrasonography in equine practice, availability of good equipment and an expanded understanding of the importance of soft tissue musculoskeletal injury in athletic horses probably accounts for this. Indications for use include:[42]

- abnormalities identified during the clinical evaluation; careful palpation and comparison between limbs is required
- history of a previous injury
- at the purchaser's request.

In addition, some veterinarians recommend ultrasonographic examination in circumstances when they suspect an injury could be present but which is not reported (e.g. event horses or race horses that have been absent from competition for extended periods, were competing but have not competed recently, or where there is an unexplained reduction in work intensity).[8,42]

It is important that the veterinarian is familiar with the requirements for distal limb ultrasonography[42,43] including equipment, scanning technique and permanent image recording. Image interpretation requires considerable experience. Acute and chronic tendon or ligament injury may have major consequences for future athletic performance. The site, severity, age and state of healing of any injury, together with the intended use of the horse, will determine the risk assessment for future problems in an individual case.

Nuclear scintigraphy is another imaging modality that could be utilized in the prepurchase examination.[25] It is not generally used and the potential use as a 'screening tool' in the context of a prepurchase examination would be problematic and is not recommended. Expense and limited availability also preclude widespread use. However, in certain circumstances nuclear scintigraphy might be valuable and these include:

- assessing the current clinical significance of apparent radiological lesions or palpable osseous abnormalities
- assessing degree of healing of a previous injury, e.g. stress fracture of the pelvis or a dorsal metacarpal stress injury ('bucked shins')
- differentiating between chronic fractures and multipartite anomalies.[25]

Endoscopic examination of the upper respiratory tract and trachea

The use of endoscopy in the prepurchase examination is variable. Some veterinarians believe that endoscopy is only indicated if clinical examination findings determine that it would be useful (e.g. nasal discharge following exercise, abnormal respiratory noise heard at exercise). However, some abnormalities of the upper respiratory tract are not always associated with an abnormal respiratory noise, especially if the horse is not exercised fast enough. These might include ethmoid hematoma, mild arytenoid chondritis, some tumors, pharyngeal cysts and some epiglottic entrapments.[12] While dressage horses and showjumpers have competed successfully with significant laryngeal hemiplegia or other respiratory impediments, abnormal respiratory noise and reduced airflow may still affect performance and be of concern to rider and spectator. Endoscopy is recommended or indicated in the following situations:

- All race horses should ideally be endoscoped before and after strenuous exercise.
- Equine athletes unable or unsuitable to be exercised strenuously. This includes yearlings at auction sales.
- Elite sport horses.
- When abnormalities in the clinical evaluation are detected, e.g. abnormal respiratory noise at exercise, nasal discharge or cough, sinus swelling.
- Purchaser's request.
- When purchase price demands a more comprehensive examination.[44]

A complete endoscopic examination of the upper respiratory tract and trachea is seldom performed. A methodical

examination of both nasal passages, ethmoid turbinate areas, openings of the guttural pouches, pharynx, larynx and cervical trachea is usually sufficient. The examiner is looking for structural and functional abnormalities that would impair athletic performance, evidence of previous surgery or the origin of any observed nasal discharge or reason for cough.[44] It is important to document only that which was inspected and to record findings accurately. Use of a checklist is best.[44]

The limitations of the endoscopic examination should be made clear to the purchaser. A resting endoscopic examination is a *static* examination. There is therefore an inherent deficiency in the procedure to detect functional abnormalities that only become a problem when the horse is exercising at maximum intensity and when respiratory airflow is at a peak. Many of these abnormalities result in an abnormal respiratory noise at exercise. This is one reason why strenuous exercise is mandatory when examining the equine athlete for purchase. In the event an abnormal respiratory noise is heard at exercise but the resting examination is normal, videoendoscopy during a treadmill exercise test is recommended.[45] Conditions that may only be apparent during maximal exercise could include dynamic collapse of the arytenoid cartilage and vocal fold, intermittent dorsal displacement of the soft palate, dynamic collapse of the pharyngeal wall, intermittent epiglottal entrapment, dynamic medial collapse of the aryepiglottic folds, exercise-induced pulmonary hemorrhage and dynamic rostral displacement of the palatopharyngeal arch.

Difficulties arise when interpretation of laryngeal function is required and only a resting examination can be performed. Typically this occurs when scoping yearling Thoroughbred and Standardbred race horses at sales. Laryngeal movement can be variable and a number of grading systems have been used to evaluate arytenoid abductor function.[44,46–48] Regardless of the system used most veterinarians agree that horses that cannot achieve full arytenoid abduction after swallowing or nasal occlusion are at a greater risk for reduced athletic performance due to dynamic collapse of the arytenoid cartilage and vocal fold. Indeed, when indices of racing performance were evaluated in Thoroughbred race horses that had endoscopic evaluations at sale as yearlings were reviewed, horses that could not achieve full arytenoid abduction (grade 3 or 4) had significantly inferior racing performance compared with those that could.[46] Unfortunately, there are 'gray zones' and laryngeal abductor function does not always fit into precise categories. Probably the best system is that used at auction sales in the United Kingdom where yearlings are trained to canter at the lunge. Evidence of a characteristic inspiratory noise at exercise *and* endoscopic evidence of impaired arytenoid abductor function is required for the horse to fail the conditions of sale and be returned to the vendor. An arbitration panel settles disputes. This system has been shown to be robust and accurate.[47] Unfortunately, the limitations of a static examination mean that some animals with clinically significant respiratory impairment at exercise will be missed. In addition, some animals with subclinical laryngeal neuropathy will progress to become clinically affected animals. Recent evidence suggests that progression of laryngeal neuropathy in non-affected or minimally affected horses may be as high as 15%. Very importantly, the progression may be rapid and can occur within weeks of purchase.[48]

Examination of the Thoroughbred race horse

Prepurchase examination of the Thoroughbred race horse includes examination of yearlings at public auction sales, examination of young race horses (2 and 3 years of age) and examination of older proven race horses. The aim of the prepurchase examination of yearlings is to identify athletic individuals who have optimal conformation and no evidence of existing cardiac abnormalities, orthopedic disease (primarily osteochondrosis), or upper respiratory tract abnormalities. The aim of the prepurchase examination of young or proven race horses is similar but the emphasis is on identification of previous injuries or 'wear and tear' that will limit future successful performance. Apart from yearlings it is always best to perform a full five-stage evaluation as described earlier.

Prepurchase examination of yearlings at public auction sales

It is very important that the examining veterinarian be familiar with the conditions of sale for each sales company. Horses are auctioned with no warranty for use or soundness other than certain conditions listed in the conditions of sale.[49] The veterinarian must be familiar with certain diseases/disorders that if not declared prior to auction and identified after sale (within a specified time) may render the purchased horse returnable. These usually pertain to vices (windsucker), ataxia (wobbler), cryptorchidism, pregnancy and laryngeal hemiplegia. The process for arbitration of purchases in dispute is also in the conditions of sale. Drug testing is available at some sales. Conditions relating to endoscopic and radiographic examinations need to be carefully understood. These are printed in the sales catalog.

A description of the horse is not performed but the lot number (hip sticker) and presented animal should always be matched to the catalog description to ensure the correct horse is examined. It is preferable to work only for buyers with whom you have a relationship and whose requirements you understand. A limited examination is more commonly performed and accepted by buyers.[7] This is because the sales venue is a difficult environment to appraise animals carefully. Young excited horses with limited education can be difficult to examine. The combination of noisy surroundings, many other horses, poor lighting and crowds of people mean a complete examination is not possible. The examination generally includes:

- visual examination of the head, neck, body, external genitalia, fore- and hindlimbs
- palpation of the head, neck, body, fore- and hindlimbs and visible abnormality elsewhere on the body that is palpable; inspection of both eyes with a penlight

- auscultation of the heart (on both sides) and on some occasions the chest
- examination of conformation, limb movements during walking and coordination.

The veterinarian should make sure to:

- Carefully inspect the feet and hoof pastern axis. 'Long toe–low heel', weak or collapsed heels, poor-quality hoof, contracted feet, clubfeet, markedly mismatched feet and overly small feet are undesirable and predispose to lameness. Horses with varus deformities of any joint seldom stay sound. Moderate to markedly 'offset knees', 'back of the knee', 'sickle hocks' or overly straight hocks may predispose to lameness and are undesirable.
- Look for enlarged pasterns, sesamoid bones and flexor tendons.
- Examine all joints for effusion. Osteochondrosis is suspected until proven otherwise.[50] Some mild effusion within carpal joints appears normal in yearlings and a variable fat pad in the stifle may mimic stifle effusion.
- Horses that either cannot or have difficulty fully abducting both arytenoid cartilages are at high risk of performing poorly. Epiglottal entrapment, persistent dorsal displacement of the soft palate, arytenoid cartilage enlargement (chondritis), rostral displacement of the soft palate, subepiglottic cyst, cleft palate and marked hypoplasia of the epiglottis are all unacceptable conditions of the upper respiratory tract which will impair athletic performance. Conditions of sale at each sales venue will determine whether an animal is returnable or not.
- Radiological lesions, which indicate a risk for future performance limitations, are listed in Table 62.2.

Examination of the mature horse

The examination procedure for prepurchase examinations of Thoroughbred race horses is similar to other athletes. However, certain injuries in Thoroughbred race horses result in reduced performance or may even prohibit successful athletic performance and are not tolerated as they might be in other equine athletes. Chronic foot problems, chronic degenerative joint disease, subchondral bone injury, sesamoiditis, tendon/ligamentous injury and dynamic collapse of the arytenoid cartilages are conditions that have a high risk of reducing athletic performance. Chronic pulmonary hemorrhage and small airways disease are also responsible for poor performance. A recent review highlights foot, fetlock, carpal and suspensory ligament injuries as the most common orthopedic injury sites resulting in lameness in Throughbred race horses.[51,52] Therefore, the veterinarian should focus on these areas during the examination procedure.

A buyer's statement should be completed and the veterinarian should discuss in detail with the potential purchaser what extra examinations are to be performed, e.g. endoscopy, radiography, ultrasonography, blood/urine tests. It should also be clear what the expectations for future training and racing will be. The vendor's statement should be completed and a full history of recent training and racing attained.

A full five-stage examination is performed and endoscopy of the upper respiratory tract and trachea (preferably before and after exercise) and radiographs of the carpi, fetlocks and front feet are usually conducted. Other areas are radiographed if the clinical examination determines this would be beneficial. For stage 3 of the examination the horse should be sufficiently warmed up and then galloped hard with the last 600 m in 39–40 seconds. The veterinarian should position him/herself so that any abnormal respiratory noise can be heard. The jockey should be asked to pull the horse up as quickly as is safe and canter back to the examiner. This is often the time when noises typical of dorsal displacement of the soft palate can be heard and as the horse slows and stops such noises can disappear. The trachea is auscultated for fluid and the chest is auscultated while the veterinarian listens carefully for disturbances in heart rhythm and heart sounds. The nostrils are checked for discharge (blood/mucopus) and the mouth and lips checked for blood. The horse should have endoscopy performed as soon as possible and arytenoid function assessed and any pharyngeal or tracheal discharges identified and noted. After the horse has been hosed down an assessment is made of recovery with heart, respiratory rates and chest sounds noted at approximately 15 min intervals. The lower limbs are checked for interference injuries. The veterinarian should make sure of the following points:

- Evaluate conformation as for yearlings but pay close attention to the feet. Mild conformational flaws especially in the well-performed horse may have little significance. Conformational abnormalities play an important role in career longevity and they should be viewed with this in mind. It is interesting to note that a study of conformation of elite young Thoroughbred race horses and sires showed that in the forelimbs most horses had mildly offset and valgus 'knees', were slightly 'over the knee', had slightly broken back hoof– pastern axes but had little deviation from the fetlock to the ground ('toe in or toe out'). In the hindlimbs being slightly 'cow hocked' and being 'toe out' was considered normal.[18]
- Acquired hoof deformities/injuries such as collapsed heels, shear heels, wry hooves, bruising and corns, medial-lateral hoof imbalance, broken hoof–pastern axes, mismatched feet, poor shoeing and evidence of previous episodes of laminitis should be noted.
- Check for muscle asymmetry, especially differences in the gluteal musculature. Differences in height of the tuber sacrale if minor and unassociated with pain are often insignificant. Palpate the croup and back checking for pain and muscle spasm. 'Cycle the back' by inducing flexion and extension and assess lateral flexibility using a blunt probe that is run along the epaxial muscles on either side.[53]
- Look carefully for evidence of joint disease, pain/enlargement of the proximal sesamoid bones and ligamentous/tendinous thickening and sensitivity on palpation. Correlate findings with manipulative tests, radiographs and ultrasonographic examinations.
- Carefully record all findings and give opinions on current or future effects on performance in terms of an assessment of risk.

Examination of the Standardbred race horse

When performing prepurchase examination on Standardbred race horses, the use of the full five-stage examination is strongly advised. A number of purchasers request less extensive examinations and while this is appropriate, stages one and two should be considered a minimum examination as this allows for a detailed clinical examination and observation in motion. Beware of examination requests such as 'heart and wind only' or 'legs and heart' as use of these tailormade types of examination allow for omission of important observations.

Clinical examination

Conformation

Limb conformational defects of particular importance to Standardbreds tend to center on the 'knees'. Pacers with 'toe out' conformation (viewed cranially/caudally when walking) may be at risk for interference due to knee strike at speed. Bench or offset knees are often associated with 'toe out' conformation and can also exacerbate knee strike. Horses with long pasterns and long toes/low heels are at risk for tendon injuries.

Skin conditions

Scars or excoriations on the side of the neck can be evidence of steering difficulties from the use of steering correction devices such as a pricker or boring pole.

Common injuries

Careful examination of the forelimb suspensory ligaments is advised as subtle evidence of previous desmitis may only show as a thickening of the width of the ligament. Non-weight-bearing palpation of the palmar flexor tendons in the pastern area may indicate previous 'low bows' (tendinitis) in a similar fashion to suspensory desmitis, as an increase in the width of the palmar flexor tendons. Any visible medial effusion of the intercarpal joint space warrants a suggestion for carpal radiography. Curbs (thickening at the plantar aspect of the tarsus) are common but are rarely of clinical concern. Partial (uni-cortical) or small midsagittal fractures of the dorsal first phalanx are common and deep palpation of the proximal dorsal cortex of P1 should be performed in all four limbs, particularly the hindlimbs. Any subtle visible bony thickening of proximo-dorsal P1 should warrant pastern radiographs. In such cases often only the lateral to medial projection shows evidence of periosteal disruption and new bone deposition on the proximal dorsal first phalanx indicative of this fracture. Hoof imbalances become more important in older Standardbreds; imbalance in younger horses is correctable and should be advised. Any effusion of the tibiotarsal joint would warrant radiographs to look for OCD, most commonly seen on the distal aspect of the distal intermediate ridge of the tibia. The interpretation of intermediate ridge OCD lesions if found is difficult as there is controversy about their clinical significance especially with respect to performance. In young, unproven race horses with intermediate ridge OCD lesions any tibiotarsal effusion may be significant to future performance while in older proven race horses with intermediate ridge OCD lesions many can have adequate 'to date' racing performances even in the face of moderate joint effusion. In a number of horses where routine hock radiographs are taken, intermediate ridge OCD lesions can show up as incidental findings.

Stage 3 exercise

Horses should be observed working under race condition where possible (e.g. fast working over 2000 m, coming home the last 400 m in 28 seconds). Working near race conditions allows for observation of respiratory noise while working, listening for knee strike and observing recovery rate post exercise. At the end of the exercise phase is an ideal time for upper respiratory endoscopic examination if it is to be performed. Observation of laryngeal function shortly after work allows evaluation of the larynx while the horse still has an elevated respiratory effort during recovery and allows checking of the trachea for blood and mucopurulent discharge, often only seen post exercise.

Ancillary tests

Electrocardiographic examination

An ECG examination as part of the prepurchase is commonly requested by Australian buyers primarily for a 'heart score' determination. Apart from the numerical heart score and assessment of T wave changes (so-called 'heart strain') the ECG does not add greatly to the prepurchase examination and its use is based mainly on purchaser's request.

Upper airway endoscopic examination

In the absence of someone reliable (bloodstock agent or prominent driver) having driven the Standardbred race horse and consequently listened to the horse's respiratory noise under raceday conditions first hand, endoscopy is normally recommended as part of the prepurchase examination. Whilst laryngeal dysfunction is not as common in Standardbreds as Thoroughbreds, endoscopic examination is a reliable screening procedure for such problems. As mentioned previously, if a full five-stage examination is performed valuable information can be gained from examination of the tracheal lumen for blood and mucopus after exercise ('hot scoping'). Luminal fluid may not be evident when examined without exercise ('cold scoping'). If a 'cold' endoscopic examination is performed (e.g. associated with a partial stages 1 and 2 examination) this should be stated in the report.

Radiography

The majority of Australasian Standardbreds examined prior to purchase are young, 'up and coming' horses with little hard racing experience. As such it is unusual to find many radiographic abnormalities indicative of chronic 'wear and tear'. For this reason recommendations on radiography are generally based on purchaser request and the personal preference of the examining veterinarian. It is common to find the presence of fetlock bony fragments (ununited plantar eminence of the proximal phalanx, and type I OCD fragments of the palmar/plantar aspect of the first phalanx),[30] especially when routine hindlimb fetlock radiographs are taken. As with distal intermediate ridge OCD the interpretation of such fetlock fragments with respect to future performance is very difficult. The majority of the fetlock fragments are incidental findings and do not appear to be of clinical significance. Interestingly, routine multiple joint radiographs are normally associated with the prepurchase examination of more expensive and often well-proven Standardbred race horses. The interpretation of any such fetlock fragments must take into account that these horses have been performing well in the upper levels of competition and that it is most likely that these fragments have been present during their most recent performances and as such their clinical significance may be questionable. As with all radiographic findings their presence needs to be stated in the radiology report.

Examination of the proven race horse

The prepurchase examination of the older proven race horse follows the principles outlined above. In line with other breeds, the examination of proven animals compared with unproven ones requires special attention to signs and consequences of 'wear and tear'.

Hoof balance and shoeing abnormalities, e.g. long toes/low heels, should be looked for, as the chronicity of these is more important to the older race horse. Deep digital palpation of the proximal row of carpal bones should be carried out to check for any withdrawal, which can indicate carpal disease and warrants radiography, especially skyline views. Another area deserving of careful deep digital palpation is the origin of the forelimb suspensory ligaments. Withdrawal to deep palpation in this area can be indicative of chronic suspensory origin desmitis. Especially scrutinize this area if there are any differences to palpation between the two front legs. Most race horses are worked (stage 3) with knee boots on and it is worth examining these at the end of the exercise phase for evidence of brushing or knee strike.

In proven race horses it is more common to undertake extensive radiographic examinations looking for signs of disease; knees and front fetlocks are normally requested.

Examination at yearling sales

Compared with Thoroughbreds, Standardbred yearlings tend to be less well handled and this limits the types of examinations possible at yearling sales. An abridged examination mostly centered on a basic clinical examination and determination of conformational defects is carried out. Base narrow conformation and toe out forelimb conformation on walking may predispose to knee strike. Bench/offset knees and 'back at the knee' are also looked upon as important knee conformational defects. Joint effusion (especially tibiotarsal) may indicate OCD. As is standard at yearling sales, endoscopy is often conducted and advised.

Examination of the sport horse prior to purchase

This section focuses on specific aspects pertaining to the examination of event horses, showjumpers and dressage horses prior to purchase. The majority of showjumpers and dressage horses competing internationally are Warmbloods, whereas most event horses competing at that level are Thoroughbreds, frequently ex-race horses. Because these two types of horses are quite different and present with their own unique conformational and soundness issues they will be discussed separately.

Examination of the three-day event horse prior to purchase

Three-day eventing combines the disciplines of dressage, showjumping and cross-country, including a steeplechase and roads and tracks phase. Therefore, the event horse must primarily be a bold and clever jumper, with plenty of scope and speed. It is because of this that Thoroughbred horses tend to excel. However, in today's competitive environment speed and braveness alone are no longer enough to succeed at the top level, and the horse must also have good basic gaits and a temperament suitable for dressage training, combined with a careful showjumping technique. Because the horses compete on extremely variable terrain and footing, three-day eventing places huge strains on the musculoskeletal system and horses with poor conformation are especially at risk of injury. The majority of injuries sustained by top-level event horses are repetitive strain injuries to soft tissues and joints, particularly to the superficial digital flexor tendons, and injuries resulting from direct trauma during the cross-country phase. Exertional rhabdomyolysis ('tying up') is also a common cause of failure to complete the event.

When examining a potential event horse prior to purchase it is important to obtain a thorough history pertaining to the horse's athletic endeavors up to the point of sale. Most horses being purchased for eventing are Thoroughbred horses that have finished their racing careers, and many race horses are retired from racing due to injury. Therefore, if possible the exact reason for the horse's retirement from the track should be ascertained. Although some race horses are just too slow or are getting too old to continue racing competitively, many suffer from some kind of disability that has reduced their racing performance and may also affect their ability to become a top-class

event horse. Superficial digital flexor tendinitis, dorsal carpal bone chip fractures and dorsoproximal first phalanx chip fractures are all common causes of lameness in race horses that may result in their retirement from the racetrack. Similarly, a poor performer on the racetrack may suffer from respiratory problems such as left-sided laryngeal hemiplegia ('roaring') or exercise-induced pulmonary hemorrhage ('bleeding'). The owner's statement should include questions that specifically address these problems; i.e. whether the horse has ever been lame, whether it has ever bled from the nostrils and whether it has ever made an abnormal respiratory noise during exercise. If the horse has already competed as an event horse it is pertinent to determine how many events it has actually completed at what level, and the reasons for not completing events, such as being withdrawn from a competition due to unsoundness or exertional rhabdomyolysis.

After establishing a thorough history, a comprehensive clinical examination should be performed at rest with particular attention to conformation. Horses with poor foot conformation, very upright hoof–pastern axes, and horses that are back at the knees typically do not stand up well to top-level competition. In our experience Thoroughbred horses often have large front feet with flat soles, long toes and underrun heels. The long-toe, low-heel syndrome in particular appears to predispose these horses to chronic bruising and caudal heel pain when jumping large fences on hard ground, and foot-related lameness is one of the most common causes of event horses failing to complete the season. Synovial effusion, especially in the carpi and front fetlock joints, and a decreased range of joint motion with signs of resistance or pain on flexion should alert the veterinarian to the possibility of degenerative joint disease subsequent to injury. The digital flexor tendons and suspensory ligaments should be carefully palpated for size and evidence of inflammation or pain, and an ultrasonographic examination of the tendons should be performed if there is any suspicion of previous injury. Following completion of the examination at rest the horse should be assessed while walking and trotting in hand on a hard, level surface (preferably concrete or asphalt), both before and immediately after flexion tests of the distal limbs and carpi in the front limbs, and full limb (spavin) tests in the hindlimbs. The horse should be ridden at a trot and canter on both reins in order to assess its paces and temperament, and if facilities permit the horse should be galloped a sufficient distance for the veterinarian to observe any abnormal respiratory noise and to evaluate heart rate, sound and rhythm following exercise. An endoscopic examination of the upper respiratory tract is usually performed immediately post-exercise to assess laryngeal function and examine for evidence of exercise-induced pulmonary hemorrhage. Once cooled off from the gallop the horse should be lunged at the trot on a 10-meter circle in both directions, preferably on a hard, level surface, to examine for low-grade lameness induced by exercise.

Given that many Thoroughbred horses are broken in and raced at a young age, most purchasers request radiographs to be taken of the most commonly injured areas, including the front feet, pastern and fetlock joints, the carpi and the hocks. Other areas may be subject to radiography if a problem is determined to exist based on the clinical examination, such as a painful splint bone exostosis or effusion in a hind fetlock joint. Commonly observed radiographic changes in Thoroughbred ex-race horses being examined prior to purchase for eventing include evidence of pedal osteitis and chronic sesamoiditis, dorsoproximal first phalanx chip fractures, dorsal carpal osteophyte formation and/or chip fractures, and osteophyte formation on the dorsoproximal aspect of the third metatarsus at the level of the tarso-metatarsal joint space. Because radiographic evidence of pedal osteitis and sesamoiditis tends to persist throughout the horse's life we feel that they are generally not clinically significant provided that there is no evidence of ongoing pain or inflammation of these structures at the time of the examination. Traumatic chip fractures of the first phalanx and carpus usually result in the development of degenerative joint disease with ongoing exercise unless they are removed arthroscopically soon after forming, therefore they must always be regarded with caution in horses expected to go on to athletic careers. Osteophyte formation on the dorsoproximal aspect of the third metatarsal bone seems to occur frequently in young Thoroughbred horses and can be present at a relatively early age. They are often bilateral and radiographically appear smooth-edged and of uniform density. In our experience, provided that the tarso-metatarsal joint space is uncompromised and well defined, and the horse exhibits no signs of lameness or abnormal response to hindlimb flexion tests, this specific radiographic change has not become clinically significant when the horses go on to become event horses.

Examination of dressage horses and showjumpers prior to purchase

A good dressage horse must possess natural balance, elegance and athleticism, as well as power and a trainable mind. The majority of dressage horses competing internationally are Warmbloods with a high proportion of Thoroughbred blood, combining the athleticism of the Thoroughbred with the trainability of the Warmblood. Through training, the horse's center of gravity is shifted caudally by increasing the degree of flexion and loading of the hindlimbs, thereby freeing the forehand to create a more airborne, uphill type of movement. As well as the general increased loading of the hindlimbs, particularly the hock joints, the lateral movements required by the sport create a unique strain on the horse's back and additional twisting stress on the appendicular joints. Because the training of dressage horses predominantly involves repetitive exercises designed to maintain suppleness and increase muscle strength, these horses rarely suffer from acute traumatic injuries but more commonly from cumulative wear and tear lesions. This is exacerbated by the fact that it takes at least 5 years for a horse to be trained to Grand Prix level and most dressage horses continue to compete to an advanced age, often as old as 20 years.

As with top-level dressage horses, the majority of successful showjumpers are Warmbloods, usually large, well-balanced, athletic individuals. The showjumper must be strong enough to jump large fences with precision and care,

both from a virtual standstill and at speed, and supple enough to make sharp turns without losing impulsion. The stresses placed on the musculoskeletal system of elite showjumpers are huge, especially on the hocks and hindlimb suspensory apparatus during take-off and on the front feet and front limb suspensory apparatus at landing. Therefore, when examining dressage horses and showjumpers prior to purchase the veterinarian should pay specific attention to the front feet, pasterns, hocks, and the front and hind suspensory ligaments. The horse should be evaluated at rest, trotting freely in hand on a hard surface, and while ridden and lunged in both directions on a hard as well as a soft surface. It is important to remember when examining a dressage horse prior to purchase that a good rider is able to correct and hide a mild gait irregularity or lameness. Therefore the veterinarian should not just focus on the limbs but also look for changes such as increased resistance to bending in either direction or reluctance to accept the bit. It is useful to lunge the horse after it has been ridden to look for any differences in the gait that may be attributable to the rider.

Foot conformation is extremely important, as many Warmbloods have small feet relative to their bodyweight. Slight differences in the size and shape of the two front feet are common and not necessarily abnormal. However, marked asymmetry of the hooves is often an acquired condition as a consequence of a previous lameness (chronic under-loading of one foot relative to the other). The horse should be lunged or ridden in small circles on hard ground in both directions to exacerbate any low-grade, foot-related lameness. High suspensory (origin of suspensory) disease in the front limbs is very common both in dressage horses and in showjumpers. It results in a mild lameness that is typically observed most easily when the horse is circling in deep footing with the affected limb on the outside of the circle. Although most cases of front limb high suspensory disease resolve over time with the horse eventually returning to its previous level of competition, they can be very slow to heal. Hindlimb proximal suspensory ligament disease is a serious condition that frequently recurs with work. It tends to be associated with a straight hock conformation and is exacerbated by collection. Lesions of the suspensory body and branches are also common and are often the cause of retirement for showjumpers. Therefore it is important to carefully palpate the entire suspensory ligament for evidence of swelling, pain or inflammation. Digital flexor tendon sheath enlargement ('windgalls') that is bilaterally symmetrical is usually benign. However, extreme unilateral distension is the result of chronic inflammation and is often associated with synovial proliferation and development of adhesions that may cause lameness. The thoracolumbar region should be carefully palpated because the back is prone to low-grade muscular injury and bony abnormalities such as impingement of the dorsal spinous processes that can cause recurrent discomfort. However, asymmetry of the tuber sacrale ('hunter's bumps') is common in showjumpers and is usually considered insignificant provided there is no evidence of lameness, loss of performance or palpable pain in the lumbosacral area.

Because the respiratory requirements for dressage horses and showjumpers are modest compared with those of three-day event horses endoscopy may or may not be requested by the purchaser. Laryngeal hemiplegia is not usually performance limiting, but the noise produced may be disturbing to the purchaser especially when the horse's head and neck are flexed. Most purchasers do request radiographs to be taken of the areas most commonly associated with decreased performance, including the front feet, pastern and fetlock joints, and the hocks.

Radiographs of the front feet and navicular bones do not correlate well with the presence of clinical signs and should be interpreted with caution, but certain radiographic lesions are a cause for concern. For example, in the dorsoproximal-palmarodistal oblique (upright pedal) view, up to seven conical nutrient foramina along the distal border of the navicular bone are considered normal. However, multiple enlarged or misshapen foramina and large central radiolucent areas (cysts) are almost always abnormal. Although many horses with mild navicular pain that are managed appropriately are acceptable for pleasure riding and lower levels of competition, the tendency to adopt a shortened stride is detrimental in a dressage horse and the pain associated with landing makes this condition incompatible with jumping big jumps. Ossification of the collateral cartilages ('sidebones') is frequently seen, especially in larger, heavier horses, but is rarely a source of lameness or related to any clinically significant foot abnormalities. Both front and hind proximal interphalangeal (pastern) joints often show slight bony modeling of the dorsoproximal articular margin of the second phalanx. Although these early radiographic changes are usually of no clinical significance, they can occasionally progress to proximal interphalangeal degenerative joint disease ('ringbone'), especially in horses with short, upright pasterns. Small, smooth-edged radio-opaque bodies are often found at the dorsoproximal aspect of the first and third phalanges in Warmbloods. They are typically not considered clinically significant provided the joints are clinically normal and there is no radiographic evidence of degenerative joint disease. Similarly, small smooth-edged osteophytes on the dorsoproximal aspect of the third metatarsal bone are frequently present without any compromise in performance. However, because degenerative joint disease of the distal intertarsal and tarso-metatarsal joints is a common cause of lameness in dressage horses and showjumpers, any associated radiographic irregularity of the joint spaces and/or positive clinical response to hindlimb flexion tests should be viewed with extreme caution in a future performance horse.

Examination of the Western performance horse prior to purchase

Western performance horses perform in a wide variety of disciplines, each of which places unique demands on the horse.

Disciplines to be discussed include: reining and cutting, roping, barrel racing, and Western pleasure. Close attention to conformation should be made in all Western performance horse evaluations. Size of the hoof in relationship to body size, hoof balance, and hoof/pastern axis should all be closely evaluated. Abnormalities in these factors may predispose the horse to navicular syndrome and to degenerative joint disease of the distal limb joints.[54] Upright rear limb conformation may predispose the horse to degenerative joint disease of the distal limbs and to bone spavin. The distal forelimbs should be evaluated closely for neurectomy scars, especially in middle-aged horses, because of the high incidence of heel pain in these horses.[55]

The genetic background of horses of the Quarter Horse breed should be scrutinized for presence of the hyperkalemic periodic paralysis (HYPP) gene. The American Quarter Horse Association registration certificate will designate if the horse has HYPP parentage or other genetic defects such as parrot mouth or cryptorchidism.[56]

Reining and cutting horses begin rigorous training as 2-year-olds to prepare for futurity competitions that begin during their 3-year-old season. These horses make rapid starts and stops, and abrupt changes in direction that will stress many of their musculoskeletal structures. Reining and cutting horses usually have a short and slight body style that allows for maximum agility. Areas of concern include: distal limbs (navicular region, distal interphalangeal and proximal interphalangeal joints), tarsal region, and stifles. Developmental orthopedic diseases such as osteochondrosis and flexural deformity must also be ruled out in young horses. Radiographic evaluations of the distal forelimbs, tarsi and stifles are commonly a part of the prepurchase examination.[57]

Roping horses need to make repeated short bursts of rapid acceleration and rapid stops. They have a more muscled and substantial body style compared with reining and cutting horses. Areas of concern on the prepurchase examination include the distal forelimbs (particularly the navicular region and the distal joints), and the tarsi. Rear limb tendinitis and suspensory desmitis commonly occur in this group of horses and these structures bear close evaluation.[57]

Barrel racing horses, and horses that compete in Western performance games (gymkhana), place a premium on short bursts of speed and the ability to make short-radius, rapid turns. All the joints from the carpi and tarsi distal need close evaluation in these horses. Degenerative joint disease, tendinitis and desmitis occur with high frequency in these athletes.

Western pleasure horses begin competition as 3-year-olds so are in training at a young age. These horses work at very slow walk, trot and canter gaits in the ring. A premium is placed on a quiet disposition. Overt signs of displeasure by the horse such as tail wringing or excessive head and mouth movements are counted against the horse during competition. Areas of concern during prepurchase examination include the distal forelimbs, tarsi and back. Ring work at slow gaits predisposes some horses in this discipline to lower back pain. When possible, Western pleasure horses should be evaluated under saddle to determine their responses during work.

References

1. Pycock JF. Evaluation of the reproductive system in stallions and mares for breeding purposes. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:138–147.
2. Asbury AC. Medical evaluation of the reproductive system relevant to purchase. Vet Clin North Am Equine Pract 1992; 8(2):395–412.
3. Mantrell JAR. The aim of the pre-purchase veterinary examination. Suffolk: EVJ Ltd; 1998:9–13.
4. Beeman GM, Soule SG, Swanson TD. History and philosophy of the medical examination of horses for purchase. Vet Clin North Am Equine Pract 1992; 8(2):257–266.
5. Anderson GF. Evaluation of the hoof and foot relevant to purchase. Vet Clin North Am Equine Pract 1992; 8(2):303–318.
6. Pascoe RR, Huntington PJ. A guide to examination of horses, 3rd edn. Artarmon: Australian Equine Veterinary Association; 1993:6–9.
7. Goulden BE. Examination of horses, 2nd edn. Palmerston North: Equine Branch New Zealand Veterinary Association; 1997:7.
8. Mitchell RD, Dyson SJ. Pre-purchase examination of the performance horse. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:951–964.
9. Kane AJ, McIlwraith CW, Park RD, et al. The effect of radiographic changes in thoroughbred yearlings on future racing performance. Proc Am Assoc Equine Pract 2000; 46:370–374.
10. Wilson HC. Legal aspects and do's and don'ts. In: Mair T, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:200–204.
11. Chandler N. The five stage prior to purchase examination. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:20–24.
12. Marks D. Pre-purchase examination of jumpers and dressage horses. Proc Am Assoc Equine Pract 1999; 45:4–12.
13. Dyson SJ. Evaluation of the musculoskeletal system part 4: The use of flexion tests and small diameter lungeing. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:95–100.
14. Schubert K. Veterinary defence society-experience of claims relating to prior to purchase examinations (PPEs). In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:205–210.
15. Ross MW. Conformation and lameness. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:15–31.
16. Marks D. Conformation and soundness. Proc Am Assoc Equine Pract 2000; 46:39–45.
17. Stashak TS, Hill C. Conformation and movement. In: Stashak TS, ed. Adams' Lameness in horses, 5th edn. Philadelphia: Lippincott Williams and Wilkins; 2002:73–111.
18. Mawdsley A, Kelly EP, Smith FH, et al. Linear assessment of the Thoroughbred horse: an approach to conformation evaluation. Equine Vet J 1996; 28(6):461–467.
19. Holmström M, Magnusson L-E, Phillipsson J. Variation in conformation of Swedish Warmblood hoses and conformational characteristics of elite sport horses. Equine Vet J 1990; 22:186.

20. Bousum P. Ancillary testing during the pre-purchase examination. Proc Am Assoc Equine Pract 1999; 45:27–30.
21. McEwen JC. Drug testing, clinical pathology and other tests: routine medical control. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:177–182.
22. Patteson M. Evaluation of the heart and cardiac disease. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:117–125.
23. Dart AJ, Snyder JR, Pascoe JR, et al. Pre-purchase evaluation of horses: 134 cases (1988–1990). J Am Vet Med Assoc 1992; 201(7):1061–1067.
24. Phillips TJ. The use of radiography in the pre-purchase examination. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:154–160.
25. Neuwirth L. Imaging and the pre purchase examination. In: White NA, Moore JN, eds. Current techniques in equine surgery and lameness, 2nd edn. Philadelphia: WB Saunders; 1998:654–671.
26. Butler JA, Colles CM, Dyson SJ, et al. Clinical radiology of the horse, 2nd edn. Oxford: Blackwell Science; 2000.
27. Kaneps AJ, O'Brien TR, Redden RF, et al. Characterisation of osseous bodies of the distal phalanx of foal. Equine Vet J 1993; 25:285–292.
28. Ruggles AJ. The proximal and middle phalanges and proximal interphalageal joint. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:342–348.
29. Jorgensen HS, Proschowsky H, Falk-ronne J, et al. The significance of routine radiographic findings with respect to subsequent racing performance and longevity in Standardbred trotters. Equine Vet J 1997; 29(1):55–59.
30. McIlwraith CW. Fetlock fractures and luxations. In: Nixon AJ, ed. Equine fracture repair. Philadelphia: WB Saunders; 1996:153–162.
31. Hardy J, Marcoux M, Breton L. Clinical relevance of radiographic findings in proximal sesamoid bones of two year old Standardbreds in their first year of race training. J Am Vet Med Assoc 1991; 198(12):2089–2094.
32. Richardson DW. The metacarpophalangeal joint. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:348–362.
33. Grondahl AM, Gaustad G, Engeland A. Progression and association with lameness and racing performance of radiographic changes in the proximal sesamoid bones of young Standardbred trotters. Equine Vet J 1994; 26(2):152–155.
34. Spike DL, Bramlage LR, Howard BA, et al. Radiographic proximal sesamoiditis in Thoroughbred sales yearlings. Proc Am Assoc Equine Pract 1997; 43:132–133.
35. Björnsdóttir S, Axelsson M, Eksell P, et al. Radiographic and clinical survey of degenerative joint disease in the distal tarsal joints in Icelandic horses. Equine Vet J 2000; 32(3):268–272.
36. Brehm W, Staecher W. Osteochondrosis (OCD) in the tarsocrural joint of Standardbred trotters – correlation between radiographic findings and racing performance. Proc Am Assoc Equine Pract 1999; 45:164–166.
37. Laws EG, Richardson DW, Ross MW, et al. Racing performance of Standardbreds after conservative and surgical treatment for tarsocrural osteochondrosis. Equine Vet J 1993; 25(3):199–202.
38. Beard WL, Bramlage LR, Schneider RK, et al. Post operative racing performance in Standardbreds and Thoroughbreds with osteochondrosis of the tarsocrural joint: 109 cases (1984–1990). J Am Vet Med Assoc 1994; 204(10):1655–1659.
39. McIlwraith CW. Clinical aspects of osteochondritis dissecans. In: McIlwraith CW, Totter GW, eds. Joint disease in the horse. Philadelphia: WB Saunders; 1996:362–383.
40. Baird DH, Pilworth RC. Wedge-shaped conformation of the dorsolateral aspect of the third tarsal bone in the Thoroughbred racehorse is associated with development of slab fractures in this site. Equine Vet J 2001; 33(6):617–620.
41. Howard RD, McIlwraith CW, Totter GW. Arthroscopic surgery for subchondral cystic lesions of the medial femoral condyle in horses: 41 cases (1988–1991). J Am Vet Med Assoc 1995; 206(6):842–850.
42. Dyson SJ. The use of musculoskeletal ultrasonography in the pre-purchase examination. In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:168–171.
43. Rantanen NW, Jorgenson JS, Genovese RL. Ultrasonographic evaluation of the equine limb: Technique. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:166–188.
44. Lane JG. Endoscopy – what role of this technique in the veterinary examination of horses prior to purchase? In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:161–167.
45. Rosenstein DS, Stick JA. Diagnostic techniques in equine upper respiratory tract disease. In: Auer JA, Stick JA, eds. Equine surgery, 2nd edn. Philadelphia: WB Saunders; 1999:314–326.
46. Stick JA, Peloso JG, Morehead JP, et al. Endoscopic assessment of airway function as a predictor of racing performance in Thoroughbred yearlings: 427 cases (1997–2000). J Am Vet Med Assoc 2001; 219(7):962–967.
47. Lane JG. The examination of Thoroughbred yearlings for respiratory impediments at auction sales. In: Proceedings. 15th Bain-Fallon Lectures, Australian Equine Veterinary Association 1993; 235–248.
48. Dixon PM, McGorum BC, Railton DI, et al. Clinical and endoscopic evidence of progression in 152 cases of equine recurrent laryngeal neuropathy (RLN). Equine Vet J 2002; 34(1):29–34.
49. Martin BB, Kimmel JC, Cheney MW. The sales yearling. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:836–837.
50. Ellis DR. Examinations at horse sales (Thoroughbreds). In: Mair TS, ed. The pre-purchase examination. Suffolk: EVJ Ltd; 1998:37–42.
51. Arthur RM, Ross MW, Moloney PJ, et al. North American Thoroughbred. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:868–879.
52. Pilsworth RC. The European Thoroughbred. In: Ross MW, Dyson SJ, eds. Diagnosis and management of lameness in the horse. St Louis: Saunders; 2003:879–894.
53. Marks D. Orthopedic concerns in the pre-purchase examination. In: Robinson NE, ed. Current therapy in equine medicine, 5th edn. St Louis: Saunders; 2003:493–499.
54. Turner TA. Shoeing principles for the management of navicular disease in horses. J Am Vet Med Assoc 1986; 189:298–301.
55. Jackman BR, Baxter GM, Doran RE, et al. Palmar digital neurectomy in horses. 57 cases (1984–1990). Vet Surg 1993; 22:285–288.
56. American Quarter Horse Association. Official handbook of rules and regulations. 2002; 50:49.
57. Black JB. Purchase examination of the western show and performance horse. Proc Am Assoc Equine Pract 1999; 45:1–3.

Appendix[7]

Buyer's statement

I, ... (Buyer/Buyer's Agent),

request that the horse..... undergo a pre-purchase examination for use as a

.....

This is to be undertaken by

Dr..... (Veterinarian)

..... (Practice)

The recipient of this report is deemed to be aware that if some stages of the standard procedure recommended by the Equine Branch of the New Zealand Veterinary Association are not carried out, any information or opinion contained in this report is based on partial examination only. Some clinical signs of disease, injury or abnormality that may have manifested themselves in the full five stage examination may not be apparent in the restricted examination.

Where this examination and report are requested for the purpose of a business they are deemed to have been carried out upon the basis that the examining veterinarian's liability, howsoever arising, shall be no greater than a sum equivalent to 100 times the fee charged for the provision of this report. In addition, liability for consequential losses of any nature is also excluded.

This contract is governed by New Zealand law.

The Buyer/Buyer's Agent irrevocably agrees that the Courts of New Zealand will have exclusive jurisdiction to hear and determine all disputes under or in connection with this contract. The Buyer/Buyer's Agent further acknowledges that New Zealand is the forum conveniens for the hearing and determination for all disputes in connection with this contract.

Ownership of X-rays: The Buyer/Buyer's Agent acknowledges that any radiographs taken in the course of this examination are the property of the veterinary practice listed herein, but it is further acknowledged by the practice that copies of the radiographs will be supplied at the Buyer/Buyer's Agent's request and expense.

Reliance upon this report will constitute an acceptance of the limitations of liability referred to above.

In addition, the nature and extent of this report has been determined by particular request. In the circumstances the examining veterinarian disclaims any liability whatsoever to any party other than the party directly responsible for requesting and paying for the services rendered.

Please indicate with a tick which aspects of the examination for purchase you do/do not wish to have carried out.

(a) Clinical Examination (which is carried out in five stages)

Indicate with a tick please		YES	NO
Stage 1	Preliminary	☐	☐
Stage 2	During walking, trotting, turning and backing	☐	☐
Stage 3	During and immediately after strenuous exercise	☐	☐
Stage 4	During period after exercise	☐	☐
Stage 5	During walking, trotting, turning and backing	☐	☐

The Clinical examination will be carried out substantially in accordance with the standard procedure recommended by the Equine Branch of the NZ Veterinary Association (1997).

(b) Ancillary Examinations

Indicate with a tick please	YES	NO
Endoscopy	☐	☐
Radiography (tick areas to be radiographed):-	☐	☐

front feet	( )	front fetlocks	( )	hind feet	( )
carpi (knees)	( )	tarsi (hocks)	( )	hind fetlocks	( )

Electrocardiography	☐	☐
Reproductive Examination	☐	☐

Other ancillary examinations (please specify)……
……..
……..
I understand the horse's usual veterinary attendant is……
(Veterinarian/Veterinarian's Practice)

Terms of payment. I understand that I will be responsible for payment for the examinations requested above.

Please note:- The certifying veterinarian takes no responsibility for, nor warrants the accuracy of, any information provided in the owner's statement including that given relating to the non-administration of drugs, freedom from vices, existing performance or suitability for intended use.

Signature……..(Buyer/Buyer's Agent)

Date……...

OWNER'S OR OWNER'S AGENT'S STATEMENT

Owner's Name ……..……..

Address……..……

Phone……..…

Horse's Name……..…...Age……..……

Sire……..….. Colour……..……

Dam……..…… Sex……..……..

Breed……..…

Agent's Name……..…….. Phone……...

Address……...

How long have you been acquainted with this horse?……..…….

How long have you had this horse under your personal care? ……..……...

Do you have knowledge of any?

1. Past or present disease?…… Has the horse ever bled from the nostrils? Yes/No
2. Lameness?…….. Has the horse ever had signs of colic? Yes/No
3. Accidents?……..…..
4. Vices (stable or being ridden)? ……
5. Abnormalities?……
6. Surgery?……...
7. Medications (particularly recent)?……...

Has this horse been recently examined by another veterinarian? ……..……

If so, for what purpose?……

Use to which you understand the horse will be put?……

Do you have any knowledge of past performance of this horse for the proposed use?

……...……

Is the horse in training/spelling?……

How long has the horse been in training/spelling?……

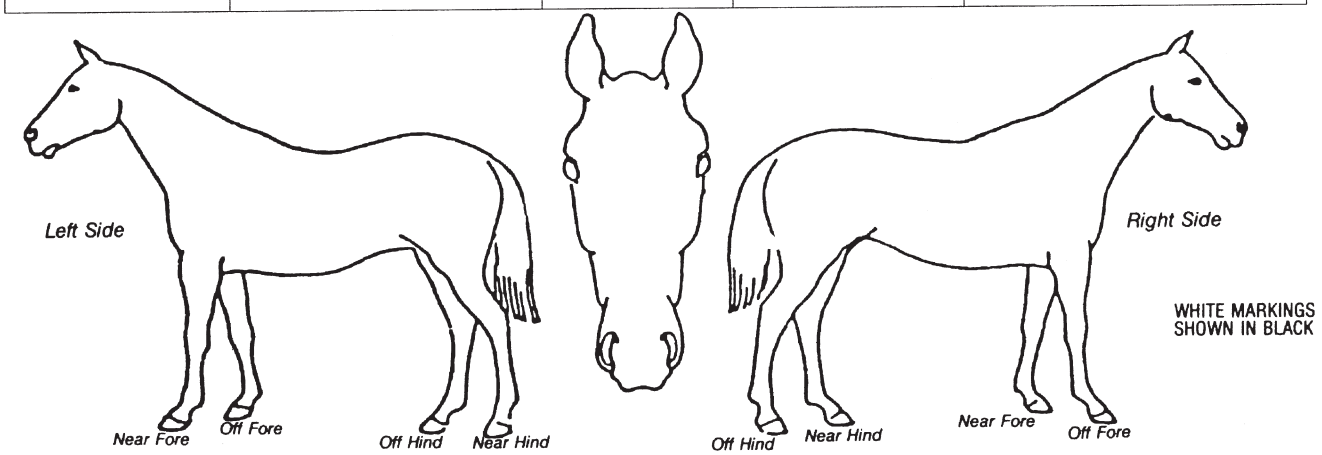
Who is the horse's usual veterinary attendant?……..…

Signature of Owner or Owner's Agent……..……

Veterinarian's record of the examination of a horse for sale

Veterinarian's Name:.....Practice Name.....
Address: .....
Horse's Name:.....
(Buyer/Buyer's Agent) .....
Description of horse said to be by ..... out of .....

COLOUR	BREED OR TYPE	SEX	AGE	APPROX HEIGHT



Markings: Head and Neck
Limbs: L.F.....
R.F.....
L.H.....
R.H.....
Body:.....
Brands: Left Shoulder ..... Right Shoulder .....
Acquired Marks: .....

STAGE 1: - The Preliminary Examination - with the horse at rest in a stall and/or outside the stall.
Complete the following with: N-Normal; AB-Abnormal; NE-Not Examined

GENERAL APPEARANCE
1. Physical Condition .....
2. Coat Condition .....

BILATERAL SYMMETRY
1. Head .....
2. Neck .....
3. Shoulders .....
4. Body .....
5. Pelvis .....
6. Legs .....

EYES
1. Symmetry .....
2. Reflexes .....
3. Lids .....
4. Mucous membranes.....
5. Cornea .....
6. Discharge .....
7. Examination with a light .....

MOUTH
1. Lips .....
2. Tongue .....
3. Teeth .....
4. Approx age by teeth .....
5. Gums .....
6. Mucous membranes.....
7. Odour .....
8. Bite .....
9. Mandible .....

NASAL & PARANASAL
1. Symmetry .....
2. Air flow .....
3. Odour .....
4. Mucous membranes.....
5. Percussion .....
6. Discharge .....

EARS
1. Symmetry .....
2. Odour .....
3. Discharge .....

PHARYNX & LARYNX
1. Palpation .....
2. Auscultation .....

NECK
1. Symmetry .....
2. Jugular furrows .....
3. Thyroid .....
4. Trachea .....
5. Withers .....
6. Poll .....

CARDIOVASCULAR
Heart
1. Auscultation .....
   a. Resting rate .....
   b. Sounds .....
Pulse
   a. Resting rate .....
   b. Quality .....
PULMONARY
1. Resting rate .....
2. Auscultation .....
3. Percussion .....
DIGESTIVE
1. Auscultation .....
2. Inspection of faeces .....
3. Perineum .....
4. Rectal Temp. .....
GENITO-URINARY
1. External genitalia .....
   a. Inspection .....
   b. Palpation .....
SKIN
1. Blemishes (saddle or girth sores etc) .....
2. Skin diseases .....
3. Hooves .....
4. Tail .....
NERVOUS SYSTEM
1. Inspection .....
2. Spine .....
3. Has horse been Denerved? .....

VICES
1. Cribbing .....
2. Aerophagia .....
3. Weaving .....
4. Head Shaking .....
5. Digging .....
6. Savaging .....
7. Other .....
8. Stable manners .....
9. Field manners .....

MUSCULOSKELETAL
Palpation & Manipulation of:
Left front leg
1. Chest & shoulder .....
2. Forearm .....
3. Carpus .....
4. Metacarpus - bone .....
   Metacarpus - tendon .....
5. Fetlock .....
6. Pastern .....
7. Foot - appearance .....
   - hoof tester .....
   - shoe type .....

Right front leg
1. Chest & shoulder .....
2. Forearm .....
3. Carpus .....
4. Metacarpus - bone .....
   Metacarpus - tendon .....
5. Fetlock .....
6. Pastern .....
7. Foot - appearance .....
   - hoof tester .....
   - shoe type .....

Left hind leg
1. Hip & thigh .....
2. Stifle .....
3. Tarsus .....
4. Metatarsus - bone .....
   Metatarsus - tendon .....
5. Fetlock .....
6. Pastern .....
7. Foot - appearance .....
   - hoof tester .....
   - shoe type .....

Right hind leg
1. Hip & thigh .....
2. Stifle .....
3. Tarsus .....
4. Metatarsus - bone .....
   Metatarsus - tendon .....
5. Fetlock .....
6. Pastern .....
7. Foot - appearance .....
   - hoof tester .....
   - shoe type .....

Flexion test results -Left fore distal limb .....
-Right fore distal limb .....
-Left fore carpus .....
-Right fore carpus .....

-Left hind distal limb .....
-Right hind distal limb .....
-Left hind hock .....
-Right hind hock .....

Remarks:
.....
.....
.....

STAGE 2 - Examination during walking, trotting, turning and backing

AT WALK
Symmetry of gait .....
Stride .....
Right fore leg .....
Left fore leg .....
Right hind leg .....
Left hind leg .....
Movement of head .....

AT TROT
Symmetry of gait .....
Stride .....
Right fore leg .....
Left fore leg .....
Right hind leg .....
Left hind leg .....
Movement of head .....
Turning .....
Backing .....

Remarks .....

STAGE 3 - Examination during and immediately after strenuous exercise

Type of Exercise (tick)
- Walk .....
- Lunge .....
- Trot or pace .....
- Canter .....
- Gallop .....

During Exercise
- Symmetry of gait .....
- Stride .....
- Breathing .....
- Rhythm .....
- Resp. noises .....

Immediately following exercise

Respiratory System
- Breathing
  - Rate .....
  - Rhythm .....
  - Sounds .....
- Auscultation of
  - Pharynx .....
  - Thorax .....

Circulatory System
- Mucous membranes .....
- Heart
  - Rate .....
  - Rhythm .....
  - Sounds .....

Remarks.....

STAGE 4 - Examination during the period after exercise

..... Minutes after		..... Minutes after		..... Minutes after	
Exercise	.....	Exercise	.....	Exercise	.....
Respiratory Rate	.....	Respiratory Rate	.....	Respiratory Rate	.....
Rhythm	.....	Rhythm	.....	Rhythm	.....
Lung sounds	.....	Lung sounds	.....	Lung sounds	.....
Heart		Heart		Heart	
rate	.....	rate	.....	rate	.....
rhythm	.....	rhythm	.....	rhythm	.....
sounds	.....	sounds	.....	sounds	.....

Evidence of cuts or marks on limbs from fast exercise .....
Evidence of epistaxis .....
Evidence of anal windsucking.....
Remarks.....

STAGE 5 - The final examination during walking, trotting, turning and backing

Walking
- Symmetry of gait .....
- Stride .....
- Right fore leg .....
- Left fore leg .....
- Right hind leg .....
- Left hind leg .....
- Movement of head .....

Trotting
- Symmetry of gait .....
- Stride .....
- Right fore leg .....
- Left fore leg .....
- Right hind leg .....
- Left hind leg .....
- Movement of head .....

Turning
- On
  - Right fore leg .....
  - Left fore leg .....
  - Right hind leg .....
  - Left hind leg .....

Backing
- Hindlimb movements .....

Remarks: .....
.....
.....

Overall comments: .....
.....
.....

Date and Time of Examination.....

Address where Examination took place .....

Signed .....

CHAPTER 63

International movement of athletic horses – quarantine and regulatory controls

Patricia M. Ellis and Keith L. Watkins

The elite athletic horse of today is a global commodity. During the 1990s, the volume of international movement of horses by air transport grew dramatically. Horses now travel for a diverse range of events including racing, dressage, eventing, show jumping, carriage driving, and endurance riding in an ever increasing number of countries. Traditionally most international events involving imported horses have been located in Europe and North America. New transport patterns are emerging with the advent of new competition venues in Eastern Europe, South America, the Arabian Peninsula, Asia, and Africa[1] and the development of complex itineraries by horses visiting multiple countries to compete in races held within a relatively short period.[2]

The modern equine athlete can move vast distances rapidly and complete journeys well within the incubation period of most infectious diseases. History has shown that without adequate safeguards this can lead to explosive outbreaks of disease.[3,4] The increased volume of horse movement in a changing world trading environment poses significant quarantine challenges to regulatory authorities, who must exclude foreign diseases from their countries without undue restriction to international trade.[1,5]

Governments and national authorities conducting international competitions have understandable concerns that:

- horses imported for a competition could bring in disease to the local population
- disease could occur in foreign horses due to exposure to a disease in the local horses
- a disease outbreak could result in cancellation of an important international event, especially if all horses (visiting and local) are held within the same competition venue
- prompt departure of foreign horses to their country of usual residency or next destination could be compromised by:
  - an outbreak of disease in the local population or in visiting horses
  - quarantine standards and management that do not meet the expectations of the horse's connections, the country of origin or country of next destination
  - inability to meet requirements for import to next destination
- horses returning from overseas could introduce disease into their country of normal residency.

Equine veterinarians in the private sector play an important role in the preparation of horses for export and in supervision of the health and welfare of horses during transport to and temporary residency in foreign countries. To avoid problems and unnecessary delays, they need to have a sound understanding of quarantine and regulatory requirements which allow horses to move safely between destinations.[6–8]

International spread of equine diseases

Economic, biological, political, and ecological factors

A variety of factors have the potential to affect the global distribution and occurrence of equine diseases including:[9]

- international trade in horses and horse semen, the single most important factor
- changes in international trading policy as a result of multinational trade agreements
- emergence of previously undescribed pathogens, such as contagious equine metritis and Hendra virus
- mutation of recognized pathogens and emergence of new biotypes
- climate-related phenomena such as global warming and the El Niño–Southern oscillation

- migration of reservoir and amplifying hosts such as birds and bats
- wind-blown carriage of insect vectors
- inadvertent introduction of exotic vectors such as ticks and mosquitos
- contamination or incomplete inactivation of vaccines
- deliberate, illegal introduction of a foreign disease, e.g. bioterrorism.

Changes in agricultural practices can indirectly influence the distribution of arboviruses by favoring the expansion of vector habitats.[10] For example, increases in irrigated rice production and expansion of the pig breeding industry are thought to have contributed to expansion of the geographic range of Japanese encephalitis in the Asian region.

Disease and horse-related factors

Potential for disease spread by international movement is influenced by the epidemiology of the disease, the intended use of horses, and whether horses are imported on a temporary or permanent basis.

The equine diseases most likely to be transferred by uncontrolled international movement are those characterized by an asymptomatic carrier state (e.g. equine infectious anemia, piroplasmosis, contagious equine metritis, equine viral arteritis, and dourine). The potential for their transfer is obviously greater if horses are imported on a permanent basis.[9] The last three diseases are transmitted by the venereal route.

Horses imported on a temporary basis for competition or performance pose little risk of introducing diseases spread by the venereal route if they are prohibited from breeding during temporary residency. Likewise, if the arthropod vectors of a disease are not present in a country, temporary import of horses that would be otherwise ineligible (e.g. horses testing positive for piroplasmosis) under controlled conditions presents a much lower risk than horses imported on a permanent basis and released into the national herd.[11] In the latter case potential for iatrogenic spread by contaminated needles would be possible.

Horses imported to a country on a permanent basis pose a far greater threat of introducing disease than horses imported for a short-term stay under appropriate conditions of management. Competition horses imported for major races and events are registered animals, travel on passports, and have a known residency, vaccination, and disease-testing history. They are kept under constant veterinary supervision before, during and after the event. During their brief residence, visiting horses have only limited exposure to the local horse population and are not used for breeding.[1,11]

Country factors

Evaluation of country factors, such as veterinary services, horse industry structure, disease control legislation, laboratory testing capacity, surveillance programs, zoning and border controls, are important inputs for assessing the likelihood of hazards being present in the horse population of an exporting country. Reliable and transparent information about the health status of a country's horses is critical for safe international movement.[12]

Impact of exotic disease outbreaks

An exotic disease outbreak can have a profound effect on the horse industry in an affected country and cause serious economic loss and disruption to normal activity.

Horses now travel from one hemisphere to another by air transport and complete their journeys within the incubation period of most major diseases. Spread of equine influenza, in particular, has increased since the introduction of air transport. In the past 20 years, the introduction of imported horses to susceptible indigenous populations has been responsible for explosive outbreaks of equine influenza in South Africa (1986), India (1987), Jamaica (1989), Hong Kong (1992), United Arab Emirates (1995/1996), Puerto Rico (1997), and Philippines (1997).[3,4,9,13]

Equine influenza was introduced to a naïve, unvaccinated South African horse population by imported horses from USA in December 1986. It spread throughout the country within a week. The explosive spread was aided by road transport from the north of the country to the south (with infected horses being offloaded at points in between), lack of an all-in, all-out postarrival quarantine policy and poor hygiene by transport operators, horse trainers, and veterinarians. Movement of horses by concerned owners from a show jumping competition that was cancelled because of horse illness also contributed. The impact of the outbreak included extensive losses of State revenue due to cancellation of race meetings and subsequent loss of wagering taxes. Normal racing schedules were only resumed in May 1987, yearling sales were delayed and many other major equestrian horse events were canceled or had to be rescheduled. The horse industry also incurred significant costs arising from veterinary treatment of sick horses and the costs of compulsory vaccination.[3]

Hong Kong suffered a similar fate in November and December 1992 when an outbreak of equine influenza, introduced by imported horses from UK or Ireland, led to a suspension of racing for 1 month. The outbreak resulted in the cancelation of seven race meetings, including an international event, with a potential loss of total betting turnover of nearly US$1 billion, over 15% of which would have been returned to the Hong Kong community by way of tax, duty, and donations.[4,14]

It is ironic that the disease which has had the most profound effect on horse movement in the new millennium is foot and mouth disease (FMD), a disease that does not infect horses. The outbreak of FMD in the UK in 2001 had a devastating effect on the horse and tourism industries, as well as on the farming community. Estimated horse industry losses reached £100 million per month in the first 3 months of the outbreak and the majority of horse-related sporting events were cancelled.[15]

International regulatory framework

The World Trade Organization

The World Trade Organization (WTO) is the body responsible for implementing international agreements resulting from the Uruguay Round of multilateral trade negotiations. In January 1995, the framework for international trade changed significantly when the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (the SPS Agreement)[16] came into force. Sanitary measures relate to human and animal health and phytosanitary measures relate to plant health.

The intent of the SPS Agreement is to minimize the negative effects of unjustified and unscientific health barriers on international trade. It requires WTO Member Countries to develop harmonized measures to protect human, animal, and plant life and health based on international standards, guidelines, or recommendations, primarily those developed by the Office Internationale Epizooties (OIE). Countries can adopt animal health measures more stringent than OIE standards if they can demonstrate a scientific need, which in practice means that quarantine conditions in excess of OIE standards should be based on a risk analysis. The SPS Agreement also promotes recognition of the concept of disease-free zones and regions within countries.[16–18]

Some authors[17,18] have noted that the SPS Agreement does not apply to international movement of competition horses as these movements are not considered 'trade'. The situation has been clarified by Sluyter.[1] Movement of horses or equine products after sale falls under the SPS Agreement. Movement of competition or breeding horses, although not considered as 'trade', also falls within the SPS Agreement if a concurrent risk of disease is involved.

Office Internationale des Epizooties

The OIE is the world organization for animal health based in Paris and was created in 1924 to address international spread of animal diseases at a time when rinderpest was a major concern in Europe. In May 2001 the number of OIE Member Countries totaled 158, each with one vote and one delegate to the International Committee (the decision-making body).[19]

A major objective of the OIE is to facilitate international trade in animals and their products by setting guidelines and standards. Historically, its primary function has been to provide Member Countries with information about the prevalence, incidence, and distribution of serious animal diseases which endanger livestock or public health.[18]

Information is sent out immediately or periodically depending on whether the disease is categorized as List A or List B (see below). Each Member Country undertakes to report important infectious diseases detected within its jurisdiction. The OIE then alerts other countries so rapid action can be taken if needed. In addition, the OIE collects and analyses scientific and technical information on animal diseases. The OIE makes this available to assist Member Countries to improve disease prevention, diagnosis and control, and provides technical support and expertise when requested.[19]

Classification and reporting of diseases

Diseases recognized internationally as being of significant importance to trade in animals are defined by the OIE as List A diseases. These are diseases that can spread very rapidly, irrespective of national borders, and that have serious socioeconomic or public health consequences. African horse sickness (AHS) and vesicular stomatitis are the important List A diseases that affect horses. OIE Member Countries are obliged to report outbreaks of these diseases to the OIE within 24 h of occurrence or reoccurrence and to supply monthly situation reports on their presence or absence.

OIE also defines a second group of diseases (List B diseases), which are considered to be of socioeconomic or public health importance within infected countries and are significant in international trade. List B diseases of equines include contagious equine metritis, dourine, epizootic lymphangitis, equine encephalomyelitis, equine infectious anemia, equine influenza, equine piroplasmosis, equine rhinopneumonitis, equine viral arteritis, glanders, horse pox, Japanese encephalitis, mange, and Venezuelan equine encephalomyelitis (VEE). List B diseases must be notified to the OIE within 24 h if they occur in a country for the first time and thereafter on an annual basis.

The Food and Agriculture Organization defines a third group of List C diseases as being significant at local level and countries report these annually. List C diseases of horses include equine coital exanthema, melioidosis, *Salmonella abortus equi*, strangles, ulcerative lymphangitis, and warble fly myiasis.[20]

In addition, each country maintains a schedule of diseases notifiable under its animal health legislation, drawn from the above lists, which have to be reported within specified periods. Because some important diseases are not universally notifiable, the Thoroughbred industry has developed its own international reporting system through the International Thoroughbred Breeders Meeting. Quarterly disease reports are submitted to a collating center at the Animal Health Trust, Newmarket, UK, and distributed to 20 participating countries.[21]

OIE international health standards

Since the formation of the WTO, the OIE has assumed significant importance in international trade as the reference organization for the WTO on animal disease issues and trade disputes. International standards developed by the OIE are now recognized by the WTO as reference international sanitary rules and can thus be used legitimately as a basis for import restrictions without constituting unjustified barriers to trade.[17–19]

OIE international health standards relevant to the international movement of horses are the International Animal Health Code and the Manual of Standards for Vaccines and Diagnostic Tests.

OIE International Animal Health Code

The OIE International Animal Health Code[22] is an essential reference for any official veterinarian involved in international trade. It is periodically updated and available online.

Part 1 contains general provisions relating to:

- general definitions and notification of animal diseases
- obligations and ethics in international trade
- import risk analysis
- import/export procedures
- risk analysis for biologicals for veterinary use.

Part 2 contains chapters for each OIE List A and List B disease and recommended wording for international veterinary certification relating to that disease. Criteria are presented which countries or zones must satisfy to be recognized as free from African horse sickness, equine influenza, dourine, glanders, and VEE.

Part 3 contains appendices to the Code. Sections relevant to the international movement of horses include:

- prescribed and alternative diagnostic tests for international trade purposes
- health controls and hygiene in establishments
- disinfection and disinsection procedures
- transport of animals.

Part 4 contains:

- a model international veterinary certificate for equines to promote international harmonization of veterinary certification
- a model passport for international movement of competition horses.

OIE Manual of Standards for Diagnostic Tests and Vaccines

The OIE Manual of Standards for Diagnostic Tests and Vaccines[23] is a companion volume to the Code and is also available online. The purpose of the Manual is to foster harmonization of diagnostic methods for OIE listed diseases and other diseases of importance to international trade. Standards are described for laboratory diagnostic tests and for the production of veterinary vaccines. Specific chapters cover each of the diseases listed in the OIE International Animal Health Code. Each disease chapter includes a well-referenced summary intended to provide information for veterinary officials and other readers who need a general overview of the tests and vaccines available for each disease. This is followed by a text giving greater detail for laboratory workers. The Manual also includes a list of OIE Reference Laboratories which have been designated by the OIE as centers of excellence in their particular field.

Import risk analysis

Risk analysis is a valuable tool for decision making that can assist global movement of horses and open up new markets without compromising the health status of importing countries.[24]

As mentioned earlier in this review, WTO Member Countries are encouraged to base quarantine conditions (SPS measures) on international standards, guidelines, and recommendations or on a scientific assessment of risk. The OIE International Health Code[22] is the international standard referenced in the SPS Agreement and contains guidelines and principles for the conduct of import risk analyses in Chapter 1.3.

The components of risk analysis are hazard identification, risk assessment, risk management, and risk communication. Briefly, the procedure should be science based and involves consideration and documentation of:

- potential exotic agents and pests of concern (hazards) that could be introduced by imported horses
- how exotic agents might be introduced into a country or zone by imported horses
- how horses in the importing country might be exposed to exotic agents thus introduced
- adverse health or environmental consequences resulting from exposure of domestic horses to such exotic agents
- how identified risks can be best managed to protect the domestic horse population without having an unjustified effect on trade.

Risk communication involves exchange of information and opinions with potentially affected and interested parties at all stages of the process.

Risk analysis has already proved its value in overcoming potential barriers to the international movement of competition horses testing positive for piroplasmosis. Government authorities in USA used risk analysis as a decision-making tool when considering import of horses for the 1996 Olympic Games.[24,25] Australia also amended its quarantine conditions to permit temporary importation of horses serologically positive for equine piroplasmosis following a detailed import risk analysis. Previous conditions banned the import of seropositive horses. The amendments were prompted by and of particular relevance to the Sydney 2000 Olympic Games. Under certain scientifically based restrictions, seropositive horses were allowed to enter Australia on a temporary basis.[26] This allowed horses that otherwise would have been ineligible to travel to Australia to compete in all three equestrian disciplines at the Sydney 2000 Olympic Games.[1] The important legacy of this risk analysis for Australia is that it also applies to future importations for other equine sports including racing.

A comprehensive risk analysis of disease risks associated with import of live horses has been completed by the Ministry

of Agriculture and Forestry, New Zealand in 2000 and was used as a basis for review of import standards.[11] The analysis includes a section relating to the temporary import of horses for racing and sporting events and recommended measures for their management.

Structured risk analysis, in compliance with OIE principles, provides countries importing horses with an objective and defensible method to assess risks associated with importation and to determine how those risks may be managed. Transparency is important. Exporting countries must be provided with clear and documented scientific reasons if import restrictions are imposed or if importation is refused.[22] Transparent decisions also assure local horse industry organizations and other interested parties that all potential risks have been evaluated and are being managed appropriately.

Regionalization

Regionalization and risk analysis are closely related.[24] Traditionally, the distribution of animal diseases has been viewed on a country-by-country basis, with the presence or absence of a particular disease anywhere within a country's borders serving to establish the status of the entire country. This conservative approach fostered an all-or-nothing standard of risk avoidance in quarantine policy development that precluded consideration of factors such as disease-free zones or regions within a country.

The contemporary approach endorsed by the OIE recognizes that there are gradations in disease risk, more often tied to climatological, geographical and biological factors and to husbandry systems than to national political boundaries. If a disease is contained within a defined zone, then export of horses from disease-free areas elsewhere in the country should not be affected. OIE guidelines relating to zoning and regionalization can be found in Chapter 1.3.4 of the OIE International Animal Health Code.[22]

Application of the concept to horse diseases was first prompted by outbreaks of AHS in previously free areas of Spain and Portugal in the years leading up to the 1992 Olympic Games in Barcelona. International movement controls relating to AHS were reviewed by the European Commission and the OIE. The OIE International Animal Health Code was amended to provide for regionalization in respect of AHS.[27] Countries allowed horses to enter Spain on a temporary basis to compete in equestrian events at the Games despite the existence of an AHS-infected area in the south of Spain.[24]

Regionalization is a valuable tool of trade for countries with significant endemic diseases of trade concern. South Africa's regionalization of AHS enabled resumption of export of horses to member states of the European Union and a number of other countries thus overcoming trade bans that had been in place for nearly 40 years. Recognition of the Cape Peninsula of the Western Cape Province as an AHS-free area was accepted by the EU (Commission Decision 97/10/EC) based on, *inter alia*:[28]

- the absence of clinical disease in the south-western part of the Western Cape Province of South Africa
- serological studies showing that AHS was not present in the area
- separation of this area by substantial geographic barriers from those parts of South Africa where AHS occurs annually
- strict movement controls to ensure that AHS is not introduced into the free area
- appropriate risk reduction measures for exported horses including minimum residency periods in the AHS-free area, quarantine in vector-protected premises, vaccination and pre-export testing
- ongoing surveillance in the free area and adjacent surveillance zone, including monthly blood testing of sentinel horses and autopsy of horses to exclude AHS as the cause of death.

Role and responsibilities of government officials, shipping agents, and veterinarians

Government officials, private practitioners, and shipping agents all share responsibility for moving horses between countries and must communicate openly and frequently during the shipping process to avoid difficulties and delays.[8]

Government officials

The chief concerns for the veterinary authorities of any country hosting an international event are potential for spread of disease, animal welfare considerations, and trade facilitation.[14]

Governments in importing countries have a primary responsibility to control the entry of foreign horses to protect the national horse population from exotic diseases. At the same time, they have to satisfy international obligations and facilitate trade. The importing country establishes import health requirements for horses by negotiation with their foreign counterparts, taking into account the disease status of the exporting and importing country and relevant international standards.[5,8,9]

An import permit may have to be obtained in advance of shipment for each consignment of horses. Often import conditions are attached to this permit. Import permits are used to ensure that only agreed and current conditions are used in trade, advance notice is given of consignments and that quarantine space is available for incoming horses (when appropriate).

The government of an exporting country is expected to act as the official independent agent of the importing country and is responsible for supplying or endorsing accurate official veterinary certification which satisfies all the health requirements of the importing country. If a problem arises with a shipment, officials in the exporting country cannot unilaterally alter agreed health conditions but must seek a dispensation from the country of destination.

Often shipments of horses transit other countries *en route* to their final destination. Governments in countries of transit may require that a transit permit be obtained in advance and/or that horses passing through meet the import requirements of the transit country in case a prolonged delay occurs due to mechanical failure of an aircraft.

Shipping agents

International transport of horses requires adequate lead time and considerable forward planning. Veterinarians approached for advice should recommend that clients engage a reputable and experienced shipping agent as the first step in commencing preparations for any international journey[6,7] as the key to success is often the competency of the shipping agent involved.[8]

A shipping agent acts as a representative of the owner and coordinates all facets of the shipping process from origin to destination. Shipping agents identify the most suitable and quickest route, prepare a travel plan, obtain all necessary permits and documentation, book road transport and air cargo space, liaise with airlines, provide shipping containers that conform to airline and welfare standards, and supervise loading. They also interact with the quarantine and customs authorities of the countries of origin and destination and coordinate arrangements for and timing of any pre-export quarantine, premises certification, veterinary examinations, testing and vaccination necessary for the completion of the official export health certification. Agents may also supply experienced attendants to escort horses during the journey.[29]

Enquiries should also be made in advance about quarantine policy in the country of destination relating to the import of tack, horse feed, supplements and veterinary medications.[30]

An additional consideration, which is sometimes overlooked, is that quarantine protocols for return of horses to their country of normal residency should be investigated before horses depart to establish whether that country imposes any special conditions on the management of horses during temporary residency in a foreign country. For instance, to return directly within a specified time period without additional testing, traveling horses may have to be isolated from other horses during a temporary absence.[30]

Equine veterinarians

In many countries, veterinarians in the private sector play a major role in preparing horses for export. Their duties may include:

- collecting blood samples for laboratory testing
- conducting or supervising pre-export treatments and vaccinations
- providing certification about the health status of horses and the premises from which they originate.

Veterinarians engaged by clients or accredited by governments to perform export duties need to work closely with quarantine authorities and shipping agents. Contact must be made with government animal health officials at an early stage to obtain or confirm the current import requirements for the country of destination. The veterinarian must understand and fulfill these requirements exactly.[8] Responsibilities include:

- being accredited for export duties (if appropriate)
- accurate completion of entries in horse passports and on other identification documents
- recording horse markings accurately by actual inspection of horses (rather than by copying other documents)
- confirming and recording the identity of each horse at the time of conducting any procedure so that any certification can be definitively linked to the animal
- collecting and submitting blood samples, performing inspections and administering vaccinations or treatments within the specified timeframes
- labeling samples clearly and accurately
- transporting samples to the laboratory using correct techniques and appropriate storage conditions
- submitting samples to approved laboratories
- requesting the tests specified in the import conditions
- providing conscientious certification about the health status of horses and premises.

Honest, accurate and reliable veterinary certification is the cornerstone of international movement.[31] Any certification provided must be completed carefully and conscientiously and match the requirements of the importing country precisely. Even if some of the requirements appear unreasonable and raise difficulties for the client, the certifying veterinarian must ensure these requirements are met or contact a government official for guidance on interpretation of the wording. Conflict of interest should be avoided and integrity of certification must not be compromised because of commercial pressures.

Misleading, inaccurate or false certification reflects adversely on the signing veterinarian and affects the reputation of the veterinary profession and government animal health services, nationally and internationally. Such certificates may result in loss of trade, spread of disease, financial loss to clients and exporters and litigation.[32]

A document entitled *The 12 Principles of Certification* was produced by the British Veterinary Association, UK Ministry of Agriculture, Fisheries and Food and the Royal College of Veterinary Surgeons in 1994.[31] A chapter on certification procedures is also included in the OIE International Health Code.[22] Both documents are recommended to veterinarians involved in the preparation or certification of animals for export as useful guides to their ethical obligations and responsibilities.

Before departure, private veterinarians traveling internationally with horses should also check whether the country of destination places any restrictions on import of veterinary medications and equipment or has any special registration requirements relating to veterinary practice by foreign veterinarians.

Equine practitioners attending recently imported horses in quarantine stations should pay close attention to personal

hygiene and comply with any operating procedures specified by quarantine management. They should be aware that a veterinarian was, in part, responsible for the quarantine breakdown that led to the disastrous South African equine influenza epidemic in 1986.[3]

Welfare legislation and standards

Welfare legislation governing international movement of horses by road and air varies from country to country. The International Air Transport Association (IATA) publishes *Live Animal Regulations* (LAR)[33] annually, which set standards for the safe and humane transport of animals by commercial airlines. The LAR contain useful information about the responsibilities of carriers and shippers, stocking density guidelines for horses, optimum temperature ranges, container standards, and specific handling procedures for horses transported by air. The LAR recommend that one competent groom be provided for each pallet of horses being shipped or, if more than four pallets are carried on the same flight, that the appropriate number of grooms (beyond four) be determined by the carrier in agreement with the shipper.

Generic recommendations for the transport of animals are presented in Chapter 1.4.1. of the OIE International Animal Health Code.[22] The Code notes that the IATA LAR are approved by the OIE and recommends their adoption. An increasing number of countries, including member states of the European Union, have formally adopted the guidelines and incorporated their provisions into legislation.

Role of horse industry organizations

For maximum efficiency, measures to prevent international spread of equine diseases require industry participation and support[5] in addition to the efforts of government veterinary authorities. At international level, the umbrella bodies of the various sporting disciplines play an important role in setting international standards for the protection of the health and welfare of horses relevant to particular disciplines. The host nation of an international event has a responsibility to provide facilities and supervision that meet these standards.

When preparing for an international event, close and continued liaison between horse industry and quarantine officials is required from an early stage to negotiate and resolve the many quarantine issues that may arise.[14,30]

In some instances, the host organization may provide and manage quarantine facilities.[14] Convenient access to good training facilities is critical for the successful participation of foreign horses. If a country that quarantines or isolates imported horses after arrival wishes to host an international event, the responsibility for establishing an approved quarantine facility for foreign horses often rests with the organization conducting that event. Most government-operated quarantine premises do not have easy access to adequate training facilities where imported horses can maintain competitive fitness in isolation.[30]

Horse industry organizations also play an important role in the regulation and control of international movement of athletic horses by issuing horse passports and by setting mandatory vaccination standards to protect the health of visiting and local horses against diseases such as equine influenza and Japanese encephalitis.

Passports

The use of passports to assist the movement of competition horses across national boundaries is well established. Internationally accepted passports must meet certain criteria set by the OIE, international horse authorities and, in Europe, by the EU.[1]

Passports are intended to serve as a unique identification document containing harmonized information about vaccinations and results of laboratory tests. They are issued by the relevant national horse industry organization of the country in which the horse is registered and should accompany a horse at all times. In some countries this is a legislative requirement. For instance, in the European Union all registered horses must have an accompanying passport during transportation.[1]

Vaccinations

In many jurisdictions, vaccination against equine influenza is compulsory for horses entering competitions or races and the vaccination status of all horses is regularly checked by horse industry officials.

It is important to establish before a horse departs on an international journey if local or foreign quarantine authorities impose any special requirements additional to or different from those known to apply to a specific discipline. For instance, because Australia is free from equine influenza, vaccination requirements for importation of horses to Australia are more stringent than those routinely required by racing authorities in Europe.[30] Likewise, in some instances, sporting authorities conducting events in certain Asian countries require vaccination against Japanese encephalitis to protect visiting horses. The recent advent of nasal vaccines for equine influenza may lead to changes in current international requirements (Roland Devolz, personal communication).

Vaccination requirements can vary from country to country and between disciplines and hence will not be detailed in this review. The main point for veterinarians is that the vaccination requirements of quarantine authorities and sporting organizations for each consignment should be established well in advance of the proposed date of horse departure. The time frames specified by quarantine authorities for courses of vaccination are not arbitrary and must be respected.

Racing authorities

The International Federation of Horseracing Authorities (IFHA) is an umbrella body for the world's Thoroughbred

racing authorities. The organization has developed an International Agreement on Breeding and Racing (IABR).[34] The general aim of the IABR is to protect the integrity of racing, thus leading to improvement of the Thoroughbred breed, enhanced welfare of trainers, riders and horses and, confidence of owners and the public in the sport. The IABR consists of a series of recommended international guidelines which are agreed and endorsed (in whole or in part) by national racing authorities and carried forward into their own rules for racing and breeding. Of particular interest to veterinarians are Article 6 of the IABR, which contains the template definition of a prohibited substance, and Articles 22 to 25, which relate to the control of infectious diseases and management of foreign race horses. Articles 22 to 25 contain general recommendations relating to passports, hygiene of transport vehicles and establishments, treatment procedures, veterinary inspections, vaccinations, health certificates, and exchange of information about equine disease outbreaks.

The IFHA has established a Permanent Liaison Committee on the International Movement of Horses (PLCIMH) to improve communication between countries conducting international races and to make recommendations about health issues that restrict trade. Significant expansion of international racing in recent years has resulted in logistical problems when horses compete in multiple countries within a short period of time before returning to their country of usual residency. Quarantine protocols vary from country to country and are usually developed to cater for direct movement to and from a specified country for competition. Complex itineraries cause logistical complications for racing authorities, government animal health services, connections of horses and shipping agents. Problems arise from variations between countries in quarantine requirements relating to health certification, minimum residency periods, testing, vaccination, housing and training during temporary residency and periods of quarantine or isolation.[2]

To address these problems and foster cooperation and international harmonization of health requirements, the PLCIMH has recently developed detailed guidelines to facilitate the safe movement of registered race horses competing on an international circuit with specific reference to testing, vaccination, certification, quarantine/isolation facilities and training of horses. The guidelines were presented to IFHA for consideration, comment and approval at its 36th Conference in Paris on 7 October 2002 and were adopted for use as a basis for discussion by IFHA member countries with their government veterinary authorities. The *Guidelines to Facilitate the Temporary Movement of Registered Racehorses for International Races* will be available online at www.horseracingintfed.com. It is anticipated that the guidelines will be reviewed and updated regularly and that IFHA will work closely with the OIE to ensure that guidelines are based on sound scientific principles.[2]

Passports have been used for the identification of Thoroughbred horses for many years. Passports have to be inspected and endorsed for foreign travel by racing authorities before each exportation and subsequently before the horse runs in a foreign country. Internationally, stud books are now moving toward an electronic identification system that incorporates DNA parentage verification and horse markings, and which also uses the number of an implanted microchip to create a unique passport number and international life number for the horse. Passport details of incoming horses can be down-loaded by registration authorities from the internet, thus speeding clearance procedures between countries.[35]

Federation Equestre Internationale

The Federation Equestre Internationale (FEI) is the international governing body of equestrian sport recognized by the International Olympic Committee and is responsible for international administration of equestrian events in the disciplines of show jumping, dressage, eventing, driving, vaulting, reining, and endurance riding. National Federations administer these disciplines at national level.[36,37]

The FEI has developed comprehensive rules and regulations to govern the above sports. Of particular relevance to equine veterinarians are the FEI Veterinary Regulations,[38] which protect the health and welfare of horses competing in international events under FEI control. The Veterinary Regulations cover, *inter alia*, the duties of veterinarians, health and hygiene requirements and responsibilities, passport control, examinations and inspections of horses during events, control of prohibited substances and treatment of horses while under FEI control.

Horses are identified by a written description and a diagram in FEI passports. Only veterinarians approved by a National Federation are authorized to complete this page and the description must be completed in accordance with the FEI Manual on Identification of Horses.[39] The vaccination section of the passport must be endorsed by a veterinarian and demonstrate that the horse has received a full course of equine influenza vaccinations in accordance with the requirements of FEI Veterinary Regulations.[38]

The FEI collaborates closely with the OIE and has played an important role in negotiating expanded international movement of horses for competition in the Olympic disciplines,[36,37] a legacy which is of benefit to athletic horses of all breeds.

Overview of quarantine controls of major equine sporting nations

There are various internationally accepted risk management strategies that quarantine authorities use to reduce disease risks associated with importation of horses.[14] Individually, each may not be perfect but, when used in combination, these measures can reduce the probability of importing an infected horse to a very low level, regardless of the starting probability. The combinations adopted vary from country

to country depending on the country's health status and quarantine policy.

Certification of origin from a disease-free source

The risk of introducing a disease agent can be reduced by sourcing horses from a disease-free country, region, zone, or premises. Alternatively, horses from an infected area may be required to be resident in an area free of the disease of concern for a specified period prior to export, a period long enough for that disease to be obvious if the horse is infected. Reliable and transparent information about the government veterinary services and disease surveillance programs in the country of export is obviously critical to the value of this strategy.

Separation

Separation of horses from other potentially infected horses (before export) and from susceptible horses (for a period after import) reduces the risk of disease transmission and the likelihood that infected horses will remain undetected. It also provides an opportunity for observation, diagnosis, and treatment (if appropriate) before imported horses are permitted to contact the domestic population. The risk of importing infected horses or releasing infected horses after arrival is thus reduced even further.

If suitable training and stabling facilities are available, separation need not disadvantage horses visiting for competition. At international race meetings in Asia[14] and Australia,[30] temporary equine imports are isolated from resident horses and horses from countries not of equivalent health status except at the time of racing.

Separation from the host population and, if there are significant variations in health status, separation of temporary residents by region, ensures the success of international competitions. It is recommended as best health practice to prevent the spread of infectious diseases and also protects the health status of visiting horses, thus assisting their prompt and uneventful departure to their next destination.

Satisfactory arrangements to separate visiting horses from the domestic population can also give foreign animal health authorities confidence that their horses can visit safely even in the face of a local disease incident. For example, prompt action by racing and animal health officials in USA salvaged European participation in an international race meeting at Arlington International Racecourse when an outbreak of equine viral arteritis occurred there in 1993.[40]

Diagnostic testing

Testing may be used to identify infected horses before or after export. The value of diagnostic tests in risk reduction depends on the availability and use of standardized tests of high sensitivity, the ability of a test to identify infected horses correctly. For example, a serological test may have a sensitivity of 99% in individual infected horses. Thus the probability of missing the disease when testing a single infected horse is 1%.

For import purposes, the negative predictive value of a test, the probability that a horse is not infected when a test result gives a negative result, is of paramount importance. Predictive values vary markedly according to the disease prevalence in the population from which the tested horse was drawn. As disease prevalence decreases, negative predictive value increases.[41] Reliable and transparent information about the prevalence of disease in the country of origin is critical for interpretation of test results.

When test results vary between different laboratories in different countries, trade problems can ensue.[9,42] Official approval of laboratories, adoption of OIE prescribed tests for international trade and use of the testing standards detailed in the OIE Manual of Standards for Vaccines and Diagnostic Tests[23] minimizes such problems.[9]

Rapid diagnostic tests are becoming more widely available and the Directigen FLU-A enzyme immunoassay[43] has been extensively and effectively utilized for both screening and diagnostic purposes of horses for the equine influenza virus both pre- and postimport in many countries since 1993.

Vaccination

Vaccination against specific disease agents such as Japanese encephalitis can reduce the risk of disease in horses sourced from or imported into an infected region. For other diseases, for example equine influenza, vaccination is of limited value as a risk management option. Equine influenza vaccination can prevent overt disease but a horse can still be infected and shedding virus at the time of import.[4,13,14]

Treatment

Treatment can be used to reduce the risk of importation of exotic parasites such as ticks. Insecticides may be applied to horses to minimize exposure to insect vectors during training sessions[30] and transport. Countries may also require horses to be treated for internal and external parasites before export.

Restrictions on destination, activity, and season of import

An example of this strategy is avoidance of exposure to insect vectors by import into a vector-free zone[26] or, by only permitting importation during a season when insect vectors are not active. Another example is requiring competition horses not to breed or be resident on breeding premises during a period of temporary residency.

Protection of health status during international travel

Government authorities may require horses to travel on approved routes through approved countries and have no contact

with other horses not of the same health status during transport. Special conditions may apply during transit of countries en route or if horses are transhipped from one aircraft to another during a transit. Conditions may be prescribed regarding cleaning and disinfection of horse transport vehicles and shipping containers, and protection of horses from insect vectors during transport.

Restrictions on duration of temporary residency

Visiting horses may only be permitted to remain in countries for a maximum specified period. The period may be set by the importing country or the country of usual residency, or both.

Contact information for major regulatory agencies

Each country has very specific quarantine conditions for temporary and permanent import of horses which are subject to change. Consequently, specific details cannot be given in this review and veterinarians should always seek advice from government officials or a reputable shipping agent before commencing preparation of horses for export. Many agencies now publish their quarantine conditions electronically. Readers are referred to contact information below. Some animal health sites on the internet such as Animal Health Australia (www.aahc.com.au) have good links to a wide range of other international animal health agencies.

Government animal health and quarantine authorities

Australia
Department of Agriculture, Fisheries and Forestry
GPO Box 858
Canberra ACT 2601
www.affa.gov.au/index.cfm

European Commission
Division Legislation Veterinaire et Zootechnique
Rue Froissart, 101, 3/56
1049 Brussels
Belgium
www.europa.eu.int/comm/agriculture/index_en.htm

Hong Kong SAR, People's Republic of China
The Government of the Hong Kong Special Administrative Region
Agriculture, Fisheries and Conservation Department
Cheung Sha Wan Government Offices
303 Cheung Sha Wan Road
5th Floor
Kowloon
Hong Kong
www.afcd.gov.hk/web/index_e.htm

New Zealand
Ministry of Agriculture and Forestry
PO Box 2525
Wellington
www.maf.govt.nz/mafnet/

Office Internationale des Epizooties
12, rue de Prony
75017 Paris
France
www.oie.int

Singapore
Agri-Food and Veterinary Authority of Singapore
Regulatory Services Branch
5 Maxwell Road #02-00 Tower Block MND Complex
Singapore 069110
www.ava.gov.sg

United Arab Emirates
Ministry of Agriculture and Fisheries
Animal Resource Department
www.uae.gov.ae/maf/

United Kingdom
Department for Environment, Food and Rural Affairs
State Veterinary Service
1A Page Street
London SW1P 4PQ
www.defra.gov.uk/

United States
National Center for Import and Export
United States Department of Agriculture
Animal and Plant Health Inspection Service Veterinary Services
Hyattsville
Maryland, USA
www.aphis.usda.gov/NCIE/

World Trade Organization
rue de Lausanne 154
CH-1211 Geneva 21
Switzerland
www.wto.org

Other organizations

Federation Equestre Internationale
Avenue Mon-Repos 24
PO Box 157
CH-1000 Lausanne 5
Switzerland
www.horsesport.org

International Air Transport Association
Cargo – Live Animals
PO Box 113
Montreal, Quebec
Canada H4Z 1M1
www1.iata.org/cargo/co/liveanimals/index

International Federation of Horseracing Authorities
46 place Abel Gance
92655 Boulogne Cedex
France
www.horseracingintfed.com

International Trotting Association
c/o Suomen Hippos ry
Tulkinkuja 3
FIN-02600 Espoo
Finland
www.intertrot.org/

References

1. Sluyter FJH. Traceability of Equidae: a population in motion. Rev Sci Tech 2001; 20(2):500–509.
2. Watkins KL, Devolz R, Ellis P, et al. Guidelines to facilitate the temporary movement of registered racehorses for international races. In: Hill DW, Hill WT, eds. Proceedings of the 14th International Conference of Racing Analysts and Veterinarians, Orlando, 2002. Newmarket, UK: R and W Publications; 2003:280–296.
3. Guthrie AJ, Stevens KB, Bosman PP. The circumstances surrounding the outbreak and spread of equine influenza in South Africa. Rev Sci Tech 1999; 18(1):179–185.
4. Powell DG, Watkins KL, Li PH, et al. Outbreak of equine influenza among horses in Hong Kong during 1992. Vet Rec 1995; 136(21):531–536.
5. Timoney PJ. Equids and equine semen. International trade vs. disease control. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:328–331.
6. Cordes T, Mitchell R. Quarantine considerations and medical management of horses during international shipment. In: Robinson NE, ed. Current therapy in equine medicine 4. Philadelphia: WB Saunders; 1997:717–719.
7. Marks D. International shipping of competition horses. J Eq Vet Sci 1993; 13:609–614.
8. Morgan AM. Regulatory aspects involved in the international movement of horses. In: Nakajima H, Plowright W, eds. Equine infectious diseases VII. Proceedings of the Seventh International Conference, Tokyo, 1994. Newmarket, UK: R and W Publications; 1994:336–338.
9. Timoney PJ. Factors influencing the international spread of equine diseases. Vet Clin N Am Equine Pract 2000; 16(3):537–551.
10. Daniels P. Emerging arboviral diseases. Aust Vet J 2002; 80(4):216.
11. Stone M. Import risk analysis: horses and horse semen. Wellington: Ministry of Agriculture and Forestry, New Zealand; 2000. Online. Available: www.maf.govt.nz/biosecurity/pests-diseases/animals/risk/index.htm#livestock 22 August 2002.
12. Ellis PM, Farr NH, Arab AA, et al. Demonstration of equine health status for international trading purposes: the United Arab Emirates strategy. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:363–366.
13. Mumford JA. Control of equine influenza from an international perspective. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:11–24.
14. Watkins KL. Endemic and exotic equine infectious diseases and their effect on international racing. In: Auer DE, Houghton E, eds. Proceedings of the 11th International Conference of Racing Analysts and Veterinarians, Queensland 1996. Newmarket, UK: R and W Publications; 1996:281–286.
15. Jeffcott L. Foot and mouth disease in Great Britain. Where are we now? The Horse 2001; 18(8):98.
16. World Trade Organization. The Uruguay Round Final Act: full texts. Online. Available: www.wto.org/ 12 July 2002
17. Chillaud T. The World Trade Organization Agreement on the Application of Sanitary and Phytosanitary Measures. Rev Sci Tech 1996; 15(2):733–741.
18. Thomson GR. The role of the Office Internationale des Epizooties in controlling important equine infectious diseases. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:339–341.
19. Office Internationale des Epizooties. What is the OIE? Online. Available: www.oie.int 10 July 2002.
20. FAO-OIE-WHO. Animal Health Yearbook. FAO Animal Production and Health Series. Food and Agriculture Organization of the United Nations; Office Internationale des Epizooties: World Health Organization; 1995.
21. Powell DG. The significance of surveillance and reporting on the prevention and control of equine diseases. Vet Clin N Am Equine Pract 2000; 16(3):389–403.
22. Office Internationale des Epizooties. International Animal Health Code. 10th edn. Paris: OIE; 2001. Online. Available http://www.oie.int 11 July 2002
23. Office Internationale des Epizooties. Manual of Standards for Diagnostic Tests and Vaccines. 4th edn. Paris: OIE; 2000. Online. Available www.oie.int 11 July 2002
24. Sutmoller P, Ahl AS. Regionalisation and risk analysis: tools to facilitate international movement of horses. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:349–358.
25. Brooks LM. The equine piroplasmosis control programme at the 1996 Summer Olympic Games. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:371–375.
26. Martin R. Equine piroplasmosis: the temporary importation of seropositive horses into Australia. Aust Vet J 1999; 77(5):308–309.
27. Rodriguez M, Ladero JL, Castaño M, et al. African horse sickness in Spain: epizootiological and regulatory considerations. J Eq Vet Sci 1992; 12(6):395–400.
28. Guthrie AJ. Regionalisation of South Africa for African horse sickness. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:376–379.
29. Santarelli JN. International movement: a shipper's perspective. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:336–338.
30. Ellis PM. Establishing a quarantine facility for imported racehorses. In: Auer DE, Houghton E, eds. Proceedings of the

11th International Conference of Racing Analysts and Veterinarians, Queensland 1996. Newmarket, UK: R and W Publications; 1996:295–298.
31. Anon. Movement of animals within the single market. Vet Rec 1994; 134(24):629–632.
32. Animal Health Australia. Accreditation program for Australian veterinarians. Initial accreditation training program. Canberra: Animal Health Australia; undated:89–190.
33. International Air Transport Association. Live animal regulations. 28th edn. Montreal: International Air Transport Association; 2001.
34. International Federation of Horse Racing Authorities. International agreement on breeding and racing. Online. Available: www.horseracingintfed.com/e-index.html 22 August 2002.
35. Anderson H. European equine identification technology. In: Proceedings of Identification and Information Expo Illinois: National Institute for Animal Agriculture; 2002. Online. Available: www.animalagriculture.org/id 22 August 2002.
36. Atock MA. FEI involvement in the international movement of horses. J Eq Vet Sci 1988; 8(3):222–227.
37. Sluyter F. International horse movement: health requirements versus impact on equestrian sport development. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:334–335.
38. Federation Equestre Internationale. Veterinary Regulations. 9th ed. Lausanne: FEI; 2002. Online. Available www.horsesport.org 20 August 2002.
39. Federation Equestre Internationale. FEI manual on identification of horses, 4th edn. Lausanne: FEI; 2000.
40. Bork RL. The Arlington experience. In: Powell DG, ed. Equine infectious disease – developing an action plan. Kentucky: Maxwell H. Gluck Equine Research Centre; 1994:13–14.
41. Smith RD. Veterinary clinical epidemiology: a problem orientated approach, 2nd edn. Boca Raton: CRC Press; 1995.
42. Edwards S, Castillo-Olivares J, Cullinane A, et al. International harmonisation of laboratory diagnostic tests for equine viral arteritis. In: Wernery U, Wade JF, Mumford JA, Kaaden OR, eds. Equine infectious diseases VIII. Proceedings of the Eighth International Conference, Dubai, March 1998. Newmarket, UK: R and W Publications; 1999:359–362.
43. Chambers TM, Shortridge KF, Li PH, et al. Rapid diagnosis of equine influenza by the Directigen FLU-A enzyme immunoassay. Vet Rec 1994; 135(12):275–279.

CHAPTER 64

Transport of horses

David J. Marlin

General recommendations for horse transport

- Prior to embarking on long distance transport (greater than approximately 12 h duration for road or flights over 3–4 h), it is advisable to ensure good respiratory health by undertaking endoscopy of the respiratory tract at least 2 weeks in advance of transport. This allows a reasonable period of time for treatment of any pre-existing conditions prior to transport.
- Owners should be advised to always take the rectal temperature of horses prior to embarking on any transport and not to risk transporting pyrexic horses unless in case of other emergency.
- Water and feed should be provided almost on an *ad libitum* basis. Water should be available at all times and not offered only when at rest stops. Damping of feeds with water and soaking of hay or feeding of haylage is important to minimize the inhaled allergen load.
- It is preferable to travel horses with the minimal amount of clothing possible. In conditions where it is unclear whether horses require rugs, then it is better to travel without than with. Under temperate conditions, the risks associated with horses becoming cold are significantly less than them becoming hyperthermic. Increased body temperature will compound the sweat and respiratory fluid losses and dehydration (due to decreased fluid intake) that usually occur in any case with transport, possibly placing the horse at an increased risk of developing colic or respiratory disease.
- If possible, monitor weight loss and recovery following transport. Horses losing more than 5% bodyweight should be considered as candidates for immediate involuntary rehydration either by administration of nasogastric or intravenous fluids.
- An appropriate period of recovery should be built into any transport plans. For road transport in excess of a days transport (~8 h) at least an overnight rest is advisable. For flying, a rule of thumb is 1 day for every 2 h of flying.
- Horses with pre-existing medical conditions, such as rhabdomyolysis or recurrent airway obstruction (RAO, formerly known as equine COPD or 'heaves'), are likely to require special care during and following transport.
- The administration of mineral oil prior to transport as a laxative is commonly undertaken. This is likely to have an effect on the gut flora. The extent to which this will aid or hamper the adjustment to a different fiber source is unknown.
- Where possible, to minimize disturbance to the gastrointestinal tract, abrupt changes in fiber source should be avoided. This is particularly relevant following air transport. If exporting of hay or preserved hay is permitted, then it is advisable to export this to the destination in advance (e.g. by road or sea). Alternatively, if export is not permitted, import a small amount of the fiber to be fed at the destination and wean horses onto it gradually prior to departure.

Almost every domesticated horse will experience some form of transportation at some time in its life. The most common reasons for transport include transport to competitions, for breeding purposes, when bought or sold, for veterinary treatment and for slaughter. The predominate means of transporting horses today is by road, with trailers or floats and

custom-made or modified lorries, trucks, vans, or articulated vehicles. However, the number of horses moved by air in the case of race horses and sport horses competing at international level is not insignificant. In some parts of the world horses are still transported by train and boat in specially adapted carriages or containers. For example, it is still possible to transport polo ponies by boat from Argentina to Europe, or between islands in Greece, and boats and trains are still used to move horses in India. In the UK it used to be common for horses to be taken to race courses by rail, and horses were also transported across the American continent by rail. However, in developed countries, sea and rail transport are now infrequently used, with the exception of horses transported in lorries on relatively short journeys (e.g. across the English Channel).

The successful transport of valuable horses by air and road requires highly skilled staff, good practice and the right fleet of vehicles. While many small transport companies exist, there are also a number of major international transporters. In road transport, the names of companies such as Sallee in the USA and Fritz Johansmann in Europe are prominent. The major airlines that move horses on a regular basis include Lufthansa, Air Canada, KLM, Air France, DHL, FEDEX, Singapore Airlines, Korean Airlines and El Al.

The last 20 years have seen major improvements in many aspects of transport as a result of research undertaken in many different countries. In the early days of transport of horses by air, the only way for the horse to be loaded was by walking across the tarmac and up a ramp. Once in the plane the air-stall was constructed around the horse. Although this type of containment is still used on smaller aircraft for short flights, for larger aircraft and longer journeys the horse is usually loaded into a modern air crate, well away from the plane and runways, which is then towed to the plane and loaded by lifting platforms (Fig. 64.1). With today's freight-movement technology and approaches to moving horses, it is possible to load a full load of horses (~80 horses) onto a Boeing 747 in approximately one and a half hours. In some cases freight is loaded off the back of the plane while horses are loaded on the front, dramatically reducing turnaround times.

There is no doubt that the majority of horses that are moved distances from as little as a few miles to thousands of miles experience little if any discomfort, stress, or ill effects. However, the effects of transport can have a noticeable negative effect on performance without obvious clinical signs of illness or disease or the effect being directly linked to pre-

Fig. 64.1
(A) Horse being loaded into an air-crate. (B) Two horses in a three-horse air-crate. (C) Three air crates containing horses being towed out to be loaded. (D) Two air crates containing horses being loaded onto a 747 cargo plane.

ceding transport. More serious consequences for health can result from transport-related effects on various body systems, most notably effects on the gastrointestinal and musculoskeletal systems, and respiratory tract.

Effects of transport on the respiratory tract

Air quality

Transport of horses by either road or air can present a significant challenge to the respiratory tract. Air quality may be compromised by inappropriate bedding, feed, and poor ventilation resulting in accumulation of irritant (e.g. ammonia from urine, dust), allergic (e.g. molds from hay and straw bedding), and infectious (e.g. bacteria) material in the traveling compartment. For example, during a horse flight from the UK to Australia, airborne bacterial and fungal colony-forming units increased by up to 20- and 7-fold, respectively, with peaks occurring during stationary periods on the ground.[1] However, even during flight when the plane's air-conditioning/circulation system was in operation, bacterial and fungal numbers of colony-forming units were up to five times higher than at the start of the flight. Warm and humid conditions that develop due to heat dissipation of the horse (i.e. sweating) and exhaled moisture can provide an ideal environment for horse to horse transmission of infectious agents.

Ammonia is a potent irritant to the respiratory tract. During 24 h of road transport by trailer, mean ammonia concentration was reported to be less than 1 ppm.[2] In another study, for horses transported 36 h by truck, ammonia concentration was reported to increase from ~0.2 to 2 ppm.[3] The bedding used in these studies was not stated and this may have a profound impact on conversion of urea into ammonia by bacteria present in the bedding. At present it is unclear whether the concentrations of ammonia reported in these studies would induce airway inflammation. However, exposure to 2–17 ppm of ammonia for 40 h has been reported to induce cough and nasal discharge and changes to cilia in the trachea.[4] The ammonia concentrations for air transport have not been reported, but with increasing journey duration significant increases in ammonia are more likely. Zeolite-containing compounds absorb and reduce airborne ammonia concentrations. The compounds are available commercially and are particularly recommended for use during moderate to long periods of transport (in excess of 8–10 h). The zeolite-containing compound is spread on the floor under the bedding (Fig. 64.2).

Fig. 64.2
Ammonia is a potent respiratory tract irritant. Zeolite-containing compounds can be laid under bedding material and help to absorb any ammonia produced from urine by bacteria, thereby reducing ammonia concentrations in air.

Table 64.1 Approximate respirable dust loads (particles per m^3) for different fiber sources, hard feeds, and bedding materials. Adapted from[51]

	Respirable dust (particles/m^3)
Fiber sources	
Haylage (silage)	~4 000
Good hay	~60 000
Alfalfa pellets	~9 000
Grains/concentrates	
Whole grains (e.g. oats)	~4 000
Rolled grains	~120 000
Molassed concentrates	~2 000
Beddings	
Wood shavings	~30 000
Good straw	~11 000
Flax straw	~9 000

Increases in airborne dust can lead to airway inflammation, increased mucus viscosity, increased mucus secretion, and mucostasis. Concentrations of airborne dust were small in horses transported by road for 36 h (0.2–0.4 mg/m^3).[3] In a subsequent study, the concentration of respirable dust (<5 μm) averaged 9 μg/L of air over 24 h of road transport.[2] In both studies it was stated that hay was fed, but not whether this was dry or soaked, nor was the bedding used stated; both can have a marked impact on the respirable dust load. The measured respirable dust loads for a number of different feeds and beddings are shown in Table 64.1. It should be noted that use of unsoaked hay, even if of good quality, and wood shavings for bedding, which are both commonly used in both road and air transport, present a considerable respirable dust load.

Mucocilary clearance

Transport is also frequently associated with dehydration, which can decrease mucociliary clearance. Following 24 h of trailer transport in which horses lost a mean of only ~3% bodyweight, lung clearance of inhaled ^{99m}Tc-DPTA from peripheral airways showed a trend to decrease by around 20%.[2] Unfortunately, clearance from the larger, ciliated

airways was not assessed and the degree of dehydration induced was much lower than can commonly occur during transport. There are currently no reports of pulmonary clearance following air transport. However, a study of mucocilary clearance of ^{99m}technetium–sulfur colloid in non-transported horses demonstrated a marked effect of head and neck position on clearance, with reduced clearance during enforced maintenance of a high head position.[5]

The drying of the airways and increases in mucus viscosity can be further exacerbated by increases in mucus production stimulated by inhalation of dust or allergic material. Warm and humid conditions inside the transport compartment can also cause the horse to increase its ventilation[6] (as a thermoregulatory response to increase heat dissipation), with the result that more particles are deposited in the airways and airway drying is further increased. In addition, maintenance of an elevated head position, as is almost universal during transport of horses, has been shown to result in marked increases in mucus and numbers of bacteria and neutrophils in the trachea within as little as 6–12 h of elevation.[5,7,8]

It is not uncommon for some horses to exhibit signs of mild airway inflammation following prolonged transport, particularly in 'heaves'-affected animals. Similarly, animals that begin a journey with pre-existing airway inflammation will almost certainly not improve and are more likely to suffer exacerbation of their condition. Generalized 'stress' responses in animals that are poor travelers could possibly contribute to pulmonary or systemic immunosuppression. At present, although there is widespread agreement that current common transport practices result in respiratory tract inflammation, there is little if any evidence to suggest that this is due to functional impairment of pulmonary defenses as a result of immunosuppression.[9–11]

Shipping fever

Transport in general has been identified by a number of authors as an important risk factor for the development of respiratory disease.[12–14] The risk clearly increases with journey duration, especially in excess of 10 h. A severe manifestation of the effects of transport on the respiratory tract may be the development of 'shipping fever'. Affected horses most usually exhibit pyrexia, depression, and reduced appetite, with or without specific respiratory signs including cough, nasal discharge, and increased respiratory rate. Shipping fever can progress to pneumonia or pleuropneumonia if not treated appropriately, and can be fatal. The reported causative agents implicated in shipping fever include *Streptococcus equi*, *Streptococcus suis*, *Streptococcus zooepidemicus*, and *Pasteurella caballi*.[15,16] However, it is generally believed that the most common agent involved is *S. zooepidemicus*.

The risk of shipping fever increases with duration of travel whether by road or air. Road transport in excess of 10 h appears to markedly increase the risk of shipping fever,[12,14] although this author has experienced horses developing shipping fever after journeys of as little as 6 h by road. In a study carried out in Japan over a 5-year period from 1989 to 1994, the incidence of shipping fever following road transport of 25–28 h was 11.9%.[17] Another study in Japan over a more recent 4-year period indicated that for all horse movements by road the incidence of shipping fever was 1.4%.[11]

The incidence of horses completing transport and showing clinical signs of respiratory disease that does not progress to shipping fever is even higher. When respiratory disease was defined on the basis of rectal temperature in excess of 38.6°C, cough, nasal discharge and lethargy, the percentage of horses showing such signs following 36 h of road transport was 45%.[3] Similarly, the prevalence of pyrexic horses was found to increase markedly beyond 20–24 h of road transport.[3]

Other risk factors for the development of shipping fever include air quality, number and density of animals in the transport compartment, and the presence of respiratory disease in individual horses prior to the onset of transport.

Effects of transport on the gastrointestinal tract

Effects of transport on the gastrointestinal tract may relate to generalized stress responses resulting in an increase in fecal water content and hence increased dehydration. Alterations in gut flora may also occur and can contribute to decreased gut transit times, increased water loss, and decreased digestibility. Decreased feed and water intake during transport may lead to decreases in intestinal motility and predispose to colic. Conversely, dehydration may decrease gastrointestinal tract water content and slow the passage of ingesta with an increased risk of impaction colic. Changes in hard feed (i.e. grains, pellets, etc.) and/or forage, imposed either due to costs of transporting feed or to import restrictions, will almost certainly cause marked disturbances to gut flora and have been identified as risk factors for the subsequent development of colic.[18] There is evidence to suggest that such disturbances may persist for 2–3 weeks following an abrupt change in feed,[19] again with implications for digestibility and gastrointestinal tract water content. This may result in horses losing weight or recovering weight slowly following transport and may have important implications for sporting disciplines in which the gastrointestinal tract serves as an important source of water to offset fluid losses through sweating, such as endurance and eventing.

Digestibility and feed intake may be further compromised when there has been a significant change in time zone to that from where the horses originated their journey. This is effectively similar to jet-lag in people. Decreased feed and water intake are not uncommon in the first few days following air transport across three or four time zones.[20] Under normal conditions, around two-thirds of a horse's water intake is associated with feed intake, and *vice versa*. The effect of disturbance to normal feed intake is likely to be worse when small numbers of large feeds are given. If the horse is nor-

mally fed at 7 a.m. and 7 p.m., and following a flight is fed at these times at the destination, then for a destination where the local time is 8 h behind, the horse will be fed at the equivalent of 3 p.m. and 3 a.m. It may therefore take horses 2–3 days to adjust to these new feeding times.

Weight loss during transport

Almost all horses, whether experienced and relaxed travelers or nervous or inexperienced travelers, lose weight during transport. Weight loss during transport may result from decreased feed and water intake, increased postural energy expenditure, and decreased digestibility of feed, although most weight loss is likely to be due to loss of fluid. This may occur because of increased fecal water content and increased thermoregulatory-associated losses (increased sweating and increased respiratory water loss). In the case of air transport, the low humidity will increase insensible water loss (water loss due to the permeability of skin to moisture) without obvious sweating.

Weight loss and recovery following road transport

A summary of studies reporting weight loss during road transport is shown in Table 64.2. Factors that increase weight loss are duration of journey, warm or hot environmental conditions, and failure to provide feed and/or water. Differences in type of vehicle used, breed, previous transport experience, fitness, distance traveled, environmental conditions, and provision of food and/or water make direct comparison between studies difficult. However, the rates of weight loss for journeys of 4.5 to 14 h[11,20–22] show a similar range of rates of weight loss of 0.33–0.42% bodyweight/h. Whereas journey times in excess of 24 h are associated with increased absolute weight loss, the rate of weight loss is reduced compared with shorter journeys[11,23–25] (Marlin, unpublished data).

It should be remembered that most studies are likely to have been conducted using professional drivers and vans, or at least by researchers driving sympathetically. In circumstances where the vehicle design is suboptimal or the vehicle is badly driven,[2,11] or there is significant turbulence in the case of flying, animals have limited space to move,[23] ventilation is poor and environmental temperature is high, rates of weight loss may be doubled.

Table 64.2 Summary of weight loss in different transport studies

Breed/Type	Vehicle	Training status	Distance (km)	Duration (h)	Weight loss (%)	Weight loss (%/h)	Weather	Fed/ Watered	Reference
TB	Trailer	Fit	1474	24	2.5	0.10	13–30°C	Yes/Yes	2
Mainly TB	Trailer	NS	240	2.4	1.5	0.63	21–27°C	No/No	21
Mainly TB	Trailer	NS	480	4.8	2.6	0.54	21–27°C	No/No	21
Mainly TB	Trailer	NS	720	7.2	3.0	0.42	21–27°C	No/No	21
TB	NS	NS	600	8.0	3.0	0.38	Hot	Yes/Yes	23
Quarter Horse and TB (to slaughter)	Trailer	NS	NS	6–30	4.0	NA	NS	NS	24
Mixed breed	Commercial van	NS	1622	24	6.0	0.25	Summer	NS	21
Mixed breed	Trailer	NS	NS	30	10.3	0.33	Hot	No/No	25
Mixed breed	Trailer	NS	NS	30	4.0	0.13	Hot	No/Yes	25
TB	NS	NS	NS	2.5	1.3	0.50	28–35°C	NS	11
TB	NS	NS	NS	4.5–6.5	1.5	0.33–0.23	28–35°C	NS	11
TB	NS	NS	NS	41	3.5	0.09	28–35°C	NS	11
TB	NS	NS	NS	60	5.3	0.09	28–35°C	NS	11
Mixed breed	Commercial van	Fit	NS	4	1.5	0.37	Hot	Yes/Yes	20
Mixed breed	Commercial van	Fit	NS	14	5.0	0.36	Warm	Yes/Yes	20
Mixed breed	Commercial van	Fit	NS	2	0.9	0.44	Hot	Yes/Yes	20
Mixed breed	Commercial van	Fit	NS	3 × 9 h (over 3 days)	0.6–1.7	0.07–0.20	Cool–hot	Yes/Yes	Marlin, unpublished data
TB	Van	Fit	NS	7	2.8	0.40	Warm	Yes/Yes	Marlin, unpublished data

NS, not stated; TB, Thoroughbred.

There are less data relating to weight loss and recovery following flying. For fit Thoroughbred racehorses transported by road and air for total durations of 6–36 h, weight loss during flying was around 3.6% bodyweight.[26] In a group of fit, three-day event horses of mixed breed with no previous flying experience and flown 9 h, the mean weight loss was 4.5% bodyweight or 0.5% bodyweight/h.[20]

The time for recovery in bodyweight following transport to that before transport depends on the duration of transport, the amount of weight lost, the environment to which the horse has traveled, the individual temperament of the horse, and possibly on previous transport experience. Changes in hay or hard feed (i.e. grains, cubes, pellets) may further delay recovery in bodyweight. Fit three-day event horses took 3 days to recover bodyweight following a road-transport-induced loss of 5% bodyweight.[20] Fit Thoroughbreds transported for 7 h by road and losing 2–3% bodyweight took less than 24 h to regain their pretransport weight (Marlin, unpublished data), whereas fit, elite three-day event horses took 24–48 h to recover following three consecutive days of road transport (Marlin, unpublished data). Foss and Lindner[21] reported that of losses in bodyweight of 1.5–3.0% induced by road transport, within 24 h in all cases the average deficit had been reduced to approximately 1.5% bodyweight, irrespective of the degree of transport-induced loss.

Weight loss and recovery following flying

Following flying and an average loss of 3.6% bodyweight, Thoroughbred race horses continued to show a deficit of 2.4% bodyweight compared to before transport at three days after arrival.[26] In a study where horses were followed for a longer period, recovery in bodyweight following a loss of 5% bodyweight was not attained until 7 days after arrival in a hot and humid climate.[20]

Diurnal changes in bodyweight

Bodyweight may vary by as much as 10–15 kg or 2% body weight in horses that are fed, watered, stabled, and rested or exercised (Marlin, unpublished data). Horses are normally found to be lightest prior to their morning feed and heaviest around 6 p.m. to 12 a.m. after consumption of feed throughout the day. Morning exercise may mean that the lowest bodyweight is recorded mid to late morning. This has some implication in assessing transport weight losses. A horse traveling morning to evening that arrives at the same bodyweight as it left has effectively lost weight, because it should arrive heavier on a normal diurnal cycle. However, in two studies where horses were kept in pens or paddocks in warm to hot conditions, weight loss was similar to those for an equivalent duration of transport. For horses kept in paddocks for 7 h at 21–27°C without food or water, weight loss was 3% bodyweight or 0.42% bodyweight/h.[21] Horses kept in paddocks for 30 h in hot conditions without water lost 12.8% bodyweight (0.43% bodyweight/h) but only 3.5% bodyweight (0.12% bodyweight/h) when allowed access to water.[25]

Fluid intake during transport

Most studies have reported a decrease in water intake during transport compared to an equivalent stabled period when horses were not transported. In one study, despite water being provided continuously, none of the horses consumed any water during an 8 h road journey, although all continued to eat.[22] This response may have been due to limited previous transport experience of this group of horses. During 7 h of road transport, mean water consumption was 23 L compared with 30 L for the same period of time in the stable (Marlin, unpublished data). In a group of elite three-day event horses transported for 9 h a day for three consecutive days, mean daily water intake was 26 L and was not different to the 3-day mean before transport (28 L) or following arrival (28 L). However, in two horses, individual water intake dropped to 7 and 11 L on the first day of transport, but in

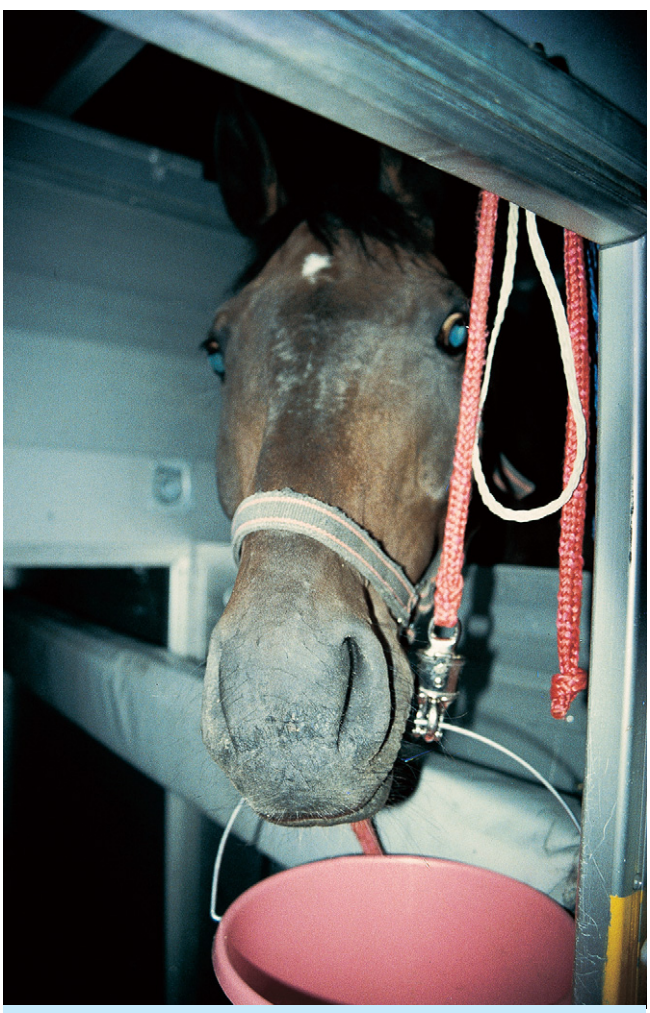


Fig. 64.3
A horse in an air crate with continual access to water in a bucket suspended within the crate from a lead rope.

both horses increased to 32 and 27 L, respectively on the second day of transport (Marlin, unpublished data). Smith et al.[2] reported that during 24 h of road transport in a two-horse trailer, water consumption was reduced to a mean of 27 L/24 h compared with 53 L/24 h before transport. In this study the horses were given access to water during 15 min stops every 3.75 h.

In spite of transport inducing dehydration, transported horses that were not permitted access to water during transport but then given water after transport, only consumed a mean of 21 L.[27] This was in contrast to horses that were kept in pens for a similar duration, which consumed a mean of 38 L. This may be related to other effects of transport, such as fatigue, not directly related to dehydration.

There is limited published information relating to water consumption during air transport. During a 9-h flight, when water and feed were provided continuously (Fig. 64.3), water intake averaged 33 L compared to 25 L for the three days prior to the flight.[20]

Effects of transport on the musculoskeletal system

Confinement and collision with internal structures of the transport vehicle might reasonably be expected to increase indicators of muscle damage such as creatine kinase (CK) and aspartate aminotransferase (AST). The extent of such increases might therefore be reasonably expected to depend on factors such as transport vehicle design; orientation within the vehicle; the nature of the flooring material; the quality of driving; road surface conditions; the amount of cornering, stopping, accelerating, braking; degree of turbulence during flying; and the age and health of the animals being transported. However, as dehydration is common during transport of horses, small increases in CK and AST following transport might be due to dehydration rather than muscle damage *per se*.

Serum CK and AST activities were not increased significantly by 14 h of road transport or 9 h of flying in a group of competing three-day event horses.[20] Mean CK and AST activities in a group of elite three-day event horses were also unchanged following three consecutive days of road travel with overnight rest stops (pretransport 34 U/L versus post-transport 26 U/L) (Marlin & Killingbeck, unpublished data). In contrast, CK activity was increased significantly in horses transported for 24 h, but only by a mean of 74 U/L and returned to pretransport activities by 24 h post-transport.[24] Similarly, CK activities increased by means of 3, 113, and 217 U/L in horses trailered by road for 2.4, 4.8, and 7.2 h.[21] However, in the same study, horses kept in pens also showed a mean increase in CK of 66 U/L over a 7.2 h period. There is also a report in the literature that indicates that both serum CK and AST activities show diurnal variation, with elevations in the afternoon compared with the morning.[28]

In race horses transported by road and air for between 6 and 39 h, CK and AST were not elevated immediately on arrival, but some horses showed an increase over the first 24 h at the destination.[26] In 12 healthy, adult horses transported by road for 130–200 km, the mean plasma CK activity increased 93 U/L.[29] Following a 300-km road journey, in a group of 40 Thoroughbred race horses the mean increase in plasma CK activity was only 60 U/L and had returned to pretransport activities by 24 h.[30] In contrast, a short 70-min road journey was reported to increase CK in a group of 30 healthy stallions.[28] Although most studies show minimal increases in CK following transport, there is one report of four horses developing rhabdomyolysis during transport.[31]

Generalized responses to transport

Heart rate and energy expenditure

Increases in oxygen consumption indicate an increase in tissue metabolic activity and energy expenditure, which can usually be ascribed to increased muscular effort, in the absence of fever. In transported horses, increases in oxygen consumption may be attributable to increased energy expenditure in order to maintain posture in response to changes in speed and/or direction. Increases in heart rate may also indicate an increase in energy expenditure, but can also be a result of reactions to external stimuli or a generalized stress response. However, it should also be noted that increases in oxygen consumption and/or heart rate may result from increased thermoregulatory demands as a result of increased temperature and humidity within the traveling compartment.

In most studies, heart rate of horses during road transport has been reported to be higher than that for the same horses either at rest in the transport vehicle or in their own stables.[2,32–37] Clark et al.[32] reported a mean heart rate during 18 min of transport in a two-horse trailer of 85 bpm in horses with little or no previous transport experience. Smith et al. reported a mean heart rate of 66 bpm for eight Thoroughbred geldings with unknown previous transport experience during 100 min of road transport in a four-horse trailer, compared to a mean heart rate of 48 bpm when the trailer was parked.[34]

However, in contrast, in a transport study of 30 mature mares and geldings, during 6 h of road transport in a large trailer, mean heart rate was only around 5 bpm higher compared to horses kept in pens for the same period of the day.[25] Similarly, in trained Thoroughbred horses with previous but no recent transport experience, mean heart rate during 7 h of road transport in a two-horse lorry was only around 5–7 bpm higher than when the horses were in their stable during the same period of the day (Marlin et al., unpublished data). Doherty et al.[33] also reported that mean heart rate in Shetland ponies during 30 min of road transport was only

approximately 5 bpm higher than when standing. However, in this study the 'resting' (standing) mean heart rate of 54 bpm would be considered high.

In many studies, the previous transport experience of horses used is not stated or possibly not known. It does appear that there are marked differences in transport responses in horses that are effectively transport naive compared with horses that are transported on a regular basis.

There is also evidence that heart rate responses to transport also depend on the stage of the journey and on the transport vehicle configuration and orientation of the animals within the vehicle. For example, heart rate has been reported to show the greatest elevation during the initial movement of the vehicle, with a gradual decline over the first 10–30 min of transport.[32,34,35]

A number of studies have investigated the orientation preference of horses during road transport and whether there are differences in behavior or physiologic or other responses assumed to be indicative of stress when horses are transported in different orientations relative to the direction of forward travel. A review of the literature indicates that multiple factors, including size and design of vehicle, space allocation, duration of transport, road conditions, journey route, and number of horses transported, as well as individual horse preferences that determine the response to or selection of different orientations during transport.[32–35,38–40]

During enforced orientation during road transport, rearward-facing transport has been reported to be associated with reductions in side and total number of impacts with the vehicle interior, losses of balance, vocalization, and movement.[32,37,38] Only one study has reported a significant reduction in heart rate during a rearward compared to forward-facing transport in a lorry for 60 min,[37] whereas others have reported trends[33] or no difference.[32,34] Two studies have, however, reported lower heart rates for rearward-facing loading and during the initial movement of the vehicle.[32,37] In relation to other indicators of stress or comfort, Clark et al.[32] reported no difference in plasma cortisol for horses transported forward- or backward-facing for 18 min by road.

In studies where horses have been allowed to select their own orientation (i.e. when transported loose), results have been highly variable. For example, Smith et al.[35] reported that out of eight horses transported loose in a four-horse stock trailer, one was in constant motion whereas five spent more than half the time during transport facing backward. In contrast, in a group of 12 horses transported in a commercial straight-deck, topless trailer, loose horses spent the greatest percentage of time (57%) facing forwards at angles of between 22° and 67° to the direction of travel.[38] In the same study, however, when horses were tied to the trailer, the side to which they were secured determined the direction they chose to face, with the greatest percentage of travel time facing backwards when tied to the left side of the trailer. Overall, these authors reported that the horses studied showed a slight preference for travel at 45° to the direction of forward movement, but no significant preference for facing toward or away from the direction of transport. Thus, whether forward- or rearward-facing transport is preferable is still unresolved and appears to depend on individual horse preference and possibly other factors such as previous transport experience, degree of acclimation transport prior to study, presence of other horses, vehicle configuration, and possibly duration of journey, as most studies cited have been relatively short.

Although it was noted previously that elevations in heart rate may be due to excitement, stress, or stimulation rather than to increased energy expenditure *per se*, a recent study utilizing EMG, heart rate, and video recording during road transport did show that muscle activity and heart rate were very closely correlated.[41] The implication from this is that most elevations in heart rate are related to the muscular efforts to adjust posture. As concluded by Giovagnoli et al., simultaneous increases in heart rate and EMG almost certainly reflect both emotional and physical stress, and are most likely primarily determined by road conditions and driving style. Whereas an increase in oxygen uptake would have been inferred by the increased EMG activity in the study by Giovagnoli et al.[41] in an earlier study, Doherty et al.[33] showed nearly a two-fold increase in energy expenditure (estimated from direct measurement of oxygen consumption) in Shetland ponies during 30 min of road transport compared to when standing.

There appears to be only one report of heart rates during air transport.[42] Heart rates were recorded during transport of horses for 12 and 24 h in enclosed containers (Airstable®) designed to prevent the ingress of insects that could act as potential vectors for equine infectious diseases. Mean heart rate for the whole period of each flight ranged from 39–57 bpm and was similar to the mean heart rate of horses on the same flights that were traveled in conventional open stalls (range 34–46 bpm). Peaks in heart rate associated with take-off and landing were around 80–100 bpm and are not considerably different from those seen in horses transported by road. This should not be surprising, as it is likely that the horse is unable to differentiate between flying and road transport but reacts simply to visual, audible, and/or mechanical cues, irrespective of their origin. Thus, in the absence of turbulence, and accepting the likelihood of poorer air quality, on a per hour basis it would be expected that horses would be less affected by flying than by road transport.

Hematology and biochemistry

Road transport

Leukogram In contrast to studies of flying, most studies of road transport have reported increases in peripheral white blood cell (WBC) count. For example, WBC count was increased in horses transported for between 5 and 32 h by road, or for 24 h by road, respectively,[24,43] although Smith et al. [2] reported no increase in WBC count following 24 h of road transport. A mean increase from 6.6 to 9.9 × 10^9 WBC/L blood following ~14 h of road transport has been reported,[20] but no change in total WBC count following 7 h of transport, although there was a significant increase in neutrophil count (Marlin, unpublished observations). Stull and Rodiek [24] reported an increase in WBC from around 8 to

13×10^9 WBC/L blood following 24 h of road transport, although it is worth drawing attention to the fact that the majority of the increase occurred in the first few hours of transport.

Hematocrit and total protein Packed cell volume (PCV) and total protein have been measured in a number of transport studies and will generally reflect the extent of dehydration. However, as it is easy to provoke an acute increase in PVC through excitement, protein measurements are likely to be more reliable as an index of hydration status. Perhaps not surprisingly, shorter duration (<7 h) journeys by road have reported no changes in PCV or total protein[30,44] (Marlin, unpublished data). Following longer-duration journeys (in excess of 24 h) PCV and total protein have not always been shown to increase in parallel. For example, both Smith et al.[2] and Stull et al.[24] found an increase in PCV but no change in total protein following 24 h of road transport. This suggests that PCV was most likely elevated either due to excitement during transport or sampling or the entrance of people into the horse compartment rather than by dehydration *per se*. In the study by Friend,[25] as would reasonably be expected, total protein was considerably higher at the end of transport in the non-watered group compared with the watered group.

Electrolytes Fewer studies have measured plasma electrolyte concentrations and results are contradictory for shorter-duration road transport.[30,44] However, for 30 h of road transport,[25] in horses receiving water, serum sodium and chloride concentrations were both increased by 8 h of transport, but were no different to pretransport after 30 h. This was in contrast to marked increases in sodium and chloride concentration at 30 h in the non-watered group. Following a 9 h flight, plasma sodium (pre 136 versus post 141 mmol/L), chloride (98 versus 104 mmol/L), potassium (3.6 versus 4.1 mmol/L), and total protein (66 versus 73 g/dL) concentrations were all significantly increased.[20] These changes were much more marked than when the same horses were transported ~14 h by road. Van den Berg and colleagues investigated water and electrolyte balance in Thoroughbred horses during 8 h of road transport in comparison to a non-transport control.[22] Dehydration was modest (~3% bodyweight loss) and intake of sodium and chloride were unaffected by transport, although potassium intake was decreased. Interestingly, sodium and potassium losses in urine and feces were similar, whether horses were maintained in stables (control) or transported, but potassium output was reduced in the transported group during the post-transport period. There do not appear to be any other reports in the literature of plasma electrolyte changes following air transport.

Air transport

There is limited published information concerning changes in hematology and biochemistry following air transport. Thornton[42] reported no changes in hematology and/or biochemistry following flights of 12 or 24 h. Leadon et al.[26] reported no changes in WBC, plasma sodium or potassium, but small increases in chloride, PCV, and fibrinogen. In a separate study the same authors also found no increase in WBC count following flying, although the WBC was decreased at 2 days postflight, suggesting that the values before flight may have been elevated. In the same study the authors reported a doubling of blood neutrophil counts and no change in globulin concentration. In contrast, following a 9-h flight, the author and colleagues have reported increases in WBC, sodium, chloride, albumin, and total protein concentrations.[20]

Hormonal responses to transport

Cortisol

Cortisol is the hormone that has been most frequently measured in transport studies. During road transport, plasma cortisol concentration has been reported to either increase or remain unchanged. In a number of shorter studies there has been a marked increase in plasma cortisol concentration in the early stages of transport,[32,44] whereas studies of longer duration have reported little or no increase in cortisol concentration[2,25] (Marlin, unpublished data). In fact, in the study by Friend[25] the greatest increase in cortisol concentration was in non-transport controls kept in pens without access to water. In one of the longer duration road transport studies which did report a large (4-fold) increase in cortisol concentration, almost half the increase occurred in the first few hours of transport.[24] When the results of the various studies are considered together, the implication is that increases in cortisol concentration are probably due to handling, loading and the initial movement of the vehicle, rather than prolonged movement or confinement.

Other hormones

With respect to other hormone measurements during transport, a decrease in serum aldosterone concentration has been reported following short-term road transport.[44] No changes were found in plasma adrenocorticotrophic hormone (ACTH), dopamine, epinephrine (adrenaline), or norepinephrine (noradrenaline) concentrations following 7 h of road transport (Marlin, unpublished data). ACTH and 11-hydroxycorticosteroid peaked within 5 h of the start of a 41-h road journey.[11] Although only 18 min of road transport doubled plasma cortisol concentration, it had no effect on plasma thyroxine concentration.[32] A combination of road and air transport of Thoroughbred race horses lasting a total of 6–39 h produced a small increase in plasma cortisol,[26] whereas there was no overall change in plasma β-endorphin in horses flown for 30 h.[42] Li and Chen reported an increase in plasma β-endorphin of around 40% only 30 min after the onset of road transport, but a decrease by 60 min of transport.[45] However, in all these examples of changes in circulating concentrations of hormones, the changes induced by transport are considerably lower than those commonly reported for exercise.

Rest stops

Perhaps surprisingly, there are no studies in the scientific literature looking at the use of rest stops during transport,

Fig. 64.4
Exercising horses by walking in hand while waiting for loading onto a cross-channel ferry from France to the UK.

although these are used to varying degrees by almost all people who transport horses. The current consensus appears to be that horses should at least be checked approximately every 4 h of transport, and preferably the vehicle stopped and the horses unloaded; this is sometimes not feasible. Ideally, horses should not be transported for more than 8–10 h at a time, particularly by road, without an overnight rest. Sometimes there are opportunities to exercise animals when waiting for a change in transport, e.g. from road to air or road to boat (Fig. 64.4), however, extreme care should be taken to evaluate the surroundings before unloading horses, especially in airports.

Immune function

The observation that horses develop respiratory disease during or following transport has led to the suggestion that the stress associated with transport may in turn lead to immunosuppression. This speculation is usually linked to the belief that increases in cortisol as part of a stress response to transport will lead directly to immunosuppression. Wheras cortisol is an immunomodulator, increased concentrations of circulating cortisol do not conclusively result in immunosuppression. Furthermore, as reviewed above, transport is not universally associated with increases in circulating cortisol.

The effects of transport on the immune system of the horse have recently been reviewed[46] and will therefore only be dealt with briefly. In relation to pulmonary immune function and in considering whether local immunosuppression contributes to the development of respiratory disease during transport (i.e. shipping fever), the role of immunosuppression is difficult to dissociate from impaired mucociliary clearance and associated bacterial proliferation.[5,8,47] Indeed, a number of studies have failed to demonstrate any impairment of alveolar macrophage function following transport.[10,48] Following 7 h of road transport, there was no change in lymphocyte proliferation in response to concanavalin A and phytohemagglutinin or in lymphocyte expression of CD4 or CD8 (Marlin, Kydd, Hannant, unpublished data). Other reports of immune function and transport in the literature are in other species, including cattle and pigs. Thus, it is conceivable that in some individuals the development of conditions such as shipping fever may be facilitated by a component of immunosuppression, but this does not appear to be a universal occurrence in transported horses.

Jet-lag, transport and possible effects of transport on performance

Transport may have a direct impact on subsequent performance due to injury, impaired respiratory health, fatigue, 'stress', and disorientation. The influence of jet-lag on the function of, for example, airline pilots[49] and performance in athletes[50] continues to be an area of interest. Although it is accepted that jet-lag occurs to some extent in all humans as a result of rapid air travel across a number of time zones, it is less clear to what extent horses are affected. It has been reported that following 9 h air transport across six time zones (i.e. –6 h at destination compared to origin) there was a reversal of the normal diurnal rectal temperature relationship, an increased frequency of uneaten meals, and changes in pattern of water consumption.[20] Although these changes may be consistent with development of jet-lag, they are impossible to differentiate from the effects of transport *per se* (i.e. fatigue, dehydration, disorientation).

Summary

The majority of horses are transported without incident. However, there may still be subclinical effects of transport, which may or may not noticeably impair performance. At the other end of the scale, a small proportion of horses become ill and may die as a result of conditions occurring that are directly associated with transport, particularly 'shipping fever'. The reasons why some transport events result in illness in some but not all individuals are presently unclear. However, the marked variation in response to transport that occurs around the world is also reflected in the marked variation between the controlled experimental studies of horse transport presented in this review. The variation in response to transport, in many cases in what appear to be similar studies, is most likely due to a combination of different factors, which could include age, breed, sex, temperament, fitness, presence of pre-existing disease, previous transport experience, external and internal environmental conditions, transport vehicle design, and the feeding and watering regimen.

References

1. Leadon DP, Daykin J, Backhouse W, et al. Environmental, hematological and blood biochemical changes in equine transit stress. Proceedings of the Annual Convention of the American Association of Equine Practitioners 1991:485–490.
2. Smith BL, Jones JH, Hornof WJ, et al. Effects of road transport on indices of stress in horses. Eq Vet J 1996; 28:446–454.
3. Oikawa MA, Kusunose R. Some epidemiological aspects of equine respiratory disease associated with transport. J Eq Sci 1995; 6:25–29.
4. Katayama Y, Oikawa M, Yoshihara T, et al. Clinico-pathological effects of atmospheric ammonia exposure on horses. J Eq Sci 1995; 6:99–104.
5. Raidal SL, Love DN, Bailey GD. Effects of posture and accumulated airway secretions on tracheal mucociliary transport in the horse. Aust Vet J 1996; 73:45–49.
6. Hobo S, Kuwano A, Oikawa M. Respiratory changes in horses during automobile transportation. J Eq Sci 1995; 6:135–139.
7. Racklyeft DJ, Love DN. Influence of head posture on the respiratory tract of healthy horses. Aust Vet J 1990; 67:402–405.
8. Raidal SL, Love DN, Bailey GD. Inflammation and increased numbers of bacteria in the lower respiratory tract of horses within 6 to 12 hours of confinement with the head elevated. Aust Vet J 1995; 72:45–50.
9. Traub-Dargatz JL, McKinnon AO, Bruyninckx WJ, et al. Effect of transportation stress on bronchoalveolar lavage fluid analysis in female horses. Am J Vet Res 1988; 49:1026–1029.
10. Crisman MV, Hodgson DR, Bayly WM, Liggitt HD. Effects of transport on constituents of bronchoalveolar lavage fluid from horses. Cornell Vet 1992; 82:233–246.
11. Oikawa M, Jones JH. Studies of the causes and effects of transport-associated stress and shipping fever in athletic horses. In: Kohn CW, ed. Guidelines for horse transport by road and air. New York: American Horse Shows Association, 2000:35–62.
12. Raphel CF, Beech J. Pleuritis secondary to pneumonia or lung abscessation in 90 horses. J Am Vet Med Assoc 1982; 181:808–810.
13. Mair TS, Lane JG. Pneumonia, lung abscesses and pleuritis in adult horses: a review of 51 cases. Eq Vet J 1989; 21:175–180.
14. Austin SM, Foreman JH, Hungerford LL. Case-control study of risk factors for development of pleuropneumonia in horses. J Am Vet Med Assoc 1995; 207:325–330.
15. Hayakawa Y, Komae H, Ide H, et al. An occurrence of equine transport pneumonia caused by mixed infection with *Pasteurella caballi*, *Streptococcus suis* and *Streptococcus zooepidemicus*. J Vet Med Sci 1993; 55:455–456.
16. Oikawa M, Kamada M, Yoshikawa Y, Yoshikawa T. Pathology of equine pneumonia associated with transport and isolation of *Streptococcus equi* subsp. *zooepidemicus*. J Comp Pathol 1994; 111:205–212.
17. Hirano S. Incidence of shipping fever in racehorses transported by road for 1000–13000 km. Eq Sci 1994; 31:445.
18. Tinker MK, White NA, Lessard P, et al. Prospective study of equine colic risk factors. Eq Vet J 1997; 29:454–458.
19. Goodson J, Tyznik WJ, Cline JH, Dehority BA. Effects of an abrupt diet change from hay to concentrate on microbial numbers and physical environment in the cecum of the pony. Appl Environ Microbiol 1988; 54:1946–1950.
20. Marlin DJ, Schroter RC, White SL, et al. Recovery from transport and acclimatisation of competition horses in a hot humid environment. Eq Vet J 2001; 33:371–379.
21. Foss MA, Lindner A. Effects of trailer transport duration on bodyweight and blood biochemical variables of horses. Pferdeheilkunde 1996; 12:435–437.
22. van den Berg JS, Guthrie AJ, Meintjes RA, et al. Water and electrolyte intake and output in conditioned Thoroughbred horses transported by road. Eq Vet J 1998; 30:316–323.
23. Stull CL. Responses of horses to trailer design, duration, and floor area during commercial transportation to slaughter. J An Sci 1999; 77:2925–2933.
24. Stull CL, Rodiek AV. Physiological responses of horses to 24 hours of transportation using a commercial van during summer conditions. J An Sci 2000; 78:1458–1466.
25. Friend TH. Dehydration, stress, and water consumption of horses during long-distance commercial transport. J An Sci 2000; 78:2568–2580.
26. Leadon DP, Watkins K. Bodyweight, rectal temperature, haematology and blood biochemistry prior to transport and for three days after arrival, in racehorses transported by air to international races in Hong Kong. In: Kohn CW, ed. Guidelines for horse transport by road and air. New York: American Horse Shows Association, 2000:71–81.
27. Friend TH, Martin MT, Householder DD, Bushong DM. Stress responses of horses during a long period of transport in a commercial truck. J Am Vet Med Assoc 1998; 212:838–844.
28. Schmidt B, Schmidt KH. Effect of road transport, lunging, tournament and daytime on activities of serum enzymes aspartate aminotransferase, creatine kinase, lactate dehydrogenase, alkaline phosphatase and serum bilirubin in warm-blooded horses. Berliner und Munchener Tierarztliche Wochenschrift 1980; 93:244–246.
29. Caola G, Ferlazzo A, Panzera M. Serum content of creatinine and creatine phosphokinase in the horse after transport. Clinica Veterinaria 1984; 107:46–48.
30. Codazza D, Maffeo G, Redaelli G. Serum enzyme changes and haemato-chemical levels in Thoroughbreds after transport and exercise. J S African Vet Assoc 1974:331–333.
31. Ito S, Fujii Y, Uchiyama T, Kaneko M. Four cases of rhabdomyolysis in the thoroughbred during transportation. Bull Eq Res Inst 1992:1–5.
32. Clark DK, Friend TH, Dellmeier G. The effect of orientation during trailer transport on heart rate, cortisol and balance in horses. Appl An Behav Sci 1993; 38:3–4.
33. Doherty O, Booth M, Waran N, et al. Study of the heart rate and energy expenditure of ponies during transport. Vet Record 1997; 141:589–592.
34. Smith BL, Jones JH, Carlson GP, Pascoe JR. Effect of body direction on heart rate in trailered horses. Am J Vet Res 1994; 55:1007–1011.
35. Smith BL, Jones JH, Carlson GP, Pascoe JR. Body position and direction preferences in horses during road transport. Eq Vet J 1994; 26:374–377.
36. Waran NK, Cuddeford D. Effects of loading and transport on the heart rate and behaviour of horses. Appl An Behav Sci 1995; 43:71–81.
37. Waran NK, Robertson V, Cuddeford D, et al. Effects of transporting horses facing either forwards or backwards on their behaviour and heart rate. Vet Rec 1996; 139:7–11.
38. Gibbs AE, Friend TH. Horse preference for orientation during transport and the effect of orientation on balancing ability. Appl An Behav Sci 1999; 63:1–9.
39. Toscano MJ, Friend TH. A note on the effects of forward and rear-facing orientations on movement of horses during transport. Appl An Behav Sci 2001; 73:281–287.

40. Waran NK. The behaviour of horses during and after transport by road. Eq Vet Ed 1993; 5:129–132.
41. Giovagnoli G, Marinucci MT, Bolla A, Borghese A. Transport stress in horses: an electromyographic study on balance preservation. Livestock Prod Sci 2002; 73:2–3.
42. Thornton J. Effect of the microclimate on horses during international air transportation in an enclosed container. Aust Vet J 2000; 78:472–477.
43. Yamauchi T, Oikawa M, Hiraga A. Effects of transit stress on white blood cells count in the peripheral blood in Thoroughbred race horses. Bull Eq Res Inst 1993:30–32.
44. White A, Reyes A, Godoy A, Martinez R. Effects of transport and racing on ionic changes in Thoroughbred race horses. Comp Biochem Physiol A, Comp Physiol 1991; 99:343–346.
45. Li WI, Chen CL. Running and shipping elevate plasma levels of beta-endorphin-like substance (B-END-LI) in thoroughbred horses. Life Sci 1987; 40:1411–1421.
46. Hines MT. Effects of transit on the immune system of the horse. In: Kohn CW, ed. Guidelines for horse transport by road and air. New York: American Horse Shows Association, 2000:93–102.
47. Raidal SL, Bailey GD, Love DN. Effect of transportation on lower respiratory tract contamination and peripheral blood neutrophil function. Aust Vet J 1997; 75:433–438.
48. Traub Dargatz JL, McKinnon AO, Bruyninckx WJ, et al. Effect of transportation stress on bronchoalveolar lavage fluid analysis in female horses. Am J Vet Res 1988; 49:1026–1029.
49. Ariznavarreta C, Cardinali DP, Villanua MA, et al. Circadian rhythms in airline pilots submitted to long-haul transmeridian flights. Aviat Space Environ Med 2002; 73:445–455.
50. Waterhouse J, Edwards B, Nevill A, et al. Identifying some determinants of 'jet lag' and its symptoms: a study of athletes and other travellers. Br J Sports Med 2002; 36:54–60.
51. Vandenput S, Istasse L, Nicks B, Lekeux P. Airborne dust and aeroallergen concentrations in different sources of feed and bedding for horses. Vet Q 1997; 19:154–158.

CHAPTER 65

Detection of drug use in performance horses

Cynthia Kollias-Baker and Scott Stanley

There is an increasing sense of concern on the part of horsemen, veterinarians, and the horse-loving public regarding the abuse of drugs and medications in horses participating in athletic competitions. Whereas it is recognized that therapeutic medications can benefit the horse, the overuse of these agents, as well as the administration of illegal drugs, have the potential to alter a horse's performance and mask serious injuries. In the show- and race-horse industries, private and government regulatory officials are responsible for developing drug and medication rules to protect the health and welfare of the horses and horsemen, assure a fair and level playing field for all competitors, and safeguard the public interest whenever pari-mutuel wagering is involved. Drug and medication rules are enforced through the testing of blood and urine samples collected from horses competing in athletic competitions for the presence of unauthorized drugs and medications and for drug concentrations greater than that permitted (overages) of authorized medications.

Enforcement is a two-step process, with all of the samples first subjected to a series of screening tests. If the results of any of these tests suggest that there is a violation of the medication rule, the sample will undergo a second confirmatory testing process. In the past few years, there have been significant technological advances in the screening and confirmation processes that have resulted in improved control over the use and abuse of medications and drugs in performance horses. These advances, however, have also led to the detection of residues of therapeutic medications and environmental contaminants. The performance horse industries and their regulatory bodies are currently trying to balance the need to control the abuse of unauthorized medications, avoid penalizing individuals for inadvertent environmental contamination, and desire to provide optimal veterinary care to equine athletes.

The drug-testing process

Sample type and collection

Sample collecting procedures must take into consideration both scientific and legal aspects. An important legal side to the process is chain-of-custody documentation, which is a tamper-resistant trail of documentation indicating where the sample has been and who has had custody of it at all times.

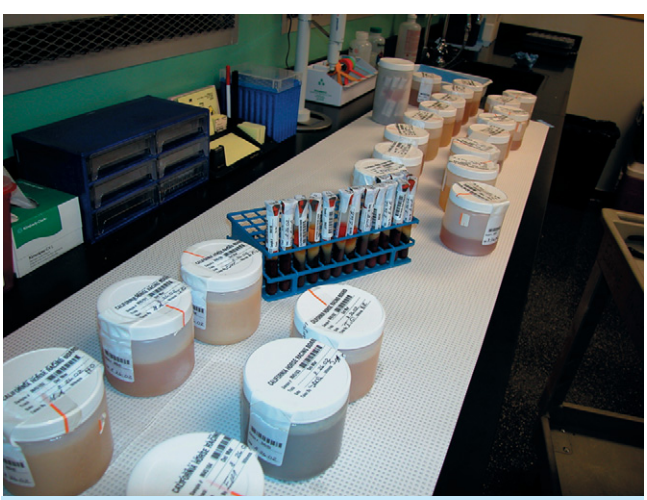


Fig. 65.1
Sample handling and chain of custody – sealed and labeled containers.

For this reason, the actual drug-testing process begins when a sample is collected. The collection container must be new, clean, and sealed and the sample must be obtained in a manner that avoids possible contamination from the environment (Fig. 65.1). It is important that drug-testing personnel maintain accurate records of sample collections, as this represents the beginning of the chain-of-custody process. Once collected, the samples are sealed with tamperproof evidence tape and secured for transport to the testing laboratory. Commercial courier services provide a complete external chain-of-custody with tracking information available through the bill of freight. The testing laboratories must also keep accurate records as to when the samples were received and document their internal chain-of-custody. In addition, security procedures must be in place to prevent the samples from being tampered with or compromised in some other manner during the collection, shipping, and testing processes.

Urine is the primary body fluid used for drug testing in most programs because it is relatively easy to obtain, and because most drugs and their metabolites are present in higher concentrations in urine than in blood. Generally, urine samples are collected from horses following competitive events. In the horse-racing industry, sample collection is usually a straightforward procedure. Following the race, the winner and one or two additional horses, which are generally chosen at random by the racing stewards, are taken to a secure and isolated detention barn where they are bathed, cooled out, and allowed access to water. Sometime during this cool-down period, most horses will void naturally. In contrast, collecting urine from show horses is often problematic. Horses to be tested are usually selected at random, although winners are always tested in some programs. Once a horse is chosen, the testers must remain with the horse until a sample is obtained or the process is halted due to the horse's failure to urinate in a timely manner. Show horses frequently compete in several classes, and often will not urinate until they are cooled out and untacked at the end of the day. Altogether, collecting urine samples from show horses can be a prolonged and time-consuming process.

Blood samples are also commonly collected if a veterinarian or veterinary technician is available to draw the sample. Because the concentration of many potent drugs in blood is too low to detect using current analytical methods, plasma or serum samples are rarely tested for unauthorized medications. For example, small doses of medications, such as detomidine, mepivacaine, and albuterol, while pharmacologically active, may not be present at detectable concentrations in the plasma or serum. Instead, blood samples are primarily used to regulate the use of authorized medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), because therapeutic plasma or serum concentrations of these agents are usually readily detectable using current analytical methods. Maximum permitted concentrations of authorized medications are established in serum or plasma, and the laboratories analyze the blood samples to ensure that these limits are not exceeded.

In the past decade, interest in the analysis of hair for detection of administered drugs has increased in forensic sciences. For example, in the USA, analysis of hair collected from cattle has been used to screen for the administration of agents, such as clenbuterol, which are banned for use in food-producing animals. In addition, in horses that were administered morphine detectable concentrations of the drug were found in mane hair samples.[1] In addition, the amount of morphine found in the mane sample correlated with the dose of morphine that was administered to the horse. The results of another study demonstrated that the ability to detect drugs in hair samples depended on the location on the body where the sample was collected (i.e. neck, back, tail and mane) as well as the season of the year.[2] For example, the tail hair was determined to be the best choice for long-term drug detection, because of its length and continuous growth. In contrast, body hair, because it is short and continually shed, was the least likely to contain detectable concentrations of any of the administered drugs. It must be remembered, however, that not all drugs administered to the horse will be incorporated into growing hair.

One major drawback to the use of hair analysis in equine drug testing is that it is difficult to determine when the drug was administered to the horse. A mane sample positive for morphine, for example, could be the result of an administration 6 months earlier, and some horses may have been bought and sold several times over that period. For this reason, the usefulness of hair analysis and the legal and ethical ramifications of proceeding with regulatory action against an owner or trainer based on a positive hair test, remain to be determined.

Occasionally, saliva samples have also been tested for the presence of unauthorized medications. The principal value of testing saliva samples is the ability to detect agents recently administered by the oral route due to residual contamination of the mouth and pharyngeal area. Saliva is collected by swabbing the horse's mouth with cotton gauze held in forceps. The main disadvantage of saliva testing is that it is difficult to obtain a useful volume, as yields rarely exceed more than 5 g of fluid.

Testing scheme overview

Over the years, the drug-testing process has evolved into a two-step procedure. When the samples arrive at the laboratory, small aliquots of each are subjected to one or more screening tests. Ideal screening test methods are rapid and sensitive, but they do not have to be highly specific, because the results are only presumptive. Regulatory actions should never be taken based on a positive result in a screening test. In North America, the three screening methods that are most commonly used to detect the presence of unauthorized substances in equine urine samples are thin-layer chromatography (TLC), enzyme-linked immunosorbent assays (ELISAs), and instrumental techniques employing mass spectrometry. If the results of all of the screening tests are negative then the sample is declared negative and no further action is taken. However, if the results of one or more of the screening tests are suspicious, the sample will undergo a second round of

testing to confirm the presence and identity of the substance. Because the confirmation test result must typically withstand legal challenge and intense scrutiny, mass spectral identification of the substance is essential. Although gas chromatography–mass spectrometry (GC-MS) has been the most commonly used method of confirmation, liquid chromatography–mass spectrometry (LC-MS) is rapidly becoming the method of choice in most laboratories testing equine samples.

Split-sample analysis

As described above, before a reputable laboratory reports that a sample contains an unauthorized drug or an overage of an authorized medication, the sample has undergone a screening and confirmation testing process using validated analytical procedures. Nevertheless, a split- or referee-sample analysis is permitted in all racing jurisdictions. The referee or split sample is a small portion of the original sample, which was poured into a separate container, or 'split off', immediately after collection (Fig. 65.2). In an ideal situation, the referee sample is stored frozen at a secure site, physically separate from the primary testing laboratory. In horse racing, if the primary laboratory reports a finding for an unauthorized substance or an overdosage of an authorized medication, the owner or trainer of the horse implicated has the option to have the referee sample sent to a second independent laboratory. The second laboratory repeats the analysis to confirm the violation. Most racing jurisdictions maintain a list of reputable and reliable laboratories, from which the owner or trainer may select. The purpose of the split-sample analysis is to verify the results of the original laboratory, and in so doing guard against laboratory mistakes or contamination of the original sample during the collection or testing process. If the second laboratory does not confirm the presence of the unauthorized substance or the overage of the authorized medication found by the primary laboratory, no regulatory action is taken.

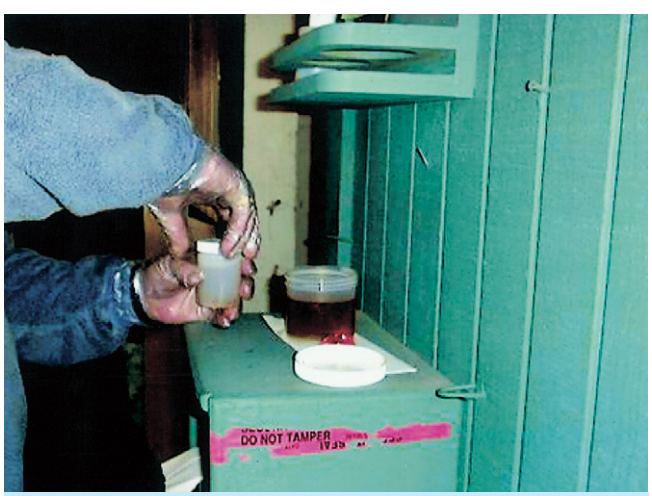


Fig. 65.2
A primary urine sample is split to create the primary and the referee or split sample.

There are several variations in split-sample analysis programs outside of the racing world. For example, under Fédération Equestre Internationale (FEI) regulations, a split-sample analysis is automatically conducted by a second FEI-associated laboratory following any finding of a violation of their drug and medication rule.[3] Should the second analysis fail to confirm the original finding, however, the rule does not stipulate whether regulatory actions will or will not be taken. For years, the American Horse Shows Association, which was the predecessor of USA Equestrian and which regulated the vast majority of horse shows in the USA, did not have a split-sample analysis program. Instead, the organization offered a reanalysis of the original sample in their primary testing laboratory. USA Equestrian, however, recently implemented a program that allows for collection of a split sample and testing of that sample at a second referee laboratory.[4] Unlike most racing jurisdictions, however, USA Equestrian does not maintain a list of approved laboratories. Instead, the rule states that the choice of second laboratory will be made by mutual agreement between USA Equestrian and the individual deemed responsible and accountable for the implicated horse. In addition, if the organization deems that only the laboratory that performed the original testing has demonstrated proficiency in performing the necessary confirmatory analysis for the drug or medication in question, then that laboratory will perform the split-sample analysis. In these aspects, the USA Equestrian rule still differs significantly from the split-sample programs utilized by most racing jurisdictions.

Analytical chemistry methods used to detect drugs and medications

Sample preparation

Sample preparation prior to testing for unauthorized medications uses variable sample volumes and can be employed for either urine or blood. The goal of the extraction process is to select and concentrate compounds of interest, often called analytes, from the sample while removing endogenous matrix materials that could interfere with the analytical process.

Liquid–liquid extraction

Probably the simplest and most traditional method of sample preparation is liquid–liquid extraction (LLE). In LLE, the aqueous sample is mixed in a glass vial with an organic solvent that is not miscible with the sample. Most drugs are more soluble in the organic solvent than in the aqueous media of the sample, and they therefore partition into and concentrate in the organic phase during the mixing process. Continuously agitating the mixture ensures that all parts of

the sample come into contact with the extracting solvent. Because the two liquids are not miscible in one another, the sample/solvent mixture will separate into two liquid layers when agitation ceases. The selection of optimal conditions, such as pH and solvent polarity, will result in the majority of any analyte present being extracted into the chosen solvent. To complete LLE, the two liquid layers are separated and the solvent layer is kept for further manipulation, such as concentration through evaporation.

Solid-phase extraction

Solid-phase extraction (SPE) is another technique used to separate and concentrate analytes from urine and blood samples. Whereas LLE uses a liquid solvent to separate the analytes from the sample matrix, SPE uses adsorption to a solid surface to achieve this same separation. The most common form of SPE is a prepackaged column containing bonded silica sorbents to which functional groups, such as hydrocarbons or ion exchange groups, have been bound. After the column of material has been conditioned, or washed and buffered to the desired pH to facilitate analyte binding, the liquid sample is passed through the bed of adsorbent particles. Analytes will be retained and contaminating matrix material will be removed by washing the column with water or some other buffer or solvent. In the final step the column is buffered to a particular pH to facilitate release of the analytes, which are then eluted into a small amount of solvent. In equine drug testing, three buffers with different pHs are used to produce an acidic, a neutral, and a basic drug fraction from each sample. Different drugs or drug classes will elute into the different fractions based on their physicochemical properties. For example, barbiturates and amphetamines will be present in the basic fraction, whereas corticosteroids will elute into the acid fraction. Each fraction then undergoes an evaporation process to further concentrate any analytes present prior to the analytical process.

Fig. 65.3
As depicted in this cartoon the final spots produced using thin-layer chromatography methods provide only average resolution, but permit the simultaneous detection of a wide range of substances in a single test.

Screening methods

Thin-layer chromatography

In TLC analysis, aliquots or small portions of the original test samples undergo a series of extractions, as described above, designed to separate any drugs present from endogenous sample matrix and concentrate them into small volumes of volatile solvent. These extracts are then applied or 'spotted' onto thin glass plates, which are coated with adsorbent material, such as silica gel, which serves as the stationary phase. The plates are then placed into a chamber with a small volume of organic solvent, which serves as the mobile phase. Drugs and other compounds are carried up the plate in the mobile phase by capillary action at a rate and distance that depends on their physicochemical properties (Fig. 65.3). Although a few agents produce visible spots, most drugs are visible only after applying certain dyes or regents. These reagents are sprayed onto the plate, where they interact with functional groups on the drug molecules to produce color changes, which make the spots visible. Different drugs may have similar migration patterns, and therefore the identification of a drug based on TLC analysis is only presumptive.

Racing laboratories have used TLC for over five decades and it remains one of the most common screening methods used in North America, despite numerous disadvantages to the methodology. For example, TLC methods require large volumes of both sample and solvent. In addition, they are time-consuming and labor-intensive, and the spots produced by the method require interpretation by the chromatographer, which can be subjective. Finally, the sensitivity of TLC is often not adequate to detect many of the more potent drugs in use today. For example, the smallest concentrations of drugs that can be detected, which are commonly referred to as limits of detection (LOD), by TLC are greater than 100 nanograms per milliliter (ng/mL) or parts per billion (ppb) for most analytes. In contrast, the LOD for ELISA and instrumental screening methods are commonly in the range of 1 to 10 ng/mL. Nevertheless, TLC remains in favor as an

analytical method because of its simplicity (extraction and spotting technicians can be trained in a few weeks), dependability (no moving parts or automation is required), relatively low cost (80% of the cost is labor), and its capacity to simultaneously detect a wide range of substances in a single analysis.

Enzyme-linked immunosorbent assay

Although ELISA testing has only been available since the 1980s, it has rapidly become an integral part of routine equine drug testing, primarily because of its simplicity and sensitivity. The majority of laboratories in North America use ELISA to complement their TLC screening methods, although several laboratories have developed screening schemes based solely on ELISA tests. The principal components in enzyme immunoassays are: (1) a drug molecule labeled with a specific enzyme conjugate; (2) a polyclonal antibody specific for the drug; and (3) a substrate, such as tetramethylbenzidine, capable of producing a measurable optical signal or color change when bound by the enzyme conjugate. The antibodies used in ELISA are specific for one drug or a drug class in which members have a similar chemical structure. In the test, the enzyme-labeled drug binds to the antibody, which results in a color change when the substrate is added. If there is drug in the test sample, it will compete with the enzyme-labeled drug for binding sites on the antibody. As a result, there will be less of the enzyme-labeled drug bound to the antibodies, and so there will be little or no color change when the substrate is added (Fig. 65.4). The testing process is simplified by the use of automated microtiter plate readers that rapidly screen the plates at their optimal wavelengths and calculate the test results with vendor-supplied software. When authentic reference standards are used to create a multipoint calibration curve, the results of ELISA testing can provide semiquantitative results or an estimation of the amount of the drug in the sample.

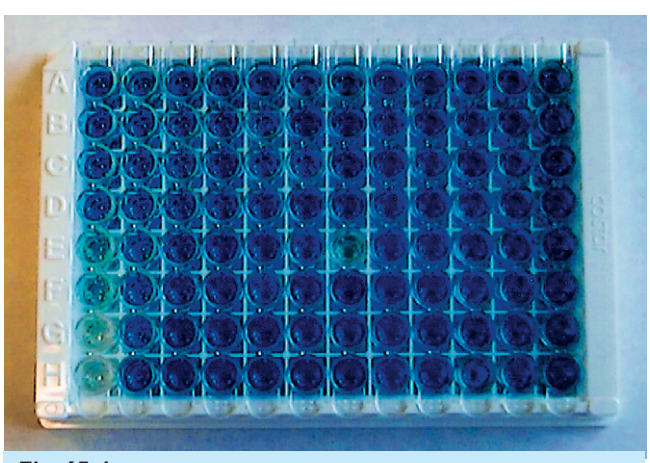


Fig. 65.4
A developed ELISA plate with a suspect sample depicted on row E, column 7. The 96-well plate configuration allows the analysis of 88 test samples and 8 reference standards, which are shown on this plate in the column on the far left.

As mentioned previously, one of the advantages of the use of ELISA testing is its superior sensitivity. The LOD for most drugs using ELISA tests are in the range of 1–10 ng/mL. When employing ELISA for specific drug or drug classes LOD of 1 ng/mL are achievable for many substances. As with any immunologically based assay, non-specific cross-reactions can occur and therefore, as with TLC, ELISA results represent only provisional drug identifications. A more specific test, generally based on mass spectrometry, must be used to confirm the presence and the identity of the drug.

Instrumental analysis

With the availability of lower-cost analytical instruments and automated sample preparation, instrumentally based drug testing programs using GC-MS and LC-MS have been employed for a number of years in Europe, Australasia, and Africa and are rapidly becoming the gold standard for equine drug testing in North America. These instrumental approaches provide a wide range of coverage (i.e. >750 drugs), excellent sensitivity, and superior specificity. Limits of detection of less than 1 ng/mL can be achieved when extraction and chromatographic separation are optimized.

Chromatographic separation

The first step in mass spectrometric analysis involves the separation of any analytes in the sample from one another and from biological matrix contaminants. The two most common instruments used for separation in equine drug testing are the gas chromatograph (GC) and the high performance liquid chromatograph (HPLC). Separation on a GC is achieved utilizing a long flexible capillary column that contains a low polarity stationary phase (i.e. 95% dimethyl 5% diphenyl-polysiloxanes). A programmed oven maintains the column at the desired temperatures (i.e. 60–280°C) according to the specific method. Following the extraction process, any analytes contained in the original sample will be present in a small volume of extraction solvent. An aliquot of each extracted sample is injected into one end of the capillary column and volatilized by heating. The volatilized sample is carried through the column by the gas mobile phase, usually helium or hydrogen, which is maintained at a constant flow.[5,6] As with any other chromatographic method, compounds travel through the column at different rates based on their physicochemical properties. The capillary columns produce excellent resolution, which is useful when trying to separate the complex matrix typical of equine urine. In a well designed GC-MS method, the chromatographic step provides sufficient separation to isolate individual compounds, and the choice of chromatographic column is the key to this separation. GC-MS systems, configured for large volume injection (~50 μL), have been demonstrated to be sensitive, precise, and rugged, making high throughputs possible. Thus, these systems are ideal for screening for drugs that are extracted into the basic fraction, because most of these agents are stable and volatile at the high temperatures used in GC-MS analysis.

The use of HPLC to produce analyte separation prior to mass spectral identification is rapidly becoming one of the most widely used analytical methods in equine drug testing, because it is applicable to a wide range of organic compounds. By some estimates, 80% or more of organic compounds can be separated by HPLC compared to only 20% by GC. The HPLC techniques can separate many drugs that are not amenable to GC separation, because they are too polar, not volatile, or have very high molecular weights (> 700 atomic mass units). In HPLC analysis, a liquid mobile phase is pumped under pressure through a column of microparticulate packings (typically 3–5 μm diameter), which serves as the stationary phase. Compounds in the extracted sample are carried in the mobile phase to the column, where they are retained on the stationary phase. Numerous types of microparticulate packing material can be used in the columns, depending on the physicochemical properties of the compounds that are to be separated. In general, different compounds will have different affinities for the microparticulate column material, and so they will be retained on it for different periods of time. The length of time that a compound is retained on the column, which is referred to as its retention time, can also be controlled by varying the composition of the mobile phase. For example, by making the mobile phase more polar, the polar compounds can be eluted off the stationary phase more quickly. There are two modes of HPLC separation, normal-phase and reverse-phase. Nearly 90% of all applications use reverse-phase, in which the mobile phase is more polar than the column packing material.

Mass spectral analysis

Following chromatographic separation, compounds isolated from the sample are serially injected into the mass spectrometer. The compounds first enter the ionization chamber where they are bombarded with an electron beam that ionizes them, causing the compounds to fragment into smaller molecules. The fragments, as well as the original ionized parent molecules, are then accelerated through a magnetic field and focused into an analyzer that measures the mass to charge ratio and abundance of each ion. A plot of the abundances of the ions versus their mass/charge ratios is referred to as the compound's mass spectrum (Fig. 65.5). The most intense peak in the spectrum is referred to as the base peak and all other peaks are reported relative to its intensity. The highest molecular weight peak in a spectrum will usually represent the parent molecule, minus a single electron (ionized), and is referred to as the molecular ion. The process of fragmentation follows predictable chemical pathways and the most chemically stable ions will always be formed. Therefore, every drug or medication has a unique mass spectrum in a manner similar to every person having a unique set of fingerprints. This is the reason that mass spectral identification is considered the gold standard for absolute drug identification during the confirmation process.

If desired, the HPLC method can be designed to produce complete separation of compounds before introduction to the mass spectrometer. This allows for the analysis of very complex mixtures, or samples with high matrix interference

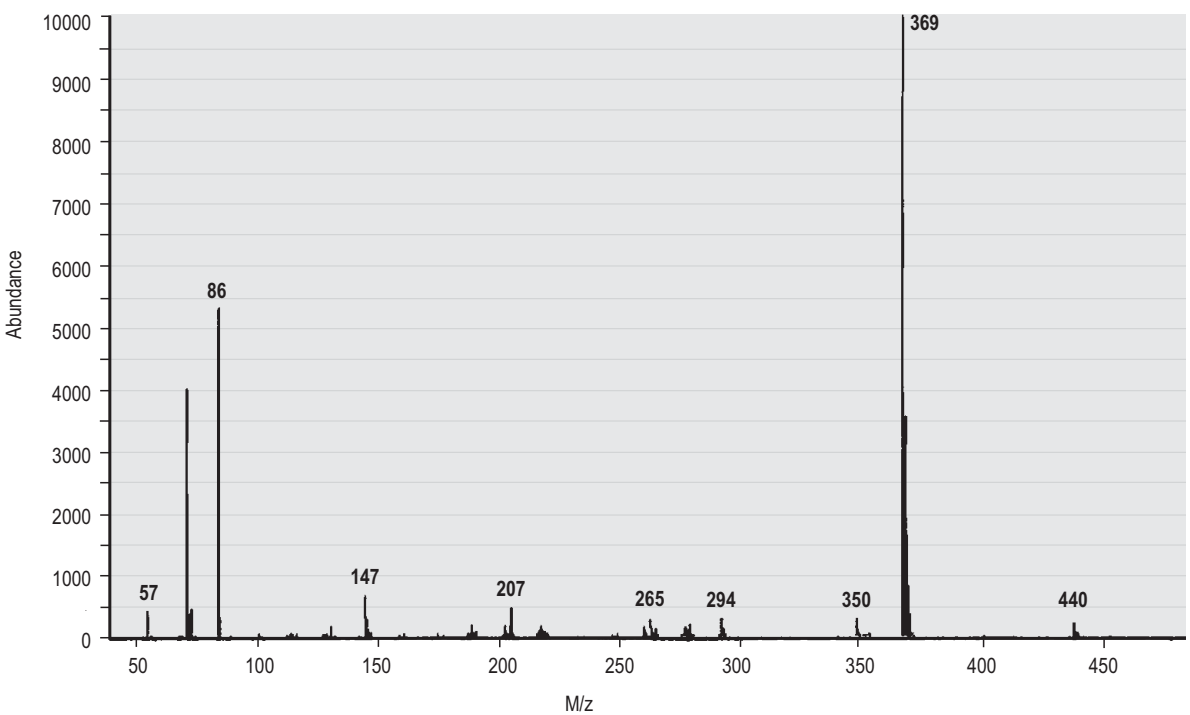


Fig. 65.5
Electron impact full scan mass spectrum of albuterol-TMS derivative as determined by gas chromatography–mass spectrometry.

or very small drug concentrations. However, because of the discriminating power of the mass spectrometer, a reduced amount of resolution may be acceptable and will have the added advantage of decreasing the time required for the compounds of interest to elute off the column. This is particularly true in MS-MS operation, because the two-stage mass analyzer provides an additional separation device.

The LC-MS ion trap mass spectrometers with an inline photodiode array detector have been employed for the combined acid/neutral fraction because this fraction by and large contains compounds that are not volatile or are otherwise unsuitable for GC-MS analysis. These ion trap methods are rapid, sensitive, and very reliable, allowing for the detection of corticosteroids, anabolic steroids, and other related drugs.

Miscellaneous testing methods

In addition to its use as a separation method prior to mass spectral analysis, HPLC is also occasionally used as a screening and confirmation method in conjunction with several different types of detectors. Ultraviolet (UV) absorption is probably the most common type of detection method used in equine drug-testing programs, because it is both sensitive and reliable with broad applicability. UV detectors are available at fixed, selectable, and continuously variable wavelengths or as diode-array detectors. Most commonly, HPLC with UV detection is used to determine the concentration of authorized medications, such as NSAIDs, in serum or plasma samples. Some laboratories, however, are still using these detectors to screen acid extracts of equine urine samples for unauthorized medications. The fluorescence detector measures the fluorescence of a drug or its derivative, if it does not naturally fluorescence. It is generally very sensitive, but it is of limited usefulness in drug-testing programs because only a few drugs naturally fluoresce and because it is difficult and time consuming to make fluorescent derivatives. Electrochemical detectors, which can only detect the limited number of substances that are electroactive at a particular electrode in response to an applied potential, are not commonly used in equine drug-testing programs.

Testing approaches

Pre-race testing

Since the 1960s, pre-race testing has been heralded as a solution to many of the drug and medication problems facing the horse-racing industry. The rationale behind this approach is to test all horses prior to racing in order to disqualify any horse with an unauthorized drug or medication in its system. Throughout the 1960s, 1970s and early 1980s, various racing jurisdictions, including Maryland, Illinois, and New York, conducted pre-race testing using a number of different methodologies, including GC, HPLC, TLC, and ELISA. By the 1990s, however, except for bicarbonate analysis, pre-race testing was largely abandoned in favor of post-race analysis for a number of reasons. First, only blood samples can be obtained in the short time period immediately prior to racing, and the concentrations of many drugs in plasma are often not detectable using current analytical methodology. Second, the process is extremely expensive, because equipment and personnel have to be near the racetrack, and testing has to be conducted during weekends and evenings to accommodate the racing schedule. Finally, there are legal ramifications to disqualifying a horse from a race based on only the results of a screening test. These results are only presumptive and are not considered definitive evidence of the presence of a drug or medication. If further definitive testing, such as mass spectral analysis, failed to confirm the presence of the drug, then an argument could be made that the owner and trainer were unjustly forced to withdraw the horse from the race. Despite the limitations and difficulties of conducting pre-race testing, it remains an attractive approach with regulators and owners, because if successful it has the potential to prevent horses from competing under the influence of unauthorized substances, instead of penalizing the owner and trainer after the fact.

In Europe and Asia, pre-race testing is carried out for a limited number of substances, such as anabolic steroids, prior to large international events. Horses are sequestered upon arrival and tested prior to selected sales and/or racing events. The timeframe for the testing is such that both screening and confirmation analysis can be completed on collected urine samples. This practice allows racing authorities to strictly control the use of these agents in horses in these jurisdictions by disqualifying any animal from the sale or race that does not meet their local criteria for medication control.

Alkalinizing substances

The oral administration of sodium bicarbonate or other alkalinizing agents to horses just prior to racing is referred to as 'milk shaking'. To control this practice, many racing jurisdictions have established venous blood gas criteria for detecting pre-race administration of alkalinizing agents. Blood samples are collected from horses pre-race, as close to race time as practical, and screened using a blood gas analyzer for bicarbonate or total carbon dioxide. Thresholds have been adopted which represent the maximum serum concentrations of these analytes that could occur naturally without the exogenous administration of bicarbonate. In the event that a horse exceeds the threshold on race day, the horse is disqualified from the event and the trainer may be fined and have his or her license suspended. The process, however, is not without controversy because the upper limits for normal serum values for bicarbonate and total carbon dioxide are not universally accepted.

Out-of-competition testing

To enforce the ban on the use of performance-enhancing drugs, such as anabolic steroids and human recombinant erythropoietin (rHuEPO), in human athletics,

out-of-competition drug testing has become standard practice. This approach was adopted because the effects of some drugs can persist beyond the length of time that current testing methods can detect them in urine or blood samples. If the goal of the drug and medication control program is to strictly prohibit the use of a particular drug by athletes, then out-of-competition testing is the only mechanism by which this can be accomplished. Despite its acceptance in human athletics, out-of-competition testing has not been generally practiced in the horse racing industry for several reasons. First, the drug and medication rules in most racing jurisdictions are worded to prohibit the presence of any unauthorized drug or medication in the horse at the time of the race. Most do not forbid or in any way limit what drugs are administered to the horse during the training period, as long as the drug is not detectable in the post-race urine sample. In addition, out-of-competition testing would increase the cost of administering a drug-testing program because more samples would need to be collected and tested. Recently, however, rumors of the use of rHuEPO have led to an exploration of out-of-competition testing for race horses. Current testing methods for rHuEPO limit the detection period to 48–72 h after administration, although the effects of repeated administrations can last for weeks. Therefore, if the racing industry and regulatory authorities determine that rHuEPO should be banned from use in race horses, out-of-competition testing will be the only feasible mechanism of controlling its use until a more sensitive test can be developed.

Authorized medications

In recent years, many USA drug- and medication-control programs have permitted a limited number of therapeutic agents to be used in horses during competitions. The NSAID phenylbutazone is the most widely used authorized medication. Other NSAIDs, such as flunixin, meglumine, and ketoprofen, are also authorized by some race- and show-horse medication rules and the diuretic furosemide (frusemide) is allowed to be administered to horses suffering from exercise-induced pulmonary hemorrhage (EIPH) in most racing jurisdictions in North America. It is the desire of these programs to control the use of these authorized medications by limiting the amounts of the drugs that can be administered. This limitation is achieved by adopting maximum serum concentration for authorized medications, such as NSAIDs, as shown in Table 65.1. Most programs collect blood samples ostensibly to regulate the use of authorized medications.

Although NSAIDs are permitted in many jurisdictions in the USA, in Europe and Australasia they are unauthorized medications and their presence at any concentration is prohibited in post-race samples. Recently published studies indicate that environmental sources of NSAIDs may result in detectable concentrations of those agents in equine urine samples. For example, in one study ibuprofen was present in urine samples collected from a horse that consumed feed that had been prepared by someone with ibuprofen gel on their hands.[7] In another study, untreated horses housed in stalls previously occupied by horses treated with therapeutic doses of flunixin had detectable concentrations of that NSAID in their urine for up to 14 days.[8] The results of these studies emphasize the importance of good barn hygiene. After administering any medication, barn workers should thoroughly was their hands. If at all possible, horses being administered medications should by segregated from untreated horses, and their stalls should be stripped and re-bedded once treatment is terminated.

Table 65.1 Plasma regulatory limits for non-steroidal anti-inflammatory agents in US racing and show horses

State	Phenylbutazone	Flunixin	Ketoprofen	Meclofenamic acid	Naproxen
AZ, AL, CO, FL, ID, IL, IN, LA, MA, MI, MN, NJ, OH, OK, OR, TX, WA, WV	5.0 μg/mL	Not authorized	Not authorized	Not authorized	Not authorized
CA	5.0 μg/mL	0.5 μg/mL	0.05 μg/mL	Not authorized	Not authorized
KY	Not regulated	Not regulated	Not regulated	Not regulated	Not regulated
MD	2.2 μg/mL	Not authorized	Not authorized	Not authorized	Not authorized
NY	< 2.0 μg/mL	Not authorized	Not authorized	Not authorized	Not authorized
PA	5.0 μg/mL	0.1 μg/mL	Not authorized	Not authorized	Not authorized
USA Equestrian	15.0 μg/mL	1.0 μg/mL	0.25 μg/mL	2.5 μg/mL	40.0 μg/mL

Furosemide

Furosemide (frusemide) is a loop diuretic that induces natriuresis, chloruresis, increased hydrogen ion excretion, and a profound diuresis.[9] These effects are mediated by the inhibition of Na^+–K^+–$2Cl^-$ transporters in the thick ascending limb of the loop of Henle. Furosemide also has important extrarenal effects. For example, it produces a significant venodilation that appears to be mediated by stimulation of prostaglandin and nitric oxide production.[9,10] This effect was dependent on the presence of a functional kidney but not on the development of diuresis. Furosemide also has been shown to prevent bronchoconstriction in humans and ponies, an effect that may be mediated by decreased production of inflammatory mediators.[11–13] In addition, furosemide was shown to improve gas exchange in anuric humans suffering from severe pulmonary disease.[14] The improvement in gas exchange was due to furosemide-induced decreases in ventilation–perfusion mismatches, and not to changes in blood volume.

In all US and Canadian racing jurisdictions, furosemide is considered an authorized pre-race medication, which can be administered to horses that suffer from EIPH. Whether or not furosemide is an effective therapy for EIPH, however, has yet to be definitively proved. For example, in 1985 Pascoe et al.[15] concluded that furosemide decreased the severity of EIPH in race horses. That study, however, used an admittedly subjective grading scale to judge the severity of the disease, and the results are therefore not conclusive. Nevertheless, if the pathogenesis of EIPH is associated with the unusually high pulmonary arterial pressures (>70 mmHg) that develop in the horse during intense exercise, as has been proposed, then there is evidence to support the use of furosemide as a therapeutic agent.[16,17] For example, multiple studies have demonstrated that furosemide decreases the peak pulmonary vascular pressures that develop in horses during intense exercise.[18,19] The mechanism by which furosemide produces this effect, however, is still unclear. The results of one study indicated that the reduction in pressure could be partially reversed by the administration of cyclooxygenase inhibitors, whereas another study concluded that prostaglandin production was not involved in the process.[20,21] Another simple explanation for the reduction in pulmonary arterial pressures is the decrease in blood volume secondary to the profound diuresis induced by furosemide.

Apart from any effects on the severity of EIPH, furosemide has also been proposed to enhance the athletic performance of horses. It is hypothesized that the diuretic-induced fluid losses result in a moderate, but significant, weight loss in the horse, which can enhance its athletic performance. In support of this theory, in treadmill exercise tests carried out in horses that did not suffer from severe EIPH, some parameters of exercise performance improved following furosemide administration.[22,23] These improvements, however, were reversed when fluid losses were replaced by intravenous administration of equivalent amounts of balanced electrolyte solutions. A field study carried out by the same laboratory also concluded that superior performances in races horses in the USA were associated with the administration of furosemide.[24] The North American racing industries, as well as some in the scientific community, however, have not generally accepted the results of this study, but given its provocative conclusions this lack of acceptance is hardly surprising.

In addition to the controversy regarding the effects of furosemide on equine athletic performance, it has been proposed that the dilute urine that follows furosemide administration may interfere with the detection of other drugs.[25,26] Therefore, the dose and timing of furosemide administration are regulated to minimize the chance that urine samples collected post-race will be dilute (i.e. urine specific gravity (SG) < 1.010). Most commonly, furosemide administration is restricted to no more than 250 mg, administered intravenously no closer than 4 h to post time. Due to the wide variability of furosemide pharmacokinetics following i.v. administration in horses, the use of serum furosemide concentrations alone is not an appropriate method to monitor compliance with furosemide dosing regulations.[25,27] The use of urine SG measurements to monitor compliance is also insufficient because of the wide range of SG measurements, obtained in both untreated control and furosemide-treated horses.[27] Despite the limitations of each test individually, screening for furosemide violations becomes much more specific by combining measurements of both urine SG and serum furosemide concentration.[28] When a urine SG less than 1.012 and a serum furosemide concentration greater than 100 ng/mL are present simultaneously, the proportion of horses expected to be erroneously classified as being in violation of furosemide dosing regulations approaches 0%.

Drug and medication rules

The Association of Racing Commissioners' International

Association of Racing Commissioners' International (ARCI) is an organization consisting of racing regulators primarily from the USA, Canada, and the Caribbean. The organization has no enforcement power but rather encourages standardization by adoption of model rules and racing polices for a broad range of topics. The organization has adopted a Uniform Classification Guideline for Foreign Substances consisting of five classes, and which currently lists over 800 agents.[29] The classification scheme is based on the potential for the agent to affect a horse's athletic performance, and whether or not it has a recognized therapeutic use. For example, drugs listed in the Class 1 category are considered to have the most potential to affect racing performance and have no accepted medical use in the horse. In contrast, drugs listed in the Class 5 category are therapeutic medications, which are considered to have very little potential to affect athletic performance. One limitation of the classification system is that it is based on the effects of the drugs on healthy horses. For example, the corticosteroid agents commonly used as

intra-articular medications, such as methylprednisolone and triamcinolone, are listed as Class 4 agents, which are described as therapeutic agents with limited ability to influence performance. Although intra-articular corticosteroids may have limited potential to alter the performance of a sound horse, they have enormous potential to alter the performance of a horse with an inflamed, arthritic joint.[30,31]

The ARCI has also adopted recommended penalties for violations based on the classification system. It does not, however, have the power to force states to adopt the guidelines or the model rules. Although few states have adopted the program in its entirety, states have used portions of it when drafting their own drug and medication rules.

Fédération Equestre Internationale

The FEI is the governing body recognized by the International Olympic Committee. It establishes the rules and regulations, including those for medication use, under which the international equestrian disciplines of Jumping, Dressage, Eventing, Vaulting, Driving and Endurance Riding compete. The organization was founded in 1921, and as of 2002 some 130 countries were members.

The stated objective of the FEI drug and medication rule is to protect the integrity of equestrian sports through controlling the use of substances capable of giving a horse an advantage or disadvantage in an event, contrary to its natural abilities.[3] The FEI considers a prohibitive substance to be any agent capable at any time of acting on one or more of the following mammalian body systems: the nervous system, the cardiovascular system, the urinary system, the reproductive system, the musculoskeletal system, the blood system, the endocrine system, the immune system (other than licensed vaccines), the digestive system (other than the orally administrated antiulcer medications omeprazole and ranitidine) and the skin. An extensive list of specific prohibited agents is approved each year. The medication rule states that the finding of a prohibited substance means the detecting of the substance itself, a metabolite of the substance, an isomer of the substance, or an isomer of a metabolite.[3] In addition, the finding of any biological or scientific indicator of administration or other exposure to a substance is equivalent to the detection of the substance itself. This latter aspect of the rule allows for methods of detection that do not specifically identify the substance itself, but rather detect some secondary physiological change that occurs following its administration.

The list of medications not considered prohibited substances is quite short and includes rehydration fluids, oxygen, antibiotics, and antiparasitics. There are limitations, however, as to how and when even these agents can be administered, so veterinarians must consult with the FEI Veterinary Delegate prior to treating any horse in an FEI event.

As discussed below, the FEI, as well as many other regulatory bodies, have adopted thresholds on a number of different substances. Unlike many other drug and medication rules, however, the FEI strictly limits the type of substances for which thresholds may be adopted. Their rule states that thresholds can only be adopted for substances endogenous to the horse, substances arising from plants traditionally grazed or harvested as equine feeds, and substances in equine feed arising from contamination during cultivation, processing, treatment, storage, or transportation.[3]

USA Equestrian

Formerly known as the American Horse Show Association, USA Equestrian is the largest regulatory organization for show horses in the USA. It is a member of the FEI and serves as the national governing body for the US Olympic Team, and also oversees much lower-caliber horse shows and events. Numerous riding and breed disciplines compete under the USA Equestrian umbrella, including Arabian, Eventing, Connemaras, Reining, and Vaulting. USA Equestrian has two drug and medication rules and each discipline chooses under which rule they wish to compete. The No Foreign Substance Rule is the same as the FEI medication rule and currently only FEI and the Endurance Riding events are conducted according to its provisions. The remaining disciplines compete under the Therapeutic Substance Rule. This rule is considered more permissive than the No Foreign Substance rule. Under this rule, forbidden substances are any stimulant, depressant, tranquilizer, local anesthetic, or psychotropic agent and/or drug that might affect the performance of a horse and/or pony or any metabolite and/or analogue of any such substance except where expressly permitted.[4] Unlike the No Foreign Substance Rule, the Therapeutic Substance rule allows for a number of permitted medications to be present in the horse's system during an event or show. For example, up to two NSAID agents are allowed to be administered to a horse, as long as the plasma concentrations do not exceed the specified maximum permitted limits.[4] The NSAIDs that are currently permitted and their respective maximum allowed serum concentrations are shown in Table 65.1. The Therapeutic Substance rule also allows the use of the muscle relaxant methocarbamol in show horses, as long as the plasma concentration does not exceed 4.0 μg/mL. USA Equestrian does not, to the authors' knowledge, provide a definitive list of forbidden substances, but will generally address practitioners' questions regarding non-permitted medications and provide withdrawal guidelines whenever possible.

Factors affecting detection times and withdrawal times

Commonly, veterinary practitioners want to know withdrawal times (how long before an event or race they should discontinue treatment) for medications to avoid having a horse test positive for that agent. Unfortunately, it is very difficult for laboratories to generate accurate withdrawal times for therapeutic medications because many different

factors can affect their detection times (how long a drug is detectable in a sample after administration). Probably the most important factor in the detection time of a medication is the sensitivity of the testing method that is being used by the laboratory. As discussed previously, there are large variations in the LOD for different analytical methods. For example, in general, TLC is much less sensitive than instrumental or ELISA analysis. Therefore, a detection time for a medication tested for by TLC in one laboratory would be significantly shorter than the detection time determined by another laboratory that used instrumental analysis as their testing method. Even if the same technique is used, differences in sample preparation can result in higher or lower analyte recoveries that can ultimately affect the detection time.

In addition, many other factors outside of the laboratory also affect detection times. For example, the higher the administered dose, generally the longer the detection time. In addition, some drugs, such as clenbuterol and isoxsuprine, accumulate in the body and after several days of administration, drug residues can persist in urine samples for 30 days or longer. There can also be large variations in the clearance rates of many drugs between different horses. The actual withdrawal time for a specific medication in a particular horse may be substantially different than the laboratory's estimated time, because laboratories often base their withdrawal times on data from only one or two horses. In summary, although many laboratories will provide withdrawal times to veterinarians, these should be used only as guidelines.

Thresholds, reporting levels, and cutoffs

As analytical chemistry methodology has improved, the smallest amount of a drug or medication that can be detected in bodily fluids has progressively decreased. Currently, the LOD in urine for most substances of concern are in the low ng/mL range. As a result of this sensitive testing, the use of drugs and medications in equine sports is considered by many to be well controlled. The side-effect of this sensitive testing, however, is also the detection of substances that were not purposely administered to the horse. In some situations these agents are contaminants in the horse's environment. For example, theobromine can be found in cocoa husks, and scopolamine and atropine occur naturally in many plants in the *Datura* genus. In addition, it is now recognized that some substances thought to be exogenous synthetic agents are actually endogenous, albeit usually only produced in very small amounts. For example, both hydrocortisone and nandrolone are now recognized as naturally occurring hormones.

As a result of the sensitive testing and the recognition that some substances may be endogenous to the horse or contaminants in its environment, almost every organizational body that regulates equestrian activities has adopted thresholds or cutoffs for a number of substances. The philosophy is to prevent horses from competing under the influence of unauthorized medications, while still allowing veterinarians to provide the best-quality medical care possible to equine athletes. Horses may compete in sanctioned events with the presence of these substances in their tissues, body fluids, or excreta provided the concentration of the substance does not exceed the predetermined threshold value. Table 65.2 lists a number of thresholds accepted by many regulatory bodies.

Table 65.2 Internationally accepted serum or urine threshold concentrations

Contaminating substance	Concentration
Dimethyl sulfoxide	15 μg/mL in urine or 1 μg/mL in plasma
Arsenic	3 μg/mL in urine
Hydrocortisone	1 μg/mL in urine
Salicylic acid	750 μg/mL in urine or 6.5 μg/mL in plasma
Testosterone	0.02 μg free and conjugated/mL in urine from geldings, and 0.055 μg free and conjugated/mL in fillies and mares (unless in foal)
Theobromine	2 μg/mL in urine

A few regulatory agencies have taken the idea of thresholds a step further and adopted reporting limits on therapeutic medications. The California Horse Racing Board, for example, has adopted urinary decision levels or thresholds on the eight medications and environmental contaminants shown in Table 65.3. The rationale behind the adoption of these levels is to allow veterinarians to administer therapeutic medications to the horse up to 48 h before a race without concern that residues of those administrations will result in positive analytical findings in post-race urine samples. Although it is likely that the urine concentrations of these agents are not associated with significant pharmacological activity, definitive evidence of this is lacking for some of these agents. Although some racing jurisdictions, especially those in Europe, have been critical of this approach, a number of others in the USA, including Washington and Ohio, have followed suit and adopted similar decision levels for therapeutic medications.

Table 65.3 Urine threshold concentrations adopted by the California Horse Racing Board for therapeutic medications and environmental contaminants

Substance	Concentration
Acepromazine	25 ng/mL
Mepivacaine	10 ng/mL
Promazine	25 ng/mL
Albuterol	1 ng/mL
Benzocaine	50 ng/mL
Procaine	10 ng/mL
Salicylates	750 μg/mL

Drugs in dispute

Recombinant proteins

The tremendous advances in molecular biology that have occurred in recent years have led to the commercial production of numerous recombinant proteins and hormones for use in treating many different types of diseases. Although most of these products are of human origin, such as rHuEPO, at least one equine product, recombinant growth hormone (rEqGH), is already available. Recombinant hormones are particularly difficult medications to control using traditional drug-testing methods for a number of reasons. First, although ELISAs can be developed for these recombinant proteins, routine mass spectrometry methods used in the confirmation process are not suitable for protein analysis. Second, the recombinant hormones are difficult, if not impossible, to distinguish from their endogenous counterparts. Obviously, equine recombinant proteins may be identical to the endogenous hormone, but because many proteins have a high degree of homology across species, it may also be difficult to distinguish a human recombinant hormone from its equine endogenous counterpart. Finally, because many of the effects of these hormones persist for weeks after administration, most of these agents would be used primarily during the training process, as opposed to during the competition. Therefore, the concentration of the hormone in urine or serum samples collected during a competition is likely to be small, making detection and confirmation difficult.

To control the use of these medications, significant changes in the traditional approaches and analytical methods of drug testing will be necessary. For example, rEqGH is indistinguishable from endogenous equine GH and has a very short serum half-life. Therefore, it would be very difficult to effectively control the use of rEqGH by adopting a maximum permissible serum growth hormone concentration consistent with a normal physiological level of the hormone. Exogenous administration of rEqGH, however, is also associated with an increase in the serum concentration of insulin-like growth factor-1 (IGF-1). It has been proposed that IGF-1 can serve as an indirect marker of rEqGH administration, with serum threshold concentrations of IGF-1 greater than 800 ng/mL being indicative of the administration of rEqGH.[32]

In addition to using non-traditional approaches, the use of alternative confirmatory methods, such as isoelectric focusing or new mass spectrometry methods, for protein sequencing may be needed to detect administration of recombinant proteins. For example, in June of 2000 Lasne and de Ceaurriz published a method that could differentiate endogenous human EPO from the rHuEPO protein.[33] This isoelectric focusing method capitalized on the subtle differences in the sialylation (sialic acids in the glycolylated side chains) between the recombinant and the endogenous human hormone that resulted in unique isoelectric points (pI). In addition, if regulators want to control the use of these substances during training they must develop a protocol for out-of-competition testing, similar to what is used for human Olympic competitors, due to the difficulty of detecting these agents on the day of a competition.

Anabolic steroids

Many drugs and hormones, such as β_2-agonists, insulin, growth hormone, and androgenic and estrogenic steroids, can induce a positive nitrogen balance in the body and are therefore said to have anabolic effects. In practice, however, the androgenic steroidal agents, which are similar in structure to testosterone, are the drugs most commonly used when anabolic effects are desired. Although testosterone is the most potent of these agents, it also produces the most androgenic effects. Synthetic agents are therefore often preferred, because modifications in their chemical structure have decreased their androgenic effects in favor of anabolic activity. Anabolic/androgenic steroids were first used in the 1940s to improve recovery from starvation, and major injuries and surgery.[34] Although their use today in human medicine is severely limited, they are still widely used in horses in North America. For example, while they are approved for use in debilitated, starved, or severely stressed animals, they are commonly administered to horses undergoing race or event training, at least in part to maintain their appetite and vigor.

In many human amateur sports, the use of anabolic steroids is strictly forbidden and rigorous out-of-competition testing is used to enforce the ban. Most of the general public assumes that equine athletic events are carried out under similar auspices. Although this is true in Europe and Australasia, this is not the case in North America. The explanation for this dichotomy is both philosophical and analytical. For example, in 1988 the European Community issued a directive banning the use of anabolic steroids in all meat-producing animals, which included the horse. This directive essentially eliminated all legal formulations of anabolic steroids for use in large animals throughout Europe.[35] The racing industries in Europe and Australasia supported the ban on the use of anabolic steroids in horses, primarily out of concern for the potential performance-enhancing effects of these agents. In response to these events, racing laboratories in these jurisdictions developed sensitive ELISA screening tests and GC-MS confirmatory methods to control the use of anabolic steroids. In contrast, in North America anabolic steroids are still used as growth-promoting agents in food-producing animals and multiple formulations are available and approved for use in the horse. In addition, the racing industry in North America has traditionally not supported tighter regulations on the use of anabolic steroids and the regulators have not viewed them as agents with significant potential to alter a horse's racing performance. For example, anabolic steroids are listed as Class 4 agents by the ARCI Drug Classification Guideline, which indicates that they are considered therapeutic medications with less potential to affect performance than drugs in Classes 1 through 3. Partly because of their classification, drug-testing laboratories in North

America have not developed or implemented sensitive testing methods for anabolic steroids. Recently, many of the breeders of performance horses in North America have begun to express concern over the rampant use of anabolic steroids and their possible detrimental effects on the integrity of the breed. Whether or not this concern eventually spreads throughout the racing industry remains to be determined.

Morphine

Opiates, such as morphine, are commonly used as analgesics and preanesthetic drugs in many species, including man. In horses, however, opiates can cause central nervous system stimulation and are therefore used only occasionally, and then generally in combination with sedatives or tranquilizers.[36] Morphine, however, has occasionally been detected in urine samples collected from horses after racing. Typically, the concentrations of morphine found in these post-race urine samples are less than 50 ng/mL, and in most cases morphine is not present in detectable concentrations in the corresponding plasma samples. The presence of any opiate at any concentration in post-race urine samples, however, is of concern to racing authorities, because in the past these drugs have been administered to horses in illicit attempts to enhance their racing performances.

The opiate morphine is derived from the opium poppy, *Papaver somniferum*, a plant native to the Far and Middle East but widely cultivated throughout the world. In addition, seeds of the plant are commonly imported into many countries for use in baking. The poppy plant and seeds contain variable amounts of naturally occurring opiates, such as morphine, codeine, and thebaine. It has been well documented that the consumption of poppy seeds by human subjects, generally in the form of baked goods, can result in the excretion of detectable concentrations of morphine in urine.[37–39] There are several ways in which horses could inadvertently consume poppy seeds. For example, bakery byproducts, which could contain poppy seeds, are occasionally used in the preparation of animal feeds. In addition, bakery products, such as bagels and muffins, are sometimes fed to horses as treats.

In one study that used GC-MS methodology, morphine was present in detectable concentrations for up to 24 h in urine samples collected from horses following administration of 1, 5, and 10 g of poppy seeds that contained approximately 73 μg of morphine per gram of seeds.[40] As shown in Fig. 65.6, 1 g is not a large volume of poppy seeds. In this same study, plasma samples collected up to 4 h after administration of 10 g of poppy seeds also contained detectable concentrations of conjugated morphine metabolites. In a different study, morphine was also detected in urine samples collected from horses administered 2 g of poppy seeds.[41]

Besides poppy seeds, it is also possible that analytical findings of morphine in post-race urine samples could result from contamination of the horse with either illegal opiates, such as heroin, or prescription medications, such as morphine or codeine, which is metabolized to morphine.[42] In humans, a unique minor metabolite of heroin, 6-monoacetylmorphine has been identified, but it has not been determined whether horses also produce this metabolite.[42] In addition, in most regulatory situations the concentrations of morphine and its major metabolites found in urine samples are quite small, and it would be unlikely that minor metabolites would be present in detectable concentrations. Of course, it is also possible that analytical findings of morphine in post-race urine samples are the result of the purposeful administration of morphine or other opiates to the horse. Thus, although there is growing evidence that there are multiple possible sources of morphine in a horse's environment, at this time it is not possible to distinguish the source of low-level morphine positives in post-race urine samples.

Fig. 65.6
One gram of poppy seeds shown in comparison to a US dime.

Cocaine

Current drug-testing methods for detection and confirmation of the primary metabolites of cocaine, benzoylecgonine (BZE) and ecgonine methyl ester (EME) are extremely sensitive. For

Fig. 65.7
Two and a half milligrams of analytical grade cocaine powder shown in comparison to a US dime.

example, when four horses were administered 2.5 mg of cocaine sublingually, urine samples contained detectable concentrations of BZE for up to 24 h postadministration (unpublished data). As shown in Fig. 65.7, this amount of cocaine is quite small and could conceivably be consistent with the residue left on a cocaine abusers hands. At the present time, only the Ohio and Louisiana Racing Commissions have officially adopted a urinary threshold of 150 ng/mL for BZE, the primary cocaine metabolite. In other racing juridictions, regulatory authorities are understandably reluctant to overlook contamination with illegal drugs. In addition, it is not possible to determine whether the source of a cocaine metabolite finding is contamination or the purposeful administration of cocaine to the horse.

Nutraceuticals

The world of human sport provides numerous examples of the hazards of nutraceuticals. For example, multiple athletes in the 2002 Winter Olympics claimed that positive tests for nandrolone resulted from consumption of nutraceuticals contaminated with the steroid. These same hazards exist for competitive equine athletes subjected to drug testing. For example, in California in 2000, a herbal supplement that contained small amounts of ephedrine and pseudoephedrine was identified as the source of exposure for numerous positive post-race analytical findings for norpseudoephedrine and phenylpropanolamine (unpublished data). The label for the product did not indicate that it contained any unauthorized medications. Unfortunately, quality control for many of these products is lacking and the presence or absence of contaminating unauthorized substances may vary from batch to batch.

Methylxanthines

Caffeine, theobromine, and theophylline are all examples of methylxanthine agents. Best known for their mild stimulatory effects on the CNS, these agents also have a number of other systemic effects including bronchodilation, diuresis, and in humans increases in the skeletal muscle workload capacity.[43] The results of several studies indicate that caffeine, in particular, may enhance certain types of athletic performance in humans. For this reason, regulators have often viewed the finding of even small amounts of methylxanthines in post-race urine samples as serious infractions of drug and medication rules. These agents, however, are pervasive in the horse's environment and opportunities for inadvertent contamination abound. Sodas, chocolate, coffee, and tea all contain varying amounts of caffeine and theobromine. In one study, horse's administered 10 peanut M&Ms, which are peanuts covered in chocolate and a thin candy shell, had detectable concentrations of theobromine and caffeine in their urine samples for up to 48 h.[44]

In some situations, trainers may not be aware that they are administering caffeine-containing substances. For example, in California in the 1990s a number of horses had detectable concentrations of caffeine in their post-race urine samples and the source of the drug was traced to an electrolyte supplement (unpublished data). The supplement contained guarana extract, which is a plant that naturally contains caffeine, although the label gave no indication that the product contained caffeine. Trainers and veterinarians need to be especially wary of any supplement that claims to have energizing effects as these often contain unauthorized substances, such as caffeine, even though the label may not indicate its presence.

Summary

Drug-testing programs are implemented in order to enforce drug and medication rules. Most programs consist of a two-part testing process, which utilizes urine as the primary sample type. All samples are tested in a preliminary screening process and any samples with suspicious results undergo an additional round of confirmatory testing.

The most common drug violations in equine drug-testing programs are overdosages of authorized medications. Veterinarians need to be aware of the drug and medication rules under which their clients compete and need to follow recommended withdrawal guidelines to avoid unintended positives.

References

1. Whittem T, Davis C, Beresford GD, et al. Detection of morphine in mane hair of horses. Aust Vet J 1998; 76:426–427.
2. Popot MA, Boyer S, Maciejewski P, et al. Approaches to the detection of drugs in horse hair. In: International Conference of Racing Analysts and Veterinarians. Newmarket, UK: R & W Publications; 2000; 13:115–120.
3. Fédération Equestre Internationale. Veterinary regulations. Lausanne: FEI; 2002.
4. USA Equestrian, Drugs and Medication Regulations. 2002.
5. Chalmers P. Use of capillary gas chromatography in drug screening. In: International Conference: Control of the Use of Drugs in Racehorses. Toronto: R & W Publications; 1983; 5:118–121.
6. Laviolette B, Fenwick J. The use of a fused silica capillary column combined with a nitrogen–phosphorous detector in drug screening. In: International Conference: Control of the Use of Drugs in Racehorses. Toronto: R & W Publications; 1983; 5:122–127.
7. Williams RB, Woodward K, Hines S, et al. Urinary detection of ibuprofen: feed contamination, topical application and oral administration. In: The 13th International Conference of Racing Analysts and Veterinarians. Newmarket, UK: R & W Publications; 2000; 13:372–376.
8. Norgren A, Ingvast-Larsson C, Kallings P, et al. Contamination and urinary excretion of flunixin after repeated administration in the horse. In: The 13th International Conference of Racing Analysts and Veterinarians. Newmarket, UK: R & W Publications; 2000; 13:377–380.

9. Hinchcliff KW, Muir WW. Pharmacology of furosemide in the horse: a review. J Vet Intern Med 1991; 5:211–218.
10. Wiemer G, Fink E, Linz W, et al. Furosemide enhances the release of endothelial kinins, nitric oxide and prostacyclin. J Pharmacol Exp Ther 1994; 271:1611–1615.
11. Broadstone RV, Robinson NE, Gray PR, et al. Effects of furosemide on ponies with recurrent airway obstruction. Pulmonary Pharmacology 1991; 4:203–208.
12. Bianco S, Vaghi A, Robuschi M, et al. Prevention of exercise-induced bronchoconstriction by inhaled frusemide. Lancet 1988; 2:252–255.
13. Anderson SD, He W, Temple DM. Inhibition by furosemide of inflammatory mediators from lung fragments. N Engl J Med 1991; 324:31.
14. Baltopoulos G, Zakynthinos S, Dimopoulos A, et al. Effects of furosemide on pulmonary shunts. Chest 1989; 96:494–498.
15. Pascoe JR, McCabe AE, Franti CE, et al. Efficacy of furosemide in the treatment of exercise-induced pulmonary hemorrhage in Thoroughbred racehorses. Am J Vet Res 1985; 46:2000–2003.
16. Jones JH, Smith BL, Pascoe JR, et al. Why are left atrial pressures high in exercising horses? Physiologist 1992; 35:25.
17. Manohar M. Pulmonary artery wedge pressure increases with high-intensity exercise in horses. Am J Vet Res 1993; 54:142–146.
18. Goetz TE, Manohar M. Pressures in the right side of the heart and esophagus (pleura) in ponies during exercise before and after furosemide administration. Am J Vet Res 1986; 47:270–276.
19. Jackson JA, Ducharme NG, Hackett RP, et al. Effects of airway obstruction on transmural pulmonary artery pressure in exercising horses. Am J Vet Res 1997; 58:897–903.
20. Olsen SC, Coyne CP, Lowe BS, et al. Influence of cyclooxygenase inhibitors on furosemide-induced hemodynamic effects during exercise in horses. Am J Vet Res 1992; 53:1562–1567.
21. Manohar M. Pulmonary vascular pressures of strenuously exercising thoroughbreds after administration of flunixin meglumine and furosemide. Am J Vet Res 1994; 55:1308–1312.
22. Hinchcliff KW, McKeever KH, Muir WW, et al. Effect of furosemide and weight carriage on energetic responses of horses to incremental exertion. Am J Vet Res 1993; 54:1500–1504.
23. Hinchcliff KW, McKeever KH. Fluid administration attenuates the haemodynamic effect of frusemide in running horses. Equine Vet J 1998; 30:246–250.
24. Gross DK, Morley PS, Hinchcliff KW, et al. Effect of furosemide on performance of Thoroughbreds racing in the United States and Canada. J Am Vet Med Assoc 1999; 215:670–675.
25. Stevenson AJ, Weber MP, Todi F, et al. The influence of furosemide on plasma elimination and urinary excretion of drugs in standardbred horses. J Vet Pharmacol Ther 1990; 13:93–104.
26. Soma LR, Korber K, Anderson T, et al. Effects of furosemide on the plasma and urinary concentrations and the excretion of fentanyl: model for the study of drug interaction in the horse. Am J Vet Res 1984; 45:1743–1749.
27. Uboh CE, Soma LR, Rudy JA, et al. Plasma concentration of furosemide versus specific gravity of urine in predicting dose of administration in race horses. Res Commun Chem Pathol Pharmacol 1992; 77:201–218.
28. Chu KK, Cohen ND, Stanley SD, et al. Estimation of the probability for exceeding thresholds of urine specific gravity and plasma concentration of furosemide at various intervals after intravenous administration of furosemide in horses. Am J Vet Res 2001; 62:1349–1353.
29. Gowen RR, Lengel JG. Regulatory aspects of drug use in performance horses. in: Hinchcliff KL, Sams R, eds. Drug use in performance horses. Philadelphia, WB Saunders; 1993:449–460.
30. Shoemaker RS, Bertone AL, Martin GS, et al. Effects of intra-articular administration of methylprednisolone acetate on normal articular cartilage and on healing of experimentally induced osteochondral defects in horses. Am J Vet Res 1992; 53:1446–1453.
31. Carter BG, Bertone AL, Weisbrode SE, et al. Influence of methylprednisolone acetate on osteochondral healing in exercised tarsocrural joints of horses. Am J Vet Res 1996; 57:914–922.
32. Popot MA, Bobin S, Bonnaire Y, et al. IGF-I concentrations measured by ELISA, IRMA and HPLC/MS: determination of a threshold value in horse plasma. In: International Conference of Racing Analysts and Veterinarians. Orlando, FL: R & W Publications; 2002; 14:26.
33. Lasne F, de Ceaurriz J. Recombinant erythropoietin in urine. Nature 2000; 405:635.
34. Strauss RH, Yesalis CE. Anabolic steroids in the athlete. Annu Rev Med 1991; 42:449–457.
35. Houghton E. Anabolic steroids in the horse – a review of current knowledge. In: International Conference of Racing Analysts and Veterinarians. New Orleans: R & W Publications; 1992; 9:3–16.
36. Clarke KW, Paton BS. Combined use of detomidine with opiates in the horse. Equine Vet J 1988; 20:331–334.
37. Struempler RE. Excretion of codeine and morphine following ingestion of poppy seeds. J Anal Toxicol 1987; 11:97–99.
38. Struempler RE. Poppy seed. [Letter] Mil Med 1990; 155:A8.
39. Lo DS, Chua TH. Poppy seeds: implications of consumption. Med Sci Law 1992; 32:296–302.
40. Kollias-Baker C, Sams R. Detection of morphine in blood and urine samples from horses administered poppy seeds and morphine sulfate orally. J Anal Toxicol 2002; 26:81–86.
41. Ginn A, Clark A, Grainger L, et al. Substances of dietary origin: morphine. In: The 13th International Conference of Racing Analysts and Veterinarians. Newmarket, UK: R & W Publications; 2000; 13:355–359.
42. Wasels R, Belleville F. Gas chromatographic-mass spectrometric procedures used for the identification and determination of morphine, codeine and 6-monoacetylmorphine. J Chromatogr A 1994; 674:225–234.
43. Serafin WE. Drugs used in the treatment of asthma. In: Hardman JG, Limbird LL, Molinoff PB, et al. eds. Goodman and Gilman's The pharmacological basis of therapeutics, 9th edn. New York McGraw-Hill; 1996:659–682.
44. Dyke TM, Sams RA. Detection and determination of theobromine and caffeine in urine after administration of chocolate-coated peanuts to horses. J Anal Toxicol 1998; 22:112–116.

CHAPTER 66

Drug effects on performance

Kenneth W. Hinchcliff

Pharmacological agents can be administered to performance horses for a number of reasons. Drugs may be administered to treat an existing condition, which may or may not impair the horse's performance. Additionally, drugs may be administered so that the apparently normal horse can attain standards of athletic performance greater than would be attained without the agent or, conversely, with the intention of decreasing performance. The Association of Racing Commissioners International has compiled a catalog in which drugs are categorized based on their ability to affect performance of race horses.[1]

Detection of drug effects on performance is difficult for a number of reasons. First, winning margins in many athletic events are small compared to the duration of the event. Consequently, small drug effects have the potential to influence performance. Second, small drug effects are difficult to detect experimentally because of the large variability in performance. Detection of a 1% improvement in performance, which would equate to almost five lengths in a Thoroughbred race, is experimentally very difficult. Studies to detect such a small effect must be designed so that the statistical power to detect a small effect on performance is optimized. Detection of such effects requires use of large numbers of horses performing under standardized conditions. A shortcoming of many studies of drug effects on the performance of horses has been inadequate statistical power as a result of use of small numbers (e.g. six) of horses. Failure to detect an effect of the drug in such instances does not mean that the drug does not have an effect – it simply means that in almost all cases the statistical power to detect a meaningful difference was inadequate. Demonstration of an effect is useful, but failure to detect an effect in such studies does not mean that the drug under study has no effect on performance that is meaningful in competition. For an effect of performance to be apparent when numbers of experimental subjects are small, the effect of the drug must be large and repeatable. The most meaningful test of drug effects on performance is undertaken using large numbers of horses (100s to 1000s) competing under conditions that mimic the conditions of interest. There are obvious financial and logistical shortcomings to this approach, although it is feasible under certain conditions.

Another approach has been to predict the effect of a drug on performance based on its effects in resting horses. This approach may be reasonable for drugs that have profound effects, for instance tranquilizers or sedatives used at therapeutic doses, but is of no use for most compounds. There has been no demonstration that drug effects, such as measured by spontaneous locomotory activity or physiological variables including heart or respiratory rates, detected in resting horses are of any use in predicting effects on performance.

Diuretics

Furosemide

Furosemide (frusemide) administration on the day of racing as prophylaxis for exercise-induced pulmonary hemorrhage (EIPH) is permitted in a number of racing jurisdictions worldwide (Fig. 66.1).[2] Within the USA and Canada, almost all Thoroughbred, Standardbred and Quarter Horse racing jurisdictions permit administration of furosemide before racing. During the late 1990s, approximately 85% of all Thoroughbred race horses in the USA and Canada received furosemide at some stage of their career and, on average, 75% of horses in a race received furosemide.[3] These proportions do not appear to have declined, making furosemide

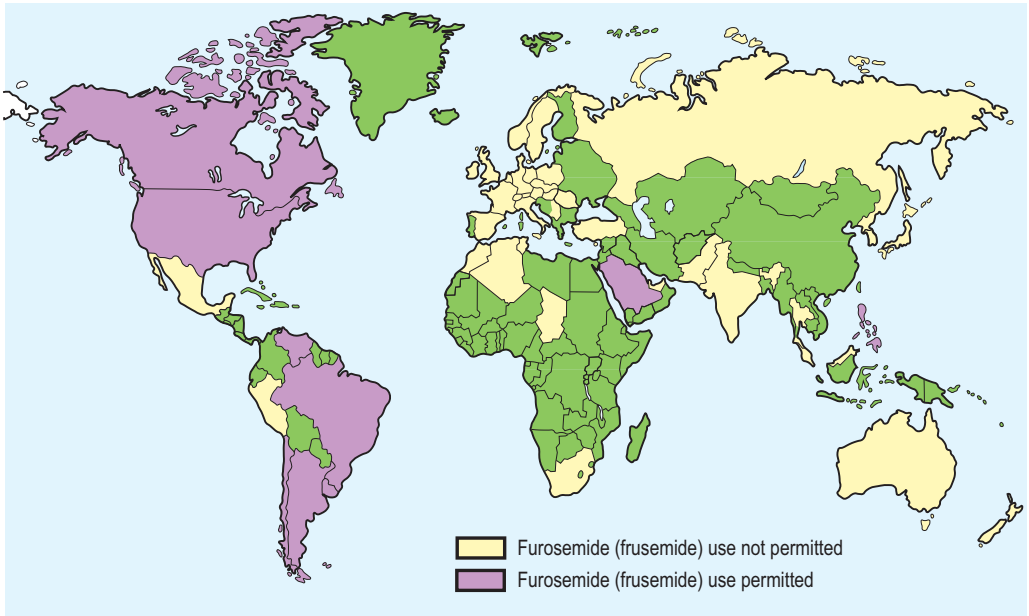


Fig. 66.1
Map showing those countries in which administration of furosemide (frusemide) to horses before racing is permitted by the rules of racing.[2]

among the most widely used drug in race horses in these regions. Although accurate numbers are not available, it appears that a smaller proportion of Standardbred and Quarter Horse race horses receive furosemide before racing. Furosemide was administered to 22–32% of Standardbred race horses and 19% of racing Quarter Horses in two racing jurisdictions in the USA.[4–6]

Pharmacokinetics and mechanism of action

Furosemide is rapidly eliminated by horses, having α, β, and γ half-lives of 5.6, 22.3, and 159 min, respectively.[7] The elimination half-life of furosemide is longer after intramuscular administration.[8] The majority of intravenously administered furosemide is eliminated unchanged in the urine within 4 h.[9] Furosemide inhibits chloride transport in a number of tissues, including the thick ascending limb of the loop of Henle, vascular smooth muscle, and tracheal epithelium by binding to the chloride binding site of the Na^+–K^+–$2Cl^-$ cotransporter. Furosemide may also exert some of its pharmacologic effects by increasing prostaglandin production, as evidenced by the antagonistic effect of drugs, such as phenylbutazone, that inhibit prostaglandin production.[10,11]

Furosemide produces a diuresis, natriuresis and chloruresis in horses,[12–16] through inhibition of the reabsorption of sodium and chloride in the thick ascending limb of the loop of Henle.[17] Urine production during the 4 h after furosemide administration (1 mg/kg, i.v.)to horses averages 25 mL per kg bodyweight.[15,18] The furosemide-induced diuresis decreases plasma volume of resting horses denied access to water.[18,19] Furosemide administration is associated with increased consumption of both salt and water in horses.[20]

Natriuresis, kaliuresis, and chloruresis is profound after furosemide administration to horses. Urinary sodium excretion increases from 8 mmol to 1629 mmol per 3 h and urinary potassium excretion increases from 222 mmol to 556 mmol per 3 h after intravenous administration of 1 mg/kg bodyweight of furosemide.[15] Similarly, intramuscular administration of furosemide (1 mg/kg) increases sodium excretion by six-fold, potassium excretion by two-fold and chloride excretion by 15-fold over the subsequent 8 h.[14] Associated with increased urinary excretion of these electrolytes are reductions in plasma concentrations of potassium, chloride, calcium, and hydrogen. Sodium concentrations are unchanged following furosemide administration to horses.[14] Furosemide administration results in increases in venous pH, Pco_2, Tco_2 and bicarbonate concentration.[5,14,21] Furosemide administration results in a transient decline in urine pH.[14]

Cardiovascular effects

In addition to its effect on the kidney, furosemide also affects the cardiovascular and respiratory systems. Intravenous administration of furosemide causes an immediate and significant dose-dependent decrease in right atrial pressure, pulmonary arterial pressure, pulmonary arterial wedge pressure, cardiac output, and stroke volume in standing horses.[16,22,23] Furosemide also modifies the hemodynamic response to exertion in both horses and ponies. Running is associated with marked changes in cardiovascular function in horses. Cardiac filling pressures increase during exercise; mean left atrial pressures exceed 70 mmHg, and mean right atrial pressures exceed 40 mmHg during intense exertion (Chapter 32). Similarly, mean pulmonary artery pressure may

exceed 80 mmHg, systolic pulmonary artery pressures may exceed 100 mmHg, and pulmonary artery wedge pressure increases from resting values of approximately 18 mmHg to 56 mmHg or higher during intense exertion. Administration of furosemide results in a significant attenuation of the exercise-induced increase in pulmonary vascular pressures, including pulmonary capillary pressure, and right atrial pressure of horses.[22,24–28] Administration of furosemide (2 mg/kg) reduces pulmonary artery and right atrial pressures during strenuous exercise by 16 and 31%, respectively, of values observed when the horses are not treated.[22] Similarly, furosemide administration reduces pulmonary capillary and pulmonary wedge pressures during exercise to 36 and 28 mmHg, respectively, from 41 and 35 mmHg in untreated horses.[25] A similar effect of furosemide is reported in other studies using different measurement techniques, although the absolute values for estimated pulmonary capillary pressure were higher.[28] The hemodynamic effects of furosemide are dose dependent,[8,22] although this effect is not consistently reported for exercising horses.[29]

The effect of furosemide on systemic hemodynamics in rats, dogs and humans is attributed to an increase in venous compliance.[30–32] However, higher concentrations of furosemide than those achieved in plasma of horses after administration of routine doses are required to exert a direct relaxant effect on preconstricted canine pulmonary vessels.[33] This finding is consistent with the conclusion that in horses the hemodynamic response to furosemide is almost entirely attributable to the diuretic effect and subsequent reduction in plasma volume.[24,34,35]

Administration of furosemide to horses results in a rapid and profound decrease in plasma and blood volume.[18,19] In horses not provided with access to water after the administration of furosemide, the reduction in blood and plasma volume persists for at least 4 h.[18,19] Based on measurement of plasma total protein concentration or hematocrit, the reduction in plasma volume persists during brief, intense exercise performed 4 h after furosemide administration.[22,24,36,37] The reduction in plasma volume is temporally associated with attenuation of exercise-induced increases in pulmonary artery and right atrial pressure and with a reduction in pulmonary artery and right atrial pressure in standing horses.[22,23,34] Furthermore, restoration of plasma volume by intravenous infusion of isotonic, polyionic fluids prevents the furosemide-induced decreases in right atrial pressure in sedentary horses and attenuation of exercise-induced increases in pulmonary artery and right atrial pressures in strenuously exercising horses.[24,34] It is likely that furosemide exerts its hemodynamic effect in horses primarily through a reduction in blood and plasma volume.

Furosemide has bronchodilatory activity in ponies with recurrent obstructive airway disease ('heaves') when administered intravenously and by nebulization. Furosemide increases dynamic compliance and decreases pulmonary resistance, but does not affect Pao_2 or $Paco_2$.[38] Dynamic compliance and pulmonary resistance of normal ponies are not affected by furosemide.[38] The bronchodilatory effect of furosemide in horses with heaves is blocked by prior administration of flunixin meglumine.[39] Furosemide administration (1 mg/kg) by inhalation to healthy horses 2 h before intense exercise on a treadmill does not affect respiratory mechanics or arterial blood gas tensions, indicating that in normal horses furosemide does not exert a bronchodilatory effect during exercise.[40]

Interaction with non-steroidal anti-inflammatory drugs

Indometacin and other non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the diuretic, natriuretic and chloruretic responses to furosemide in laboratory animals and humans.[41,42] The mechanism of this interaction is inhibition of loop prostaglandin synthesis; indometacin does not inhibit the tubular secretion of furosemide.[42] Phenylbutazone, administered in high doses (8.8 mg/kg, q12 h for two doses, one oral and the second intravenous), inhibits the cardiovascular and renal effects of furosemide in standing horses.[11,16] Furosemide-induced reductions in right atrial pressure and increases in diuresis, natriuresis, and chloruresis are attenuated by phenylbutazone administration. Phenylbutazone reduces by 25% the amount of furosemide excreted in the urine, but does not affect the efficacy of excreted furosemide, indicating that in horses phenylbutazone does not influence the activity of furosemide in the renal tubule.[11] The mechanism of phenylbutazone's antagonism of furosemide's renal and hemodynamic effects in horses is likely a result of the reduction in diuresis.[35]

The effect of prior administration of phenylbutazone or flunixin meglumine on the hemodynamic effect of furosemide in exercising horses is unclear, with conflicting results reported. Administration of phenylbutazone (4 mg/kg i.v.) or flunixin meglumine (1.1 mg/kg, i.v.) before exercise and before administration of furosemide abolishes the effect of furosemide on right atrial and pulmonary artery pressures during exercise.[43] However, others have not detected an effect of flunixin meglumine administration (1.1 mg/kg q8 h for 3 days, i.v.) on the furosemide-induced attenuation of increases in pulmonary vascular pressures during exercise.[44] The differing results likely reflect different experimental protocols and measurement techniques. The weight of evidence from both horses and other species supports an effect of non-steroidal anti-inflammatory drugs in attenuating the renal and cardiovascular effects of furosemide.

Furosemide and exercise-induced pulmonary hemorrhage

Furosemide is the most commonly used drug to prevent or treat EIPH.[45] The pathogenesis of EIPH and treatment of EIPH are reviewed in Chapter 29. The efficacy of furosemide in treatment of EIPH is uncertain. While field studies of large numbers of horses do not demonstrate an effect of furosemide on the prevalence of EIPH,[46,47] studies of Thoroughbred horses running on a treadmill provide evidence that furosemide reduces the severity of EIPH.[48,49] Under field conditions, based on tracheobronchoscopic evaluation of the severity of bleeding, furosemide has

been reported to reduce or have no influence on the severity of bleeding.[47,50] The apparent inconsistency between field studies and those conducted on horses running on a treadmill may be attributable to measurement of red blood cell counts in bronchoalveolar lavage fluid of horses that have run on a treadmill not being representative of effects of furosemide under field conditions. The weight of evidence from field studies does not support a role for furosemide in preventing or reducing the severity of EIPH.

The mechanism by which furosemide may reduce the severity of EIPH is unknown although it is speculated that furosemide, by attenuating the exercise-induced increase in pulmonary artery and pulmonary capillary pressure of horses, reduces the frequency or severity of pulmonary capillary rupture.[25,51]

Effect on performance

The widespread use of furosemide in race horses raises the question of the effect of furosemide on performance. A number of studies have attempted to address this issue, although most were hindered by low statistical power because of the small number of horses examined. Small differences in speed, that may have an important effect on the outcome of a race, are difficult to detect unless large numbers of horses are examined. The studies in which no effect of furosemide was detected examined either small numbers of horses or analyzed race times collected retrospectively and not corrected for variables that may have affected speed.[8,52] In contrast, studies with adequate statistical power demonstrate clearly that furosemide administration before racing is associated with superior performance in both Thoroughbred and Standardbred race horses.[3,4,46,53]

The effect of furosemide on performance is not consistent within and among studies with the effect of furosemide varying depending upon breed, sex, quality of horse, age, and length of the race, among other factors. Furosemide administered to Thoroughbred horses with EIPH resulted in a decrease in race times corrected for track variant and length of the race in horses in the higher of two value categories.[53] Speed was compared in five races before diagnosis of EIPH with that of five races immediately after diagnosis of EIPH. Horses were administered furosemide before each of the races after the race in which EIPH was diagnosed. Diagnosis of EIPH and administration of furosemide were associated with a significant reduction in adjusted race times. It is likely that furosemide caused the reduction in race times after diagnosis of EIPH but the effect of other treatments is unknown. Importantly, diagnosis of EIPH and furosemide administration did not affect race times in the horses of lower value with EIPH nor in any of four groups of horses with epistaxis.[53] Thus, the effect of furosemide in this study was not consistent and an effect of other factors associated with the diagnosis of EIPH cannot be excluded.

Similarly, Sweeney et al examined the effect of furosemide on corrected racing times of 79 Thoroughbred horses that did not have EIPH.[46] Horses raced on three occasions and received furosemide before the second race only. Geldings had

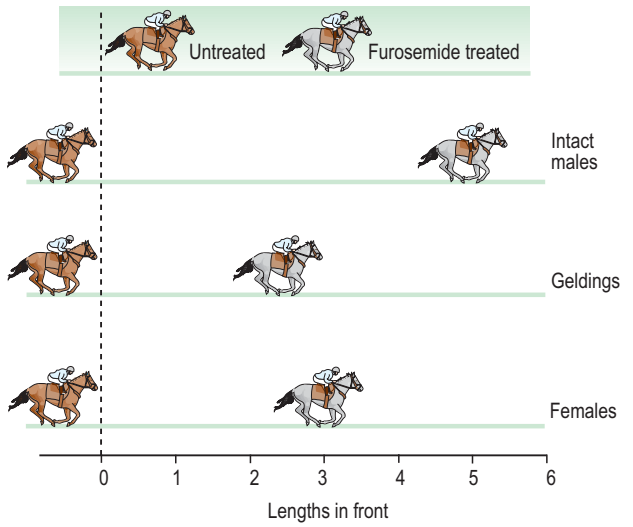


Fig. 66.2
The relative association between furosemide (frusemide) administration and 1200 m (6 furlong) race time for Thoroughbred intact males, geldings, and females. Data from Gross et al.[3]

shorter race times during the second race, after furosemide administration, compared to race times during the first race. However, the reduction in race time was also present in the third race when furosemide was not administered. There was no difference between race times in the second and third races. Thus, an effect of furosemide is likely but debatable, given that the absence of furosemide administration in the third race did not result in a return of race times to values similar to those of the first race. Alternatively, an effect of furosemide may have persisted during the third race, although this possibility appears unlikely.

An examination of the race times of 22 589 Thoroughbred horses racing on dirt tracks in North America between 28 June and 13 July 1997 revealed a significant effect of furosemide on speed, probability of winning or placing, and amount of money won.[3] The magnitude of the effect of furosemide varied by sex of the horses (fillies or mares, geldings, and stallions) with horses administered furosemide racing 0.0006 to 0.00116 furlongs per second faster than horses that did not receive furosemide. When standardized to a race distance of 6 furlongs (1200 m), horses receiving furosemide finished the race in 0.56 to 1.09 s less than horses not receiving furosemide, a difference equivalent to 3 to 5.5 lengths (Fig. 66.2).[3] No attempt was made to determine whether horses in this study were affected with EIPH at the time the study was conducted.

A similar effect of furosemide on race times is evident for Standardbred pacers with treated horses pacing 0.67 s faster for the 1 mile race.[4] The effect of furosemide varied by sex and age, but race times were consistently shorter in treated horses. Furthermore, treated horses finished on average 3.4 lengths behind the winner, compared with 5.0 lengths for non-treated horses.

There is strong and persuasive evidence that furosemide improves the performance of Thoroughbred and Standard-

bred race horses. An effect of furosemide to reduce race times is apparent in horses with and in horses without EIPH at the time of study.[46,53] Therefore, the effect of furosemide on race times appears to be independent of whether the horse has EIPH, raising the question of the mechanism of furosemide's effect on race time.

Mechanism of furosemide's effect on race times

Furosemide is a potent diuretic that alters cardiovascular and respiratory function and acid–base status of horses, as described above. A number of these effects could account for the ergogenic activity of furosemide.

Urine production and reduction in bodyweight The reduction in bodyweight associated with furosemide administration is attributable to increased production of urine.[14,54] The diuretic effect of furosemide is short lived with most urine being produced within the first 30 min of intravenous administration, the rate of urine production returning to baseline values or less within 2 h.[8,14–16] If horses are not permitted to drink after furosemide administration, the diuresis is associated with a marked reduction in bodyweight.[20,22,54] The reduction in bodyweight of horses after administration of furosemide varies between 1 and 5.5%, with the larger reductions occurring after administration of larger doses (2 mg/kg) or intramuscular administration.[14,21,22,36,54] Standardbred horses administered furosemide 4 h before racing have a reduction in bodyweight of 1.3% compared to 0.2% in untreated horses.[55]

Effect of bodyweight changes on energy metabolism The amount of energy needed to run is directly related to the weight being moved (horse, rider, and handicap) and the speed at which it is moved. Increasing weight, for a given speed, results in a proportionate increase in the amount of energy required. Thus, horses that are lighter require less energy to cover a given distance at a specified speed, leading to speculation that furosemide administration may be associated with a reduction in the amount of energy needed for a horse to run a given distance at a given speed.[54,56]

Energy for running is provided by a combination of aerobic and anaerobic metabolism. At speeds achieved during racing, it is estimated that 70–80% of energy is supplied by aerobic metabolism with the balance being supplied by anaerobic metabolism. The rate of aerobic metabolism during racing is believed to be at its maximum as racing occurs at an exercise intensity above that which induces the maximal rate of oxygen consumption ($\dot{V}O_{2max}$). The maximal rate of oxygen consumption is considered an important indicator of athletic capacity.

The maximal rate of oxygen consumption is expressed as either an absolute number (liters of oxygen consumed per minute per horse) or relative to bodyweight (milliliters of oxygen consumed per kilogram bodyweight per minute). Expression of the rate of oxygen consumption as a function of bodyweight provides an index of the maximum rate of energy generation from aerobic metabolism, per kilogram of bodyweight. Increases in the maximal rate of oxygen consumed per kilogram of bodyweight may therefore be consistent with an increase in athletic capacity. During an incremental exercise test, furosemide administration (0.5 mg/kg, intravenously) results in an increase in the maximal rate of oxygen consumption expressed as a function of bodyweight.[56] Furosemide also increases the maximal relative rate of oxygen consumption, but not the maximal absolute rate of oxygen consumption, of horses during a high-speed exercise test on a treadmill.[36] These data demonstrate a physiologically important effect of furosemide in increasing aerobic capacity of horses.

Furosemide administration also reduces the accumulated oxygen deficit and rate of appearance of lactate in blood of horses during a 2-min, high-speed exercise test on a treadmill.[36] A reduction in the accumulate oxygen deficit indicates a reduction in the amount of energy supplied by anaerobic metabolism during the exercise test. The effect of furosemide on accumulated oxygen deficit was directly attributable to furosemide increasing the maximal relative rate of oxygen consumption by the horses during the exercise test. Further evidence that furosemide decreases the use of anaerobically supplied energy during exercise is the observation that furosemide decreases the rate of carbon dioxide production and blood lactate concentration of horses performing an incremental exercise test.[54]

The furosemide-induced reduction in bodyweight may be the cause of the increase in relative aerobic power of horses.[36,56] This is supported by the observations that carriage of weight equal to that lost as a result of furosemide administration normalizes the relative rates of oxygen consumption during a high-speed exercise test and the relative rate of carbon dioxide production and blood lactate concentration during an incremental exercise test.[36,54] While normalization of the rate of oxygen consumption by weight carriage does not conclusively demonstrate that it is weight loss that causes the increase in aerobic power, it does suggest a means of correcting for the effects of furosemide on aerobic power.

Table 66.1 Pharmacologic effects of furosemide (frusemide) in horses

Body system	Effect
Renal	Diuresis
	Natriuresis
	Chloruresis
	Kaliuresis
	Decreased specific gravity
	Increased urine acidity
Electrolyte and acid–base	Hypokalemia
	Hypochloremia
	Increased serum bicarbonate
	Alkalosis
Cardiovascular	Decreased blood volume
	Decreased plasma volume
	Decreased right atrial pressure
	Decreased left and right end-diastolic pressure
	Decreased pulmonary artery pressure

Furosemide-induced alkalosis Alkalosis induced by furosemide administration persists during both strenuous, incremental exercise and brief, high-speed exercise on a treadmill.[37,57] Bicarbonate and base excess concentration and pH are both higher during exercise in horses administered furosemide than in horses not administered furosemide.[37,57] The effect of furosemide to attenuate exercise-induced decreases in blood pH and bicarbonate and base excess concentrations is inhibited when the horses carry weight equal to that lost after furosemide administration.[57] The effect of induced alkalosis on athletic capacity of horses is unknown.

Reduction in severity of EIPH The effect of furosemide on prevalence and severity of EIPH is dealt with elsewhere (Chapter 29). For furosemide to affect athletic performance by decreasing the severity of EIPH, it is necessary that EIPH impair performance and that furosemide reduce the severity of EIPH. Neither of these presumptions have been conclusively demonstrated.

Bumetanide and ethacrynic acid

Bumetanide and ethacrynic acid are structurally different to furosemide, but both are potent diuretics that inhibit chloride transport in the loop of Henle, as does furosemide. Ethacrynic acid given orally to adult horses induces a dose-dependent diuresis; 400 mg (p.o.) induces a diuresis that, assessed subjectively, is maximal 1 h after dosing and persists for 3 h.[58] Ethacrynic acid also increases urinary sodium excretion of ponies.[13] Bumetanide is a benzoic acid derivative with potent diuretic activity.[59] Bumetanide is a potent diuretic when administered intravenously or intramuscularly to horses at dose rates of 10 to 20 μg/kg.[60] Bumetanide is a potent saluretic and kaliuretic in humans and likely exhibits similar activity in the horse, although this activity has not been conclusively demonstrated in horses.[13] The elimination half-life of bumetanide in horses is 6.3 min after intravenous administration and 11 to 27 min after intramuscular administration.[60] The effect of these compounds has not been reported in exercising horses.

Non-steroidal anti-inflammatory drugs

Phenylbutazone and other NSAIDs are among the most commonly used drugs in athletic horses. Phenylbutazone was administered to 50% of 14 600 Thoroughbred horses racing at tracks in the USA and Canada that permitted use of this drug, or presence of the drug in the horse's blood, on race day.[3] The high proportion of athletic horses receiving phenylbutazone is likely a reflection of the frequency of musculoskeletal disorders in these animals and the efficacy of phenylbutazone and similar drugs in alleviating signs of inflammation including heat, pain, and swelling. Phenylbutazone and other non-steroidal drugs are potent analgesics, in addition to inhibiting inflammation, and are especially effective for treatment of disorders involving the musculoskeletal system. Administration of phenylbutazone is associated with a marked reduction in signs of pain and permits more normal gait in horses with induced carpal disease.[61] Treatment with these drugs minimizes tissue damage and may hasten recovery, permitting continued training and racing of the treated horse.

The efficacy of phenylbutazone, and related compounds, is attributable to their ability to penetrate damaged and inflamed tissues and inhibit prostaglandin production. Inhibition of prostaglandin production in inflamed or damaged tissue, and the consequent therapeutic effect, persists after concentrations of drug have reached undetectable levels in plasma. The prolonged effect of phenylbutazone is due to ion 'trapping' of the drug in inflamed tissue – the pH of the inflamed tissue is such that more of the ionized form of phenylbutazone is present in that tissue. Ionized forms of phenylbutazone or its active metabolites cross lipid membranes more poorly than does the unionized form, with the result that the concentration of phenylbutazone is higher in inflamed tissue. Administration of phenylbutazone, which has an elimination half-life of approximately 6 h in horses, inhibits prostaglandin E production in inflamed tissue for up to 24 h.[62,63] Thus, administration of phenylbutazone provides long-lasting inhibition of inflammation and pain.

NSAIDs act by inhibiting the activity of cyclooxygenase enzymes (COX-1, COX-2), thereby reducing the rate at which various prostaglandin compounds, such as prostacyclin, prostaglandin $F_{2\alpha}$, prostaglandin E, and thromboxane are formed from arachidonic acid. Inhibition of prostaglandin synthesis is thought to be the principal mechanism by which the NSAIDs exert their potent anti-inflammatory, antipyretic, and analgesic activities. COX-1 is a constitutive enzyme involved in production of prostaglandins necessary for normal physiologic activity, whereas COX-2 is an enzyme whose production is induced by tissue damage. Consequently, COX-1 is always present in certain tissues, such as the kidney and gastrointestinal tract, in which it mediates or modulates various normal physiologic functions, whereas COX-2 is only present after injury or damage to tissue. The enzymes are genetically and functionally distinct. Recognition of these two forms of this enzyme has resulted in production of compounds that selectively inhibit COX-2 with the intention of maximizing therapeutic efficacy and minimizing adverse side effects.[64] Use of these compounds in horses has, to date, been limited. NSAIDs used in horses and with some selectivity for COX-2 include etodolac, meloxicam, and carprofen.[64]

While there is an extensive body of literature about NSAIDs and their use in horses,[64] there is limited information of the effect of these drugs in exercising horses.

Exercise and prostaglandin production

Prostaglandin production is altered by exercise, although the effects on plasma or urine concentrations are variable among species and exercise type and intensity. The plasma

concentrations of PGE_2, 6-keto $PGF_{1\alpha}$, and $PGF_{2\alpha}$ of humans increase during running and exercise increases the urinary excretion rate of a metabolite of prostacyclin, 2,3-dinor-6-keto-prostaglandin $F_{1\alpha}$, but not of the metabolite of thromboxane, 2,3-dinor-thromboxane B_2.[65–67] Exercise on a stationary cycle induces a two-fold increase in femoral venous PGE_2 concentrations over those measured at rest, indicating a net production of PGE_2 in working muscle.[68] In horses, plasma concentration of 6-keto-prostaglandin $F_{1\alpha}$ increases during incremental treadmill exertion,[69,70] although others have not detected a similar effect of exercise on this metabolite of prostacyclin (PGI).[71,72] However, both intense exercise and endurance exercise increase the plasma concentrations of thromboxane A2.[69,71,72]

Cardiovascular system

The increases in prostaglandin production and/or plasma concentration during exertion likely indicate a physiologically important role for the prostaglandins in exercising horses. Inhibition of prostaglandin synthesis alters the physiological responses to exertion in horses and other species.[73–76] In general, prostaglandin E_2 and prostacyclin (also known as PGI_2) are vasodilatory compounds, whereas prostaglandin $F_{2\alpha}$ and thromboxane are vasoconstrictor compounds. Prostanoids are produced by endothelium of blood vessels (thromboxane is produced by platelets) and contribute to maintenance of vascular tone in a number of vascular beds including pulmonary, skeletal muscle and renal.[77] The importance of these actions is illustrated by the observation that inhibition of production of vasodilatory prostanoids by indometacin results in flow-induced vasoconstriction in skeletal muscle blood vessels.[78] Indometacin and aspirin similarly inhibit exercise-induced increases in calf muscle and forearm blood flow in humans and indometacin accentuates the exercise-induced increase in systolic and diastolic arterial pressures and decreases the heart rate response to exercise.[79]

The issue of alteration by NSAIDs of the hemodynamic responses to exercise is important given the number of horses that exercise or race after administration of phenylbutazone. However, to date, studies of the impact of non-steroidal anti-inflammatory drugs on the hemodynamic responses of horses to exercise have revealed only minor effects on heart rate and right atrial pressure. Phenylbutazone and flunixin meglumine accentuate the exercise-induced increase in heart rate of horses,[76,80,81] and decrease the treadmill velocity at a heart rate of 200 beats per min (V200).[82] However, this effect is not consistent among studies, perhaps reflecting the different exercise and drug administration protocols used.[83,84] Meclofenamic acid does not affect heart rate of horses during an incremental exercise test on a treadmill.[85] Phenylbutazone administration accentuates the exercise-induced increase in right atrial pressure, but does not affect systemic vascular or pulmonary arterial pressures of exercising horses.[76,83,84] The effect of phenylbutazone on right atrial pressure has not been consistently detected.[83] The lack of an effect of the NSAIDs on pulmonary vascular pressures suggests that these compounds should not be expected to exacerbate the severity or increase the frequency of exercise-induced pulmonary hemorrhage. However, this aspect of the pharmacology of these drugs has not been examined in detail.

Oxygen consumption

Phenylbutazone and meclofenamic acid do not alter the rates of oxygen consumption or carbon dioxide production during moderate to intense submaximal exercise.[76,85] Flunixin administration does not affect peak oxygen consumption or carbon dioxide production of horses during an incremental exercise test.[69]

Blood lactate, electrolytes, and acid–base balance

The administration of NSAIDs may alter the blood or plasma lactate response to exercise. However, this effect is variable among studies and may depend on the exercise intensity and duration and the drug and dosage administered. Administration of flunixin meglumine (1 mg/kg, i.m.) or meclofenamic acid (2.2 mg/kg, p.o.) before running results in lower venous lactate concentrations after exercise than occur during drug-free trials.[80] Meclofenamic acid also increases the running speed at which a blood lactate concentration of 4 mmol/L is achieved and decreases the extrapolated venous lactate concentration at V200.[80,85]

Lactate concentration is not altered by phenylbutazone administration before 1 h of submaximal exercise.[84] Nor was blood lactate concentration after a simulated race on a track altered in Standardbred trotters nor in horses performing an incremental exercise test on a treadmill.[76,86]

Gait

A further factor to consider when discussing the effect of the NSAIDs on athletic performance is the ability of these drugs to decrease the pain associated with musculoskeletal disease. Flunixin meglumine restores the stride length of horses with induced carpal inflammation and similar results have been reported for phenylbutazone.[61,87] Flunixin meglumine administration is associated with decreased stance time and increased swing time and range of limb angles in apparently normal Standardbred horses trotting over ground.[81] These results demonstrate that administration of NSAIDs to horses with musculoskeletal pain may restore gait to more normal parameters.

Traditional wisdom is that lame horses do not perform as well in athletic competition as sound horses. The administration of phenylbutazone, or other NSAIDs, to lame horses may therefore allow them to compete more effectively. However, the risks of further injury to the horse if it is allowed to race after administration of NSAIDs have not been determined. It is possible that allowing a horse with clinically significant lameness, such as would need to be treated by administration of a NSAID, to race could exacerbate the injury.

Performance

There was no detectable effect of phenylbutazone on performance of 14 600 Thoroughbred horses racing in North America at tracks that permitted presence of the drug in the horse at the time of racing.[3] Similarly, flunixin meglumine does not affect run time to fatigue of Thoroughbred horses during an incremental exercise test on a treadmill.[69]

Hormones and analogs

Anabolic steroids

Anabolism, the production or generation of tissue, can be stimulated by a variety of anabolic steroids. While estrogens and related steroids have an anabolic effect, the androgenic steroidal hormones are more potent anabolic agents and are therefore more commonly used for this purpose. The anabolic/androgenic steroids are a group of compounds similar in structure to testosterone. Modification of the testosterone molecule has resulted in the production of compounds with reduced androgenic activity but maintained anabolic activity.[88] Various modifications have been made to the basic steroid structure to enhance its lipid solubility, thereby rendering it more soluble in the lipid vehicles used for parenteral injection, or reducing its rate of metabolism by the liver, thereby decreasing the 'first-pass effect' and permitting oral administration.[88] While oral administration of anabolic steroids to horses is unusual, with the exception of use of ethyestrenol in Australia, and steroid-induced hepatopathy has not been reported, the relatively constant rate of absorption from a site of intramuscular injection is an important aspect of the pharmacology of these drugs.

After parenteral administration the duration of effect of the anabolic steroid depends to a large extent on the rate with which it is released from the injection site. The rate of release is determined by the chemical nature of esters of the compound: acetic and propionic acid esters permit rapid absorption and a short duration of action (several days); phenylpropionic, cyclopentylpropionic, and undecylenic acid have a duration of approximately 2–4 weeks; and laureate, decanoate, and heptanoate esters slow absorption and extend the duration of action to 1 month or longer.[88] The ester used has important consequences for both the duration of action of the steroid and the period for which it can be detected. Undeclared substitution of nandrolone decanoate for nandrolone undecylenate, as may occur with some veterinary products produced by unreliable manufacturers, may result in nandrolone being detectable in the urine of treated horses for longer than expected. It is important to recognize that even using the same product the period during which steroid can be detected after intramuscular administration of anabolic steroids to horses is highly variable and unpredictable.

Testosterone is the archetypical androgenic/anabolic steroid. It exerts potent anabolic and androgenic (masculinizing) effects. The androgenic activity of testosterone or other androgenic steroids results in development of masculine characteristics in females or geldings, or prepubertal males. These changes include development of male behavioral traits including aggressiveness, frequent flehman exhibitions, mounting and erections (in geldings) and clitoral enlargement.[89,90] Because of testosterone's potent androgenic effects, use of anabolic steroids with lesser androgenic activity is often preferred.

The steroid hormones exert their effect by binding to intracellular (cytoplasmic) protein receptors. The hormone–receptor complex then interacts with nuclear material in a hit-and-run fashion to induce the synthesis of specific RNA and, consequently, proteins.[91] Testosterone acts in most body tissues, although the active intracellular hormone depends on the tissue. Testosterone is metabolized to the more active 5α-dihydrotestosterone by 5α-reductase in reproductive tissues, whereas in muscles, which have little 5α-reductase activity, testosterone is the predominant anabolic hormone.[88] This difference in tissue sensitivity to testosterone is important in mediating the effect of the synthetic anabolic/androgenic agents. Synthetic anabolic steroids that are resistant to reduction by 5α-reductase therefore exert minimal androgenic activity in reproductive and central nervous system and may exert considerable anabolic activity in muscle cells.

Effect on performance

Administration of anabolic steroids to men and women results in an increase in lean body mass and decease in body fat percentage.[92] While most studies of horses have found that administration of anabolic steroids to healthy horses does not enhance muscle development or increase bodyweight,[90,93–95] nandrolone laurate (0.3 mg/kg q7 days) increases the cross-sectional area of type 1 fibers and the percentage of type IIA fibers in trotting horses.[96] It also increases red cell volume of Finnish trotters in race training over that of similarly trained, untreated horses.[97] Furthermore, the rate of repletion of muscle glycogen after exercise is enhanced by administration of nandrolone laurate (1 mg/kg q7 days).[98] This effect is associated with higher plasma insulin concentrations after exercise and, the authors speculate, greater liver glucose production, although this was not measured.[98] Nandrolone administration also increases citrate synthetase and 3-hydroxyacyl-CoA dehydrogenase activity in muscle.[98] These are critical enzymes in energy transduction in muscle and increases in their activity may indicate increased capacity for energy metabolism by muscle of anabolic steroid-treated horses.

Administration of anabolic steroids to human athletes improves performance in sports that depend on optimal skeletal muscle function.[92,99–101] Administration of anabolic steroids increases muscle mass and improves strength and power output of both male and female human athletes.[99–101] However, an effect of anabolic steroid administration on athletic performance of horses has not been detected in any of the three published studies that have examined this variable.[94,95,97] This apparent lack of effect of anabolic steroids

on performance of horses may be a result of study design and the inability of studies of small numbers of horses to detect what would be, under racing conditions, important effects of the treatment.

The contrasting effects of anabolic steroids in horses and humans may well be due to species differences in response to the drugs, but more likely is a result of dosage. Human athletes often take doses of anabolic steroids (e.g. 3–6 mg/kg testosterone weekly) that may be 10–40 times the therapeutic dose (the amount needed to support physiologic function in agonadal males). Additionally, human athletes often 'stack' steroids, a practice in which the athletes take more than one anabolic steroid at a time.[92] It may be that administration of larger doses of anabolic steroids, simultaneous administration of more than one anabolic steroid, or prolonged administration may have detectable effects on body composition and athletic performance of horses.

Adverse effects

The use of anabolic/androgenic steroids is associated with a number of adverse side-effects. Virilization (masculinization) is often pronounced in females, castrated males, and prepubescent males.[89,97,102] Impaired reproductive function is noticeable in both fillies and stallions and is attributable to the direct effect of anabolic/androgenic hormones on the pituitary–gonadal axis.[89,103] These adverse effects dissipate and both stallions and mares appear to have normal fertility after cessation of treatment, although this return to normal fertility may take many months.[104]

Long-term administration of anabolic steroids has been associated with adrenal insufficiency in a horse.[105] Confirmation of the tentative diagnosis is based on lack of an increase in serum cortisol concentration in response to administration (1 IU/kg) of adrenocorticotropic hormone (ACTH). However, this case is unusual and short-term administration of stanozolol or boldenone undecylenate is not associated with changes in serum cortisol or ACTH concentrations.[106]

Liver disease, including cholestasis, hepatitis and neoplasia, occurs, albeit uncommonly, in humans ingesting C-17 α-alkylated anabolic steroids.[107] There are no reports of liver disease associated with anabolic steroid administration to horses.

Recombinant human erythropoietin (rhEPO)

Erythropoietin is a glycoprotein growth factor synthesized by cells adjacent to the proximal tubular cells in the kidney.[108] Production of erythropoietin increases in response to stimuli associated with reduced oxygen-carrying capacity of blood. Erythropoietin binds to specific receptors on erythroid precursors in bone marrow and other erythropoietic tissues stimulating the progenitor cells to continue their development to erythrocytes.[108] In the absence of stimulation by erythropoietin, the erythroid precursor cells die. Plasma erythropoietin concentrations in humans increase in an exponential manner with decreases in hematocrit such that hematocrits of less than 20% are associated with 100-fold increases in plasma erythropoietin concentration.[108]

Recombinant human erythropoietin (epoietin) was marketed for use in humans in 1985 and other products (darbopoietin) have been developed since that time. These products have been administered to horses in an apparent attempt to increase performance by increasing hematocrit and oxygen-carrying capacity. Administration of recombinant human erythropoietin to horses results in increases in red cell count, red cell mass and hematocrit.[109,110] This effect is achieved with administration of one dose of 120 IU/kg or dosages of 30 IU/kg three times weekly for 4 weeks.[109,110]

Plasma concentrations in clinically normal horses are 3.6 ± 2.3 (mean ± standard deviation) mIU/mL with 102 of 104 horses having values of 9 mIU/mL or less.[110] However, the range of values from normal horses likely depends on the methodology used to measure equine erythropoietin. Peak concentrations of recombinant human erythropoietin in horse plasma after administration of 30 IU/kg range from 25 to 120 mIU/mL, and decline with a half-life of approximately 13 h.[111]

Administration of recombinant human erythropoietin (15 IU/kg, three times weekly for 3 weeks) to splenectomized horses increases hematocrit from 37% to 46% and $\dot{V}O_{2max}$ by 19%,[109] suggesting the potential of this compound to improve athletic capacity. Similarly, administration of recombinant human erythropoietin (50 IU/kg, three times per week for 3 weeks) to horses with a spleen increases red cell mass, $\dot{V}O_{2max}$, and speed at $\dot{V}O_{2max}$.[112]

Adverse effects of administration of recombinant human erythropoietin to horses are potentially fatal. While there is substantial similarity and cross reactivity of erythropoietin among species,[113] administration of recombinant human erythropoietin to horses may induce production of products, likely anti-erythropoietin antibodies, that inhibit the activity of endogenous erythropoietin.[114] Administration of human recombinant erythropoietin is therefore associated with severe anemia secondary to red cell aplasia in an unknown proportion of horses to which it is administered (see Chapter 44).[114] The anemia may be refractory to treatment and result in death of the horse.[115]

An additional concern is that polycythemia induced by erythropoietin administration may increase blood viscosity with subsequent exacerbation of exercise-induced increases in pulmonary artery pressure and a worsening of exercise-induced pulmonary hemorrhage.[116] However, such concerns have not been substantiated at this time.

Growth hormone (somatotropin)

Growth hormone is a protein produced by the anterior pituitary gland. It is essential for normal growth and development in young individuals through both direct effects on tissue and effects mediated by somatomedins including insulin-like growth factor-1 (IGF-1).[117] Growth hormone

increases the rate of protein synthesis in cells, mobilizes fatty acids from adipose tissue, decreases glucose utilization, and influences fluid and electrolyte balance.[117] Recognition of the potential for growth hormone to exert anabolic effects lead to its use by human athletes.[92] However, studies of highly conditioned athletes have demonstrated that growth hormone administration does not increase fat-free mass, skeletal muscle protein synthesis, or strength in highly trained humans.[118,119] Growth hormone is effective in the treatment of individuals with a documented deficiency of the hormone but currently is considered ineffective as an anabolic agent in clinically normal human athletes.[92]

Recombinant equine growth hormone (eST) is available commercially. Although growth hormone deficiency has not been documented in horses, this compound has been administered to both old and young horses in studies of mineral balance, growth, immune function, bone mineralization, wound healing, and exercise capacity.[120–125] There is no detectable effect of growth hormone administration on athletic capacity of immature Standardbred or geriatric Standardbred and Thoroughbred mares.[124,125] However, studies of the effect of eST on exercise capacity of mature, athletic horses have not been reported.

Administration of growth hormone may be detected by measurement of serum concentrations of insulin-like growth factor.[126,127] Plasma concentrations of IGF-1 are increased for hours to days after administration of eST, whereas eST has a very short half-life and detection of increased concentrations is therefore difficult.[126] Concentrations of IGF-1 vary with age in horses, and normal values have been established.[126,128]

Sympathomimetics

The sympathetic nervous system mediates many of the homeostatic functions vital for existence. Exercise is a potent stimulus of increased sympathetic activity with large increases in concentrations of epinephrine (adrenaline) and norepinephrine (noradrenaline) occurring soon after the start of exercise.[129] Most of the actions of the sympathomimetic amines – the naturally occurring catecholamines and drugs that mimic their actions – can be explained through their effect to mimic the activity of the sympathetic nervous system. Catecholamines and the sympathetic amines produce, among other effects, bronchodilation, positive inotropy and chronotropy, altered vasomotor tone (either vasodilation or vasoconstriction, depending on the vascular bed and agent), and altered carbohydrate and fat metabolism.[130] Both epinephrine and norepinephrine, and the sympathetic amines isoprenaline (isoproterenol), clenbuterol, salbutamol, and terbutaline exert one or more of these effects in horses.[130–132] The predominant use of catecholamines or sympathetic amines in horses is in the relief of airway constriction attributable to bronchoconstriction. Sympathomimetic agents used to effect bronchodilation in horses include clenbuterol, albuterol (salbutamol), salmeterol, terbutaline, and isoproterenol.[132]

Clenbuterol hydrochloride

Clenbuterol hydrochloride is a β_2-adrenergic agonist used for the treatment of respiratory disease associated with bronchoconstriction in horses.[133] It has an elimination half-life of approximately 10.4 h, although the drug may be detected for up to 11 days in urine of horses administered multiple doses.[134,135]

Clenbuterol has pronounced cardiopulmonary effects in horses.[136] Intravenous administration of clenbuterol to healthy horses (0.8 μg per kg) minimally reduces non-elastic pulmonary resistance although this effect persists for longer than 3 h.[136] In horses with airway obstruction (heaves) clenbuterol decreases the maximal change in pleural pressure during respiration, airway resistance and the work of breathing. These effects are mediated by relaxation of constricted bronchial smooth muscle, with effects in vitro being maximal at 100 nM and not detectable at concentrations less than 0.1 nM.[137,138] Plasma concentrations achieved with twice daily administration of 0.8 μg/kg, orally, are 1.0 to 1.5 nM.[135] Notably, the bronchodilatory effect of clenbuterol in horses with no evidence of respiratory disease is minimal, although detectable, while the effect in horses with airway obstruction associated with bronchospasm is much greater.

Clenbuterol has minimal effect on respiratory variables during exercise by fit horses free of detectable respiratory disease. Blood gas tensions ($Paco_2$ and Pao_2) are not affected by clenbuterol administration, with the exception of one report of slightly lower $Paco_2$ during submaximal exercise.[135,139–141] Similarly, with the exception of one report of clenbuterol increasing tidal volume of normal horses during exercise, there is no effect of clenbuterol on respiratory mechanics during strenuous exercise on a treadmill.[135,139,141] The lack of effect of clenbuterol on respiratory variables of normal horses during intense exercise is not surprising given the minimal effect of clenbuterol in standing normal horses and the intense adrenergic stimulation associated with large increases in sympathetic tone and plasma epinephrine and norepinephrine concentrations during exercise.[129] The intense sympathetic stimulation during strenuous exercise may result in maximal bronchodilation, leaving no margin for a pharmacologic effect of clenbuterol. However, the effect of clenbuterol on responses to exertion of horses with chronic obstructive airway disease (heaves) is not reported.

Clenbuterol does not affect the rate of oxygen consumption during incremental exercise tests performed on a treadmill.[135,139–141] However, the effect of clenbuterol on the maximal rate of oxygen consumption, an indicator of maximal aerobic capacity, has not been reported.

Clenbuterol causes a transitory increase in heart rate and decrease in mean arterial pressure in standing healthy horses, but does not affect right atrial or pulmonary arterial pressures, after intravenous administration.[136,139,142] Clenbuterol has minimal cardiovascular effects on healthy horses during exercise. It causes a slight increase in heart rate, over that of untreated horses, at low work intensities but this effect is not apparent at higher work intensities.[139] Clen-

buterol does not attenuate the exercise-induced increases in pulmonary artery, pulmonary capillary or pulmonary wedge pressure in horses running on a treadmill,[142] nor does it alter furosemide's hemodynamic effect in exercising horses.[143]

Administration of clenbuterol (2.4 μg/kg, orally twice daily, 5 days per week) for 8 weeks to Standardbred horses is associated with left ventricular dilation, and increases in left ventricular free wall thickness at the end of systole and aortic root diameter.[144] These changes are interpreted as potentially detrimental to the horse's wellbeing.[144] A deleterious effect of chronic or repeated, high-dose, β-adrenergic stimulation on myocardium of dogs, sheep, rats, and mice is reported.[145,146] Changes observed include necrosis and hypertrophy of myocardial cells. However, the doses used were, on a body-weight basis, much larger than those associated with cardiac disease in horses. The importance of the changes in heart and aortic size reported with clenbuterol administration to horses remains to be determined.

Clenbuterol is a potent repartitioning agent in a number of species including mice, cattle, and horses.[147,148] Clenbuterol increases muscle mass, muscle protein synthesis and body-weight and decreases fat mass in these species. At a dose of 2.4 μg/kg orally twice daily, 5 days per week for 8 weeks, clenbuterol increases fat-free mass and decreases fat mass and the proportion of fat in the body in unexercised horses. Similar effects are noted in horses that trained while being administered clenbuterol.[147] The importance of this change in body composition on athletic capacity is not reported.

Chronic administration of clenbuterol decreases both endurance and sprint running capacity of rats.[145] The effect of clenbuterol on exercise capacity of horses or humans has not been reported.[149] While extrapolation of results obtained during submaximal exercise should be done with caution, results of none of the studies to date clearly indicate a likely effect of clenbuterol to increase athletic capacity of horses.

Albuterol (salbutamol)

Albuterol (salbutamol) is a β_2-adrenergic agonist administered to horses orally, intravenously, intratracheally, or by inhalation for treatment of bronchoconstriction.[150] The plasma elimination half-life is not reported but the drug is not detectable in urine 24–48 h after the last dose, although this will vary depending on the dose, animal characteristics, and method of detection used.[151]

After inhalation by horses with recurrent airway obstruction, bronchodilation occurs within 5 min and persists for 30 min to 3 h.[150] However, no effect of albuterol (360, 720, or 900 μg total dose by inhalation) on respiratory mechanics, $\dot{V}O_{2max}$, maximum heart rate, or blood lactate concentration has been reported in healthy horses running on a treadmill.[152,153] By contrast, others have reported a significant effect of albuterol (900 μg total dose by inhalation) on $\dot{V}O_{2max}$ and run time to fatigue of healthy horses.[154] $\dot{V}O_{2max}$ increased from 122 to 130 mL/kg/min and run time to fatigue increased from 406 to 431 s. The reason for these disparate results is not apparent, although it is speculated that the horses in the later study may have had some degree of bronchoconstriction that was relieved by albuterol administration.[153]

Amphetamines

Amphetamine is an indirectly acting sympathomimetic amine; its mechanism of action involves release of norepinephrine from storage sites in nerve terminals.[155] Consequently, the effects of amphetamine administration are predominantly those of α- and β_1-adrenergic stimulation, including increases in both systolic and diastolic blood pressure and a reflex reduction in heart rate.[155] However, the primary effect of the amphetamines is in the central nervous system.[156] Central effects of amphetamine include medullary and cortical stimulation and possibly reticular activating system stimulation. Stimulation of these areas results in mood elevation, euphoria, and decreased sense of fatigue in humans. Amphetamines also increase metabolic rate, oxygen consumption, and plasma free-fatty acid concentration.[157]

In resting horses amphetamine increases respiratory rate slightly (9 breaths per minute) without altering the heart rate.[158,159] Amphetamine sulfate administered intravenously 30–60 min before a gallop produces an immediate post-race heart rate that is significantly less than that of controls.[158,159] Smetzer and Senta reported a similar observation with doses of amphetamine of 150 and 300 mg per horse.[159] However, in another trial in which amphetamine was administered intravenously (0.55 mg/kg) 20 min before a submaximal exertion test, the heart rates of the treated horses were higher than those of control horses after completion of the run.[160] Cardiac arrhythmias occur during the immediate postexertion period in amphetamine-treated horses.[158,159] The arrhythmias included second-degree atrioventricular (AV) block, sinus arrhythmia, and ventricular or AV junctional beats.[159] The arrhythmias resolved in 3 to 5 min.[158] Amphetamine also increases respiratory rate, rectal temperature, and blood lactate concentration immediately after high-speed trotting or pacing.[161]

Amphetamine has been used by human athletes because of its ability to reduce fatigue and enhance athletic performance.[156,162] Amphetamines may be ergogenic in human beings, improving acceleration and increasing lactate accumulation and time to exhaustion, but not muscular power, speed, or maximal aerobic capacity.[156] Amphetamine administration is also associated with significant increases in knee extension strength, acceleration, anaerobic capacity, time to exhaustion, and pre-exercise and maximum heart rates.[157] Lactate accumulation during an incremental exercise test is increased, but $\dot{V}O_{2max}$ is not.[157]

Administration of amphetamine to Thoroughbred horses before each of five trials increased the speed over the corresponding control gallop, however, the overall difference was not statistically significant and the statistical power was

low.[158] The effect of amphetamine administration on equine athletic performance is unknown.

Methylamphetamine

Methylamphetamine, a derivative of amphetamine, produces variable effects on recovery heart rates when it is administered before exercise. The effect of methylamphetamine on heart rate appears to depend on the intensity and possibly the duration of the exertion involved.[163] Methylamphetamine improves performance in a variety of submaximal speed tests at doses of 0.1 to 0.4 mg/kg, intramuscularly,[164] but the importance of this action to competitive endeavors is unknown.

Methylphenidate

Methylphenidate is structurally related to amphetamine and its pharmacologic effects are essentially those of the amphetamines. There has been minimal evaluation of the effect of methylphenidate in horses. The time for cardiac deceleration after lungeing is longer in horses administered methylphenidate than in untreated horses.[163] Methylphenidate increases recovery heart rate, respiratory rate, venous lactate concentration, rectal temperature, and cardiac output over those values in untreated horses after a submaximal exercise test by trained Standardbred horses.[160] These results suggest that methylphenidate may have a detrimental effect on these variables during exercise and therefore has the potential to impair performance. However, methylphenidate consistently increased the speed of running in four types of submaximal exercise tests.[163]

Ephedrine

Ephedrine is both an α- and β-adrenergic agonist that stimulates heart rate and increases cardiac output of non-exercising human beings. The administration of ephedrine to horses does not affect heart and respiratory rates after lungeing, nor speed performance of horses.[164]

Cocaine

Cocaine is a naturally occurring alkaloid with potent peripheral sympathomimetic activity and central nervous system stimulating effects. Cocaine is also an effective local anesthetic, an effect enhanced by cocaine's induction of localized vasoconstriction and consequent delayed absorption and dissipation from the site of application.[165] The mechanism of the peripheral systemic effects of cocaine is unclear but may be due to inhibition of reuptake of norepinephrine at presynaptic terminals of sympathetic nerves, direct stimulation of release of catecholamines from peripheral nerves, or centrally mediated release of adrenal catecholamines.[156] Whatever the mechanism, cocaine administered intravenously to humans and horses elevates blood pressure and heart rate, and may induce arrhythmias.[166,167] The central nervous system effects of cocaine administration to humans includes euphoria, a positive alteration in mood, and a decreased sense of fatigue. These effects are likely the result of cocaine inhibiting reuptake of dopamine in the CNS, with a resultant increase in dopamine concentration at dopamine (D2) receptors.[156]

Cocaine enhances athletic capacity for short-term, intense exertion but not for prolonged, submaximal activities by humans.[156] However, this effect does not appear to be related to increased aerobic capacity.[168] Cocaine increases heart rate and mean arterial pressure of horses during an incremental exercise test and decreases the anaerobic threshold in a dose-dependent fashion.[167] Cocaine-treated horses have higher blood lactate concentrations at maximal, fatiguing, work intensities.[167] Notably, endurance time, as measured by time to fatigue during an incremental exercise test, is significantly prolonged by cocaine administration.[167] This study provided persuasive evidence of an ergogenic effect of cocaine that is dose related. Interestingly, cocaine also demonstrates dose-related effects on spontaneous locomotor activity of horses, with the highest no effect dose being 0.02 mg/kg.[169]

Sympatholytics

The adrenergic receptors, via increased sympathetic nervous system activity and increased concentrations of circulating epinephrine and norepinephrine, play a significant role in mediating the physiologic and metabolic responses to exertion. Therefore, it is not surprising that β-blockade modifies these responses and impairs exercise performance.[170–173] Furthermore, given that the β-adrenergic system comprises two receptor subtypes, β_1 and β_2, which subserve different physiologic functions, it is apparent that non-selective and selective β-blockade have the potential to modify different physiologic responses to exertion. The modification of the physiologic responses by both selective and non-selective β-blockade during exertion has been extensively investigated in humans, in part because of the importance of β-blockade and exercise in cardiac rehabilitation programs. The effects of a number of different β-blockers on the physiologic responses to exertion have been examined in humans and animals.

β-Blockade attenuates the exertion-induced increase in heart rate and cardiac output of horses,[174] and reduces heart rate during the recovery period from exercise.[173] Propranolol (0.22 mg/kg, i.v.) attenuates the elevation in pulmonary artery flow velocity (an indicator of cardiac output) and right ventricular dP/dt, while augmenting the increase in mean pulmonary artery and right ventricular pressures of ponies during an incremental exercise test.[175] Propranolol did not alter the response of the mean systemic arterial pressure to exertion.[175]

The effect of β-blockade on $\dot{V}O_{2max}$ has not been reported for horses. However, $\dot{V}O_2$ is maintained at submaximal work intensities through an increase in oxygen extraction by tissue, manifest as a reduction in venous oxygen content.[174] At maximal work rates, however, the increased arterial–venous oxygen difference can no longer compensate for the decreased cardiac output and maximal oxygen consumption in humans is diminished.

β-Adrenergic blockade has significant effects on exercise-induced changes in metabolism.[173,174,176] Propranolol increases plasma glucose concentrations, decreases plasma insulin concentrations, attenuates the increase in plasma glucagon and free fatty acid concentration in horses during submaximal exercise.[176] The rate of appearance of glucose in blood was increased from 30.5 +/– 3.6 to 42.8 +/– 4.1 μmol/kg/min during exercise at 50% $\dot{V}O_{2max}$, and from 54.4 +/– 4.4 and 73.8 +/– 4.7 μmol/kg/min during exercise at 65% by prior propranolol administration.[176] Similarly, the rate of disappearance of glucose from blood, an indicator of skeletal muscle uptake of glucose, during exercise was approximately 40% higher after propranolol administration. Propranolol also augmented carbohydrate oxidation, with a concomitant reduction in fat oxidation, during exercise. Muscle glycogen utilization was similar between trials and therefore the increase in carbohydrate oxidation with propranolol administration was due to increased use of plasma glucose. Evidently, beta-adrenergic mechanisms restrain glucose uptake by tissue during exercise.[176]

Propranolol administration also decreases blood and muscle lactate accumulation during brief, intense exercise, and attenuates the decrease in arterial and venous pH.[174] However, these effects are likely attributable, at least in part, to the shorter duration of exercise in propranolol-treated horses.[174] Similarly, the rise in blood glucose, glycerol and lactate concentrations immediately after exercise over values before exercise is reduced by both propranolol and metoprolol administration, but these changes could be attributable to the slower speed at which horses ran after treatment.[173]

In horses sweating is under β_2-adrenergic control.[177] Propranolol reduces the sweating response of isolated equine skin after stimulation with either epinephrine or terbutaline,[177] and of horses to exertion.[173] Metoprolol does not decrease sweat production, consistent with the β_1 selectivity of this drug.[173] Reduction in the rate of sweat production is likely the reason for elevated body temperature of horses during exercise after administration of propranolol.[174,176,178]

Beta-adrenergic blockade reduces exercise performance in both humans and horses.[173–176,178,179] Non-selective β-blockade (propranolol) causes a greater reduction in exercise performance than selective (metoprolol) β-blockade.[172,173,180] The reduction in exercise capacity of horses occurs during both moderate- and high-intensity exercise. Run time of Thoroughbred horses running on a treadmill at a speed equivalent of 105% $\dot{V}O_{2max}$ was reduced from 119 to 82 s by propranolol administration.[174] Similarly, exercise duration for horses running on a treadmill for 30 min at 50% $\dot{V}O_{2max}$ and then 30 min at 65% $\dot{V}O_{2max}$ was reduced to 49 min by propranolol administration.[176] Ponies that could easily complete an incremental exercise test to 3.4 m/s on a treadmill were only able to achieve 2.8 m/s after propranolol administration.[175] The speed of galloping by Thoroughbred horses was reduced by 7% after propranolol administration and 5% after metoprolol administration.[173] The effect of β-blockade on exercise performance is likely the result of impaired cardiovascular, metabolic and thermoregulatory responses to exercise.

Sedatives and tranquilizers

The sedatives and tranquilizers used frequently in equine practice are phenothiazine derivatives (promazine, chlorpromazine, acepromazine, fluphenazine) and the α_2-adrenergic agonists (xylazine, detomidine, and romifidine).[181]

Promazine, acetylpromazine, chlorpromazine, and fluphenazine

The predominant mechanism of action of the phenothiazine derivatives is as dopamine antagonists in the mesolimbic–mesocortical, and nigrostriatal regions of the brain.[181] The mesolimbic–mesocortical pathway is involved in behavior, whereas the nigrostriatal pathway is integral to the coordination of voluntary movement. The phenothiazines therefore reduce spontaneous motor activity in horses.[182] Phenothiazines also block the peripheral actions of catecholamines, an action that may account for acepromazine's hypotensive effect.[183,184] The phenothiazine derivatives have little or no analgesic activity.[185]

Fluphenazine is a potent dopamine antagonist used in human medicine as an antipsychotic. Long-acting preparations (ethanate or deconoate) suitable for intramuscular use are available and are administered to horses to induce prolonged, mild sedation. Extrapyramidal signs occur in humans administered fluphenazine and include grimacing and muscle spasms of the head, neck, jaw and proximal extremities, and motor restlessness evident as pacing or rocking.[186] Fluphenazine-induced extrapyramidal signs have been reported in Thoroughbred racehorses.[187,188]

The terminal half-life of acepromazine in serum is approximately 150 min,[189] although the drug or its metabolites may be detectable for much longer (120 h) in urine.[190] Repeated administration of acepromazine may further prolong the period for which it can be detected in plasma or urine.

There are few studies of the effect of the promazine tranquilizers on physiologic responses to exercise. Acepromazine (0.0066 mg/kg i.v. 20 min before exercise) decreases plasma lactate concentration of Thoroughbred horses 2 and 30 min after galloping 1000 m.[191] However, there was no effect of acepromazine on plasma potassium, cortisol, norepinephrine or epinephrine concentrations.[191] Similarly, promazine does not influence a number of physiologic variables of horses during a submaximal exertion test,[161] but does increase the heart rate immediately after completion of a high-speed run.[158] Chlorpromazine increases the heart rate and causes penile ptosis of male horses during submaximal running on a track.[192]

Sedatives may reduce athletic performance of horses, depending on the nature and intensity of the exercise and the personality of the horse. Acepromazine increased the time taken for Thoroughbred horses to run 1000 m by 0.6 s, although this was not statistically significant.[191] Interestingly, two nervous horses had improved run time after acepromazine administration, whereas more relaxed horses had markedly worsened run times when affected by acepromazine.[191] Both acetylpromazine and promazine reduce performance in horses subjected to a short gallop or cavalleti.[163] Promazine significantly decreases speed of Thoroughbred horses when administered 30–60 min before a simulated race.[158] Chlorpromazine has a pronounced effect in decreasing running speed of Thoroughbred horses.[192]

α_2-Adrenergic agonists

The α_2-adrenergic agonists exert their sedative and analgesic effects by binding to α_2 receptors in the central nervous system and suppressing axonal release of norepinephrine and dopamine.[181] α_2-Adrenergic receptors are found in many other tissues of the body and this likely accounts for the endocrine and cardiovascular effects of the α_2-agonists.[193] The cardiovascular effects of the α_2-agonists are due to the combined effects of inhibition of central nervous system sympathetic tone and norepinephrine release from peripheral sympathetic nerves, and an apparent reflex increase in vagal tone secondary to α_2-agonist-induced increase in systemic blood pressure.[193]

Xylazine, detomidine, and romifidine are α_2-agonists available for use in horses.[181] Although their relative potency varies, all three drugs are potent analgesics and sedatives in horses. Both xylazine and detomidine exert dose-dependent effects on systemic hemodynamics of conscious horses. Xylazine and detomidine cause an initial brief increase in systemic arterial pressures, which is followed by a more prolonged hypotension.[194] Heart and respiratory rate and cardiac output are reduced, while cardiac filling pressures are increased by xylazine or detomidine administration to horses.[194] These drugs also decrease intracranial pressure in conscious horses,[195] cause hyperglycemia and reduced insulin secretion, and transiently increase urine output.[196,197]

While the α_2-agonists are drugs frequently used in performance horses the effect of α_2-agonists on athletic capacity of horses has not, to our knowledge, been reported. However, the profound sedative, hemodynamic and endocrine effects of these drugs in resting horses would suggest that they have the capacity to reduce maximal athletic capacity.

Reserpine

Reserpine is a compound used to produce long-lasting sedation in horses, for which it is sometimes used as an aid in training young or fractious horses. Reserpine depletes norepinephrine, dopamine, and serotonin stores in synapses resulting in long-lasting (10 days) sedation.[181] There is a lag time between administration of reserpine and onset of sedation. Administration of reserpine (5 mg, i.v., single dose) decreases spontaneous motor activity of horses with maximal sedation occurring 3–5 days after injection.[198] Sedation occurs even after reserpine is no longer detectable in blood or urine, although the period during which reserpine can be detected depends on the method of analysis of samples.[199,200] There are no reports of the effect of reserpine on athletic capacity, however it could be expected to reduce maximal athletic capacity. Reserpine toxicosis is characterized by bradycardia, depression, miosis, ptosis, and paraphimosis.[201]

Methylxanthines

Theophylline (and its salt, aminophylline), theobromine, and caffeine are methylxanthine alkaloids that share similar structures, pharmacologic effects, and mechanisms of action. All act as stimulants of the central nervous system and heart, relax smooth muscle, induce diuresis, and increase basal metabolic rate and plasma concentrations of free fatty acids, probably mediated via antagonism of adenosine.[202,203]

Caffeine

Ingestion of caffeine by humans causes increased alertness (i.e. less drowsiness and clearer thought), but impairs coordination and task performance.[156] Increasing doses of caffeine increase central nervous system stimulation resulting in, progressively, nervousness and anxiety, restlessness, insomnia, tremors, hyperesthesia, and convulsions.[203] Caffeine also affects skeletal muscle function. In vitro caffeine potentiates twitch tension, and in vivo it increases muscle force output at low electrical frequencies (10–59 Hz) but does not alter the strength of maximum voluntary contractions.[156] Caffeine does not improve short-term or maximal power output of humans, and it may or may not improve endurance performance.[156,204]

Caffeine is often detected in urine samples collected as a result of drug-control procedures. In many instances, these positive findings are a result of dietary caffeine, such as feeding horses chocolate treats, rather than deliberate administration of caffeine.[205] The elimination half-life of caffeine in horses is approximately 10 h.[206]

Caffeine spontaneously increases locomotor activity of horses, but the effect is short lived and apparent only after intravenous injection of the drug.[206] The highest no-effect dose for spontaneous locomotor activity of horses is 2.0 mg/kg i.v.,[207] although the relationship between this variable and racing performance is unknown. Caffeine (2.5 and 5.0 g/horse, s.c.) enhances running performance, as assessed by timed runs of Thoroughbred horses running at submaximal speeds,[208] likely reflecting an increased alertness or willingness to run rather than a change in exercise capacity. Heart rates during submaximal exercise and recovery are higher after caffeine administration than during drug-free trials.[208] Variable effects on performance and heart and respiratory rates were observed in two horses

administered caffeine (4.0 and 16.0 mg/kg, p.o.), although there are insufficient data to draw any conclusions.[164]

Theophylline

Theophylline is a potent dilator of constricted airways, and is often used in the treatment of recurrent obstructive pulmonary disease (heaves, COPD) of horses. Theophylline, like caffeine, has pronounced effects on other body systems, including the central nervous system, heart, and kidneys. Theophylline induces dose-dependent increases in heart rate, sweating, sensitivity to auditory and visual stimuli, urine flow, and muscle tremors in horses.[209] The suggested upper therapeutic plasma concentration of theophylline in horses is 15 μg/mL.[210]

Theophylline affects some of the physiological responses of horses to exertion. Theophylline accentuates both the heart rate and blood lactate concentration responses of horses to incremental exertion on a treadmill.[80,211] The effect of theophylline on athletic performance of horses is unknown, although in humans intravenous aminophylline does not increase maximal oxygen uptake, maximum work rate, or maximum minute ventilation.[212]

Alkalinizing agents

Sodium bicarbonate

Bicarbonate is an endogenous substance present at predictable concentrations in blood and body fluids. Endogenous bicarbonate is produced as a result of the hydration of carbon dioxide:

$$CO_2 + H_2O \Leftrightarrow HCO_3^- + H^+$$

This reaction is catalyzed by the enzyme carbonic anhydrase. This enzyme is highly active in red blood cells and renal tubular cells, among other tissues, where it has important action in carbon dioxide transportation and maintenance of acid–base balance. Bicarbonate is eliminated by the reverse reaction occurring in the lungs, with subsequent exhalation of carbon dioxide. Bicarbonate is also eliminated by renal excretion. Variable proportions of bicarbonate filtered at the glomerulus are then reabsorbed in the proximal tubule. Excess bicarbonate is not reabsorbed and is excreted as predominantly sodium or calcium bicarbonate in urine.

The concentration of bicarbonate in blood depends on the rates of production from carbon dioxide in red blood cells and plasma, elimination of carbon dioxide from the lungs, and excretion in urine. Formation of bicarbonate from carbon dioxide produced in metabolically active tissues is quantitatively important in the transport of carbon dioxide and its elimination in the breath.

Exercise, which is associated with increases in carbon dioxide production, increases bicarbonate concentration in venous blood. This increase in plasma bicarbonate concentration is short lived, resolving within seconds to minutes of the cessation of exercise (see Chapter 39) as the excess carbon dioxide is exhaled. The increase in venous blood bicarbonate concentration is proportional to the intensity of exercise and partially attenuates the exercise-induced acidemia associated with intense exercise.

A number of factors, including exercise, diet, ambient temperature, administration of supplements and medications, and disease have been demonstrated or claimed to effect blood bicarbonate concentrations. The potential for these factors to affect blood bicarbonate concentration has important consequences for regulation of administration of alkalinizing agents to horses and have therefore attracted considerable attention. The influence of a number of these factors has been described elsewhere.[213–216]

Pharmacokinetics

Alkalosis and increased blood bicarbonate concentrations persist for periods varying with dose and route of administra-

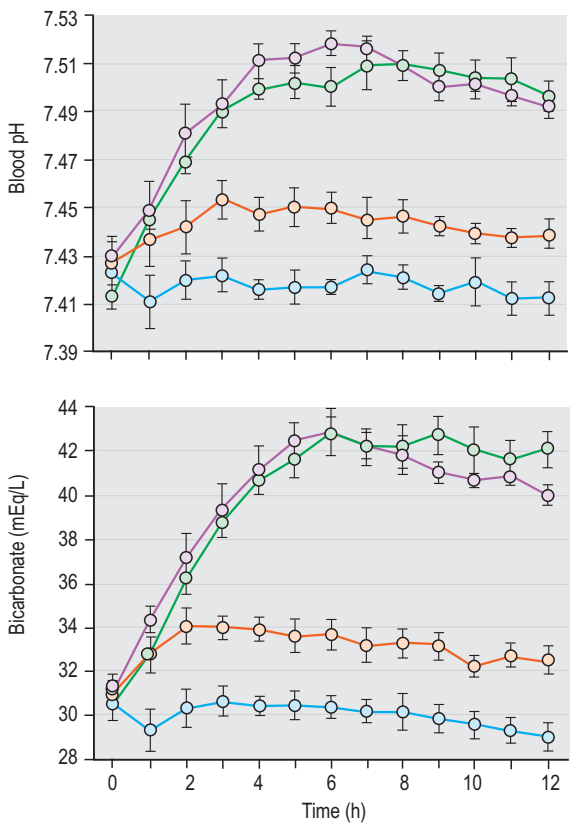


Fig. 66.3
Effects of dosages of sodium bicarbonate of 250, 1000, and 1500 mg/kg bodyweight administered orally to horses. Notice the prolonged time to peak concentration with larger doses and the lack of a higher peak with dosages above 1000 mg/kg. ●, sodium bicarbonate, 1500 mg/kg, orally; ●, sodium bicarbonate, 1000 mg/kg, orally; ●, sodium bicarbonate, 250 mg/kg, orally; ●, water, 3L, orally.
Data are from Rivas et al.[219]

tion and whether the horse is permitted to drink water after receiving sodium bicarbonate. Increases in blood bicarbonate concentration are detectable within 1 h of administration of bicarbonate orally.[217–220] Peak blood bicarbonate concentrations occur at times proportional to the dose of bicarbonate. Smaller doses of sodium bicarbonate result in lower peak concentrations achieved sooner after administration. Dosages of 400 mg/kg, orally, result in peak concentrations of bicarbonate in blood 2–4 h after administration, whereas after dosages of 1000 to 1500 mg/kg, orally, peak blood bicarbonate concentrations are not achieved for 6–8 h (Fig. 66.3).[217,219–221] Alkalosis persists for more than 12 h after administration of ≥ 250 mg/kg sodium bicarbonate orally to horses that are then not provided access to water.[217,219,220,222] The alkalinizing effect of orally administered sodium bicarbonate is not affected by feeding.[217]

The alkalinizing effect of sodium bicarbonate is proportional to the dose administered, up to a dosage of 1000 mg/kg.[219] Dosages of sodium bicarbonate of 250–300 mg/kg, orally, induce an increase in blood bicarbonate concentration of approximately 4 mEq/L, a dose of 0.5 mg/kg increases blood bicarbonate concentration by 8 mEq/L, whereas increases of 10–12 mEq/L are detected after oral administration of 1000–1500 mg/kg.[217–219,223] Dosages of 1500 mg/kg, orally, do not induce greater increases in blood bicarbonate concentration than do dosages of 1000 mg/kg, perhaps because of limits to the rate of absorption of sodium bicarbonate from the small intestine.[219]

Effect on blood and urine constituents

Administration of sodium bicarbonate has profound effects on blood pH and serum electrolyte and protein concentrations, osmolality and hematocrit, as well as urine composition and volume. Serum concentrations of sodium and plasma protein increase whereas serum potassium concentration declines after administration of sodium bicarbonate. Serum osmolality increases, with greater increases observed in horses that are not permitted to drink after administration of sodium bicarbonate.[217,219] Urine flow increases, regardless of whether the horses are permitted to drink, whereas urine osmolality may drop, remain unchanged, or increase slightly, depending on the dose of sodium bicarbonate and whether the horses have access to water.[217,219]

Blood pH, both arterial and venous, increases in a dose-dependent fashion up to dosages of sodium bicarbonate of approximately 1000 mg/kg, orally. Venous pH increases by approximately 0.04 units after dosages of 250–300 mg/kg, orally, and by 0.1 units after dosages of 1000–1500 mg/kg, orally.[214,217–221,223,224] However, the effect of dose is not entirely predictable, although being a major component of any increase in pH, and other factors may influence the increase in blood pH after administration of sodium bicarbonate.

Venous Pco_2 increases after administration of sodium bicarbonate. Venous Pco_2 increases by 4 to 8 mmHg after administration of 250–1500 mg/kg of sodium bicarbonate orally.[214,217,219,220,224–226] Increases in arterial Pco_2 have been reported, but are variable and inconsistent among studies.[227]

Increases in serum sodium concentration after administration of sodium bicarbonate vary to some extent with the dose administered. However, it is not possible to determine the dose of sodium bicarbonate from serum concentrations of sodium in the horse. Dosages of 1000 mg/kg increase serum sodium concentrations by approximately 10 mEq/L in horses not provided with access to water.[219,225] Similarly, dosages of 500 mg/kg increase serum sodium concentration by approximately 6 mEq/L.[217] However, the increase in serum sodium concentration is attenuated when sodium bicarbonate is administered with water.[225]

Serum potassium concentration declines after administration of sodium bicarbonate with greater declines occurring after larger doses.[219,225] Serum potassium concentration may decrease to less than 2.5 mEq/L in resting horses administered sodium bicarbonate. Serum chloride concentrations usually decline after administration of sodium bicarbonate, especially when horses are allowed to drink or water is provided with the sodium bicarbonate.[217,225] The decline in serum chloride concentrations is approximately 5–9 mEq/L. Others have not detected a decline in serum chloride concentration.[219]

Consistent with the increase in serum sodium concentration is an increase in serum osmolality, the magnitude of which depends on dose and access to water. Administration of dosages of 250 mg/kg increase serum osmolality by less than 10 mOsmol/kg whereas administration of 1000 to 1500 mg/kg increases serum osmolality by approximately 25 mOsmol/kg.[219] Access of the horses to water attenuates the increase in serum osmolality.[217]

Plasma protein concentrations are unchanged in horses that are not provided access to water after administration of sodium bicarbonate.[219] However, plasma protein concentration declines by approximately 1.0 g/dL (10 g/L) after administration of 500 mg/kg of sodium bicarbonate in horses that are permitted to drink.[217] The decline in plasma protein concentration is likely secondary to an increase in plasma volume, although such changes have not been detected by direct measurement of plasma volume.[225]

Urine flow increases after sodium bicarbonate administration, regardless of whether the horses have access to water.[217,219] Urine volume in the 12 h after administration of 3 L of water, 250, 1000, or 1500 mg/kg of sodium bicarbonate in 3 L of water was 3.3, 3.5, 7.7, and 9.3 L, respectively.[228] Horses provided access to water after administration of sodium bicarbonate increase their water consumption from control levels of 0.5 L/h to 2.3 L/h.[217] The rate of water consumption returns to control levels by 18 h.[217] Horses administered sodium bicarbonate and denied access drink readily when subsequently provided with water likely indicating enhanced thirst.

Increases in urine volume are associated with increases in sodium excretion. During the 24 h after administration of 500 mg/kg of sodium bicarbonate, horses excreted 3400 mmol of sodium, compared with 600 mmol during an equivalent control period.[217] The excretion of sodium is dose dependent, with 12-h sodium excretion of 198, 457, 1700,

and 2400 mmol after oral administration of 3 L of water, or 250, 1000, or 1500 mg/kg orally, respectively, of sodium bicarbonate.[228] The increase in sodium excretion is associated with increased urine osmolality in horses not provided access to water,[228] and decreased osmolality in horses permitted to drink.[217]

Urine pH increases by 0.5 to 0.8 units after administration of 250 to 1500 mg/kg, although there does not appear to be a dose-dependent effect.[217,228] The increase in urine pH is associated with an increase in urine bicarbonate concentration, with the effect increasing with increasing dosage up to a dosage of 1000 mg/kg, orally.[228] Bicarbonate excretion in urine is 604, 1034, 2734, and 3370 mEq in the 12 h after administration of 3 L of water or 250, 1000, or 1500 mg/kg of sodium bicarbonate, respectively.[228]

Effect during exercise

Sodium bicarbonate administered a sufficient time before exercise to induce alkalosis at the start of exercise attenuates the acidosis induced by intense exercise, and increases blood lactate and sodium concentrations during exercise.

The venous and arterial pH of horses is higher during intense exercise after sodium bicarbonate administration than in untreated animals. This attenuation of acidemia is associated with higher venous and arterial concentrations of bicarbonate and higher Pco_2 tensions during and immediately after both intense, but submaximal exercise, and during work at speeds greater than that which induces $\dot{V}o_{2max}$.[214,218,227,229,230] Sodium bicarbonate attenuates the exercise-induced decrease in venous pH (6.97 and 7.06, respectively, for water or bicarbonate) at the end of a sprint in horses running on a treadmill.[227] Similarly, the decrease in both arterial and venous blood bicarbonate concentration is attenuated by sodium bicarbonate administration with values of 24.5 and 29.7 mEq/L (venous) at end of sprinting after administration of water or $NaHCO_3$, respectively.[227]

Blood lactate concentrations during exercise are higher in horses administered sodium bicarbonate.[223,224,227,229,231,232] Blood, plasma or serum lactate concentrations are typically 3–6 mmol/L higher in horses administered sodium bicarbonate, with the increase depending in part on the dose of sodium bicarbonate, the intensity of exercise and therefore lactate concentration, and on whether lactate was measured in whole blood, plasma, or serum. Generally, the increase in blood lactate concentration is larger when lactate concentrations are higher, as occurs during intense exercise. Not all investigations have detected an effect of sodium bicarbonate administration on blood lactate concentrations, possibly because these studies used low dosages of bicarbonate (300–600 mg/kg).[226,230,233] Increases in blood lactate concentration have been attributed to increased movement of lactate from sites of production in muscle to the blood after sodium bicarbonate administration. However, muscle lactate concentrations are not affected by sodium bicarbonate administration.[226,231,233] The lack of apparent effect of alkalinization on muscle lactate concentrations may be attributable to the insensitivity of measurement techniques to detect a reduction secondary to enhanced efflux of lactate from the muscle. Enhanced rates of lactate efflux and lower lactate concentrations in muscle have been detected using isolated dog or rat muscle.[234]

Sodium bicarbonate administration attenuates the ionized calcium concentration of serum of horses during intense exercise (iCa of 1.58 and 1.44 mmol/L before exercise, and 1.69 and 1.49 end sprint, for water and $NaHCO_3$ treatments, respectively), but does not affect total calcium concentrations in serum.[227] Bicarbonate administration decreases plasma ammonia concentrations during and after intense exercise, although this effect is not consistently reported.[224,231] Sodium bicarbonate administration does not affect blood hypoxanthine or xanthine concentrations at rest or during and after exercise.[233]

Muscle concentrations of adenosine-5-monophosphate and inosine-5-monophosphate are lower after exercise in horses administered sodium bicarbonate.[231] However, muscle concentrations of glucose-6-phosphate, creatine phosphate, and ATP before and immediately after intense exercise are not detectably affected by sodium bicarbonate administration.[226,233]

Mechanism of action

Muscular work is associated with increases in the concentration of lactate and hydrogen ions in muscle cells. These changes occur as energy for muscle contraction is provided by anaerobic glycolysis, the metabolism of glucose to lactate and pyruvate. Under aerobic conditions lactate is metabolized, and hydrogen ions are consumed, via pyruvate and the citric acid cycle to carbon dioxide. However, if the oxygen supply is limiting, as may occur in muscles during intense exercise, then lactate and hydrogen ions accumulate in the muscle cells. When the buffering capacity of the cell is exceeded then the intracellular pH falls, the activity of pH sensitive processes in the cell declines, and the cell's ability to generate power diminishes.[235] Sodium bicarbonate may delay the onset of fatigue by providing additional buffering and thereby slowing the decline in intracellular pH. However, whereas metabolic alkalosis favors the release of lactate from muscle cells, it does not affect cellular creatine phosphate and ATP concentrations, nor does it increase muscle performance.[236] The mechanism by which sodium bicarbonate exerts any ergogenic effect is unclear.

Effect on exercise performance

There have been numerous studies of the effect of sodium bicarbonate on athletic capacity of human beings (see Heigenhauser[234]). The findings of these studies are inconsistent and often contradictory. Comparison of the studies is confounded by the range of doses of sodium bicarbonate used, including doses that are now regarded as ineffective (0.2 g/kg and less), the variable time between ingestion and the exercise test, and the variety of exercise tests employed. A meta-analysis of studies of the effects of sodium bicarbonate ingestion by humans on anaerobic performance found that overall performance was enhanced although the effect size

Table 66.2 Effect of sodium bicarbonate on exercise capacity of horses

Dosage (mg/kg body-weight)	Number of horses	Breed	Type of exercise	Exercise intensity	Effect	Effect relative to control treatment	Comments	Reference
1000	6	TB	Treadmill	Incremental to 110% $\dot{V}O_{2max}$	P	+42 s (+32%) time to exhaustion	$P < 0.02$. Control was sodium chloride	229
1000	6	TB	Treadmill	Incremental to 110% $\dot{V}O_{2max}$	N	–40 s (–22%) time to exhaustion	$P = 0.05$. Control treatment was water	229
600	5	STB	Treadmill	Incremental exercise	N	–12 s (–5%) run time to fatigue	$P > 0.05$. Control was water	233
300	6	QH	Treadmill, 4.5 m/s, 11° incline	Submaximal	P	+26.7 s (+2.2%) run time to fatigue Control run time was 1191.8 s	No type 1 error rate reported, presumably greater than 0.05. Control was water and corn syrup	223
1000	12	TB	Treadmill	115% $\dot{V}O_{2max}$	N	–10 s (–10%) time to fatigue	$P > 0.05$. Control was no treatment	218
1000	8	STB	Treadmill	113% $\dot{V}O_{2max}$	N	–9 s (–6%) time to fatigue	$P > 0.05$. Control was water	227
600	24	TB	1000 m match race	Maximal	N	+0.1 s (+0.1%) race time	$P > 0.05$. Control was water	224
300	22	STB	1 mile match race	Maximal	P	–1.1 s (–0.8%) race time	$P < 0.1$. Control was powdered dextrose, salt, and 10 mL water	230
400	6	TB	1600 m on track	Maximal	P	–2.7 s (2.4%) time to cover 1600 m	$P < 0.1$. Control was water	226
400	16	TB	Simulated race, 1600 m	Maximal	P	–0.06 s (–0.004%) race time	$P > 0.05$. Control was water	221
1000 (approx)	12	STB	Simulated 1 mile race	Maximal	N	+0.2 s (+0.02%) race time	$P > 0.05$. Control was water	214
600	6	STB	Simulated race, 1000 m	Maximal	NE	0 min/km (0%) mean finishing speed for last 1000 m	$P > 0.05$. Control was no treatment	241

N, negative effect on performance measure; NE, no effect on performance measure; P, positive effect on performance measure; QH, Quarter Horse; STB, Standardbred; TB, Thoroughbred.

ranged from –0.12 to 2.86, with a mean increase in time to exhaustion of 27 ± 20%.[237] Although the effect on time to exhaustion was only weakly related to the degree of induced alkalosis, studies that demonstrated an effect on performance employed larger dosages and were associated with a greater decline in pH during exercise (indicating more strenuous exercise).[237]

Similar to the use of sodium bicarbonate in human beings, studies of the effect of sodium bicarbonate on athletic capacity in horses have produced conflicting results (Table 66.2). The conflicting results are attributable to differing study designs using varying breeds of horses, a wide range of dosages of sodium bicarbonate and differing means of assessing athletic capacity. Studies that use the time to fatigue of horse performing exercise above 100% $\dot{V}O_{2max}$ have an effect range of –22 to +32% (time to fatigue compared to control), with four studies demonstrating a negative effect of sodium bicarbonate on time to fatigue and one demonstrating a prolongation of time to fatigue. Not all these results were statistically significant. In five studies examining the effect of sodium bicarbonate on times in simulated or match races, the effect size varied from –2.4 to +0.1%, with two studies finding longer race times and three detecting shorter times to cover a defined distance. Again, not all of these results were statistically significant.

Adverse effects

Gastrointestinal discomfort is frequently reported in human beings who ingest large quantities of sodium bicarbonate (>0.4 g/kg) or insufficient water. Theoretically, cardiac arrhythmias will develop secondary to the serum electrolyte abnormalities encountered after sodium bicarbonate ingestion, but sodium bicarbonate-induced arrhythmias are not reported in the horse. The concurrent administration of furosemide and sodium bicarbonate to horses induces a profound metabolic alkalosis and severe serum electrolyte abnormalities, and is associated with dehydration, synchronous diaphragmatic flutter, and mild diarrhea.[238] Concurrent administration of sodium bicarbonate and furosemide should be avoided. Mild diarrhea is reported after administration of oral sodium bicarbonate to horses.[219,230] Fatal aspiration pneumonia has been observed in horses after the inadvertent intratracheal administration of sodium bicarbonate solution.

Other alkalinizing agents

Administration of sodium citrate, potassium bicarbonate, ammonium chloride, and tromethamine (TRIS buffer, THAM) may induce alkalosis in horses.[239] However, administration of sufficient quantity of these compounds increases blood pH and bicarbonate concentrations, which are detectable with appropriate testing. There are no reports of the effects of these compounds on athletic capacity. Administration of calcium carbonate does not affect blood pH or bicarbonate concentration of horses.[240]

References

1. Anonymous. Uniform Classification Guidelines for Foreign Substances. Vol. 2003: Association of Racing Commissioners International. www.arci.com
2. Anonymous. International agreement on breeding and racing and appendices. Vol. 2002: International Federation of Horse Racing Authorities, 2002. www.horseracingintfed.org
3. Gross DK, Morley PS, Hinchcliff KW, Wittum TE. Effect of furosemide on performance of Thoroughbreds racing in the United States and Canada. J Am Vet Med Assoc 1999; 215:670–675.
4. Soma LR, Birks EK, Uboh CE, et al. The effects of frusemide on racing times of Standardbred pacers. Eq Vet J 2000; 32:334–340.
5. Soma LR, Uboh CE, Nann L, Gerber AL. Prerace venous blood acid–base values in Standard-bred horses. Eq Vet J 1996; 28:390–396.
6. Sime D, Engen R, Miller-Graber P. Frequency and use of medications in horses racing in Prairie Meadows. Iowa State Univ Vet 1994; 54.
7. Chay S, Woods WE, Rowse K, et al. The pharmacology of furosemide in the horse. V. Pharmacokinetics and blood levels of furosemide after intravenous administration. Drug Met Dis 1983; 11(3):226–231.
8. Tobin T, Roberts BL, Swerczek TW. The pharmacology of furosemide in the horse. III. Dose and time response relationships, effects of repeated administration and performance effects. J Eq Med Surg 1978; 2:216–226.
9. Roberts BL, Blake JW, Tobin T. The pharmacology of furosemide in the horse. II. Its detection, pharmacokinetics, and clearance from the urine. J Eq Med Surgery 1978; 2:185–194.
10. Hinchcliff KW, Mitten LA. Furosemide, bumetanide, and ethacrynic-acid. Vet Clin N Am Eq Pract 1993; 9:511–522.
11. Dyke TM, Hinchcliff KW, Sams RA. Attenuation by phenylbutazone of the renal effects and excretion of frusemide in horses. Eq Vet J 1999; 31:289–295.
12. Garner HE, Hutcheson DP, Coffman JR, et al. Urine electrolyte and diuretic responses to seven dosage levels of lasix. Proc Annu Meeting Am Assoc Equine Pract 1975; 21:87–90.
13. Alexander F. The effect of ethacrynic acid, bumetanide, frusemide, spironolactone and ADH on electrolyte excretion in ponies. J Vet Pharmacol Therap 1982; 5:153–160.
14. Freestone JF, Carlson GP, Harrold DR, Church G. Influence of furosemide treatment on fluid and electrolyte balance in horses. Am J Vet Res 1988; 49(11):1899–1902.
15. Kurosawa M, Ohtake I, Tsuji T, Murakami M. The diruetic effect and fate of furosemide in horses. Jpn J Equine Sci 1991; 2:49–57.
16. Hinchcliff KW, McKeever KH, Muir WW. Pharmacological interaction of furosemide and phenylbutazone in horses. Am J Vet Res 1995; 56:1533–1539.
17. Weiner IM, Mudge GH. Diuretics and other agents employed in the mobilization of edema fluid. In: Gillman AG, Goodman LS, Rall TW, Murad F, eds. The pharmacological basis of therapeutics. New York: Macmillan Publishing; 1985:887–907.
18. Hinchcliff K, McKeever K, Muir WW. Furosemide-induced changes in plasma and blood volume of horses. J Vet Pharmacol Ther 1991; 14:411–417.
19. Muir WW, Kohn CW, Sams R. Effects of furosemide on plasma volume and extracellular fluid volume in horses. Am J Vet Res 1978; 39(10):1688–1691.
20. Houpt KA, Northrup N, Wheatley T, Houpt TR. Thirst and salt appetite in horses treated with furosemide. J Appl Physiol 1991; 71:2380–2386.
21. Rose RJ, Gibson KT, Suann CJ. An evaluation of an oral glucose-glycine-electrolyte solution for the treatment of experimentally induced dehydration in the horse. Vet Rec 1986; 119:522–525.
22. Olsen S, Coyne C, Lowe B, et al. Influence of furosemide on hemodynamic responses during exercise in horses. Am J Vet Res 1992; 53:742–747.
23. Muir WW, Milne DW, Skarda RT. Acute hemodynamic effects of furosemide administered intravenously in the horse. Am J Vet Res 1976; 37(10):1177–1180.
24. Hinchcliff KW, McKeever KH. Fluid administration attenuates the hemodynamic effect of frusemide in running horses. Eq Vet J 1998; 30:246–250.
25. Gleed RD, Ducharme NG, Hackett RP, et al. Effects of frusemide on pulmonary capillary pressure in horses exercising on a treadmill. Eq Vet J 1999; Suppl. 30:102–106.
26. Goetz TE, Manohar M. Pressures in the right side of the heart and esophagus (pleura) in ponies during exercise before and after furosemide administration. Am J Vet Res 1986; 47(2):270–276.
27. Manohar M. Effect of furosemide administration on systemic circulation of ponies during severe exercise. Am J Vet Res 1986; 47(6):1387–1394.
28. Manohar M, Hutchens E, Coney E. Furosemide attenuates the exercise-induced rise in pulmonary capillary blood pressure in horses. Eq Vet J 1994; 26:51–54.
29. Manohar M, Goetz TE, Sullivan E, Griffin R. Pulmonary vascular pressures of strenuously exercising thoroughbreds after administration of varying doses of frusemide. Eq Vet J 1997; 29:298–304.
30. Dikshit K, Vyden JK, Forrester JS, et al. Renal and extrarenal hemodynamic effects of furosemide in congestive heart failure after acute myocardial infarction. N Engl J Med 1973; 288:1087–1090.
31. Johnston GD, Hiatt WR, Neis AS, et al. Factors modifying the early nondiuretic vascular effects of furosemide in man. The possible role of renal prostaglandins. Circ Res 1983; 53:630–635.
32. Bourland WA, Day DK, Williamson HE. The role of the kidney in the early nondiuretic action of furosemide to reduce elevated left atrial pressure in the hypervolemic dog. J Pharmacol Exp Ther 1977; 202:221–229.
33. Greenberg S, McGowan C, Xie J, Summer WR. Selective pulmonary and venous smooth muscle relaxation by furosemide: a comparison with morphine. J Pharmacol Exp Ther 1994; 270:1077–1085.

34. Rivas L, Hinchcliff K. Effect of furosemide and subsequent intravenous fluid administration on right atrial pressure of splenectomized horses. Am J Vet Res 1997; 58:632–635.
35. Hubbell JAE, Hinchcliff KW, Grosenbaugh DA, et al. Ureteral ligation prevents the haemodynamic effect of frusemide in pentobarbitol anaesthetised horses. Eq Vet J 2002; 34:580–586.
36. Hinchcliff K, McKeever K, Muir W, Sams R. Furosemide reduces accumulated oxygen deficit in horses during brief intense exertion. J Appl Physiol 1996; 81:1550–1554.
37. Harkins JD, Hackett RP, Ducharme NG. Effect of furosemide on physiologic variables in exercising horses. Am J Vet Res 1993; 54:2104–2109.
38. Broadstone RV, Robinson NE, Gray PR, et al. Effects of furosemide on ponies with recurrent airway obstruction. Pul Pharmacol 1991; 4:203–208.
39. Rubie S, Robinson NE, Stoll M, et al. Flunixin meglumine blocks frusemide-induced bronchodilation in horses with chronic obstructive pulmonary disease. Eq Vet J 1993; 25:138–142.
40. Bayly WM, Slocombe RF, Schott HC, et al. Effects of inhalation of albuterol sulphate, ipratropium bromide and frusemide on breathing mechanics and gas exchange in healthy exercising horses. Eq Vet J 2001; 33:302–310.
41. Kirchner KA. Indomethacin antagonizes furosemide's intratubular effects during loop segment microperfusion. J Pharmacol Exp Ther 1987; 243(3):881–886.
42. Chennavasin P, Seiwell R, Brater DC. Pharmacokinetic-dynamic analysis of the indomethacin–furosemide interaction in man. J Pharmacol Exp Ther 1980; 215:77–81.
43. Olsen S, Coyne C, Lowe B, et al. Influence of cycloxygenase inhibitors on furosemide-induced hemodynamic effects during exercise in horses. Am J Vet Res 1992; 53:1562–1567.
44. Manohar M. Pulmonary vascular pressures of strenuously exercising Thoroughbreds after administration of flunixin meglumine and furosemide. Am J Vet Res 1994; 55:1308–1312.
45. Hinchcliff KW, McKeever KH, Muir WW, Sams RA. Effects of furosemide on athletic performance and exercise-induced pulmonary hemorrhage in horses. J Am Vet Med Assoc 1999; 215:630–635.
46. Sweeney CR, Soma LR, Maxson AD, et al. Effects of furosemide on the racing times of Thoroughbreds. Am J Vet Res 1990; 51:772–778.
47. Birks EK, Shuler KM, Soma LR, et al. EIPH: postrace endoscopic evaluation of Standardbreds and Thoroughbreds. Eq Vet J 2002; Suppl 34:375–378.
48. Kindig CA, McDonough P, Fenton G, et al. Efficacy of nasal strip and furosemide in mitigating EIPH in Thoroughbred horses. J Appl Physiol 2001; 91:1396–1400.
49. Geor RJ, Ommundson L, Fenton G, Pagan JD. Effects of an external nasal strip and frusemide on pulmonary haemorrhage in Thoroughbreds following high-intensity exercise. Eq Vet J 2001; 33:577–584.
50. Pascoe JR, McCabe AE, Franti CE, Arthur RM. Efficacy of furosemide in the treatment of exercise-induced pulmonary hemorrhage in thoroughbred racehorses. Am J Vet Res 1985; 46(9):2000–2003.
51. Manohar M, Hutchens E, Coney E. Pulmonary hemodynamics in the exercising horse and their relationship to exercise-induced pulmonary hemorrhage. Br Vet J 1993; 149:419–428.
52. Milne DW, Gabel AA, Muir WW, et al. Effects of furosemide on cardiovascular function and performance when given prior to simulated races: A double-blind study. Am J Vet Res 1980; 41(8):1183–1189.
53. Soma LR, Laster L, Oppenlander F, Barr-Alderfer V. Effects of furosemide on the racing times of horses with exercise-induced pulmonary hemorrhage. Am J Vet Res 1985; 46(4):763–768.
54. Hinchcliff K, McKeever K, Muir WW, Sams R. Effect of furosemide and weight carriage on energetic responses of horses to incremental exertion. Am J Vet Res 1993; 54:1500–1504.
55. Coleman RJ, St. Lawrence AC, Lawrence LM, Roberts AM. Effect of frusemide on bodyweight loss and recovery in racing Standardbreds. Eq Vet J 2002; Suppl. 34:165–167.
56. Bayly WM, Slocombe RF, Schott HC, Hodgson DR. Effect of intravenous administration of furosemide on mass-specific maximal oxygen consumption and breathing mechanics in exercising horses. Am J Vet Res 1999; 60:1415–1422.
57. Hinchcliff K, McKeever K. Frusemide and weight carriage alter the acid:base responses of horses to incremental and to brief intense exertion. Eq Vet J 1999; 30:375–379.
58. Todi F, Fenwick J. Excretion of three diuretics, furosemide, trichlormethiazide and ethacrynic acid in the horse. 5th International Conference on Control of Drugs in Racehorses. Toronto, 1983. Association of Official Racing Chemists.
59. Frey HH. Diuretic effect of high-ceiling diuretics in ponies. J Vet Pharmacol Ther 1983; 6:157–158.
60. Delbeke FT, Debackere M, Desmet N, Stevens M. Pharmacokinetics and diuretic effect of bumetanide following intravenous and intramuscular administration to horses. J Vet Pharmacol Therap 1986; 9:310–317.
61. Toutain PL, Autefage A, Legrand C, Alvinerie M. Plasma concentrations and therapeutic efficacy of phenylbutazone and flunixine meglumine in the horse: pharmacokinetic/pharmacodynamic modelling. J Vet Pharmacol Ther 1994; 17:459–469.
62. Soma LR, Gallis DE, Davis WL, et al. Phenylbutazone kinetics and metabolite concentrations in the horse after 5 days of administration. Am J Vet Res 1983; 44:2104–2109.
63. Higgins AJ, Lees P, Taylor JB. Influence of phenylbutazone on eicosanoid levels in equine acute inflammatory fluid. Vet Rec 1984; 113:622–623.
64. Moses VS, Bertone AL. Nonsteroidal anti-inflammatory drugs. Vet Clin N Am: Eq Pract 2002; 18:21–37.
65. Demers LM, Harrison TS, Halbert DR, Santen RJ. Effect of prolonged exercise on plasma prostaglandin levels. Prostaglandin Med 1981; 6:413–418.
66. Ritter JM, Blair IA, Barrow SE, Dollery CT. Release of prostacyclin in vivo and its role in man. Lancet 1983; 1:317–319.
67. Wennmalm A, Fitzgerald GA. Excretion of prostacyclin and thromboxane A2 metabolites during leg exercise in humans. Am J Physiol 1988; 255:H15–H18.
68. Nowak J, Wennmalm A. Effect of exercise on human arterial and regional venous plasma concentrations of prostaglandin E. Prostaglandins Med 1978; 1:489–497.
69. Colahan P, Bailey J, Chou C, et al. Effect of flunixin meglumine on selected physiologic and performance parameters of athletically conditioned thoroughbred horses subjected to an incremental exercise stress test. Vet Therapeutics 2002; 3:37–48.
70. Birks EK, Giri S, Li C, Jones JM. Effects of exercise on plasma concentrations of prostaglandins and thromboxane B2. In: Persson SDG, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications, 1991:374–379.
71. Mitten L, Hinchcliff K, Pate J, et al. Effect of exercise intensity on plasma prostaglandin concentrations in horses. Am J Vet Res 1995; 56:122–126.
72. Hinchcliff K, McKeever K, Muir WW. Effect of phenylbutazone on the haemodynamic, acid–base and

eicosanoid responses of horses to sustained submaximal exertion. Res Vet Sci 1994; 56:352–362.
73. Stebbins CL, Longhurst JC. Bradykinin-induced chemoreflexes from skeletal muscle: implications for the exercise reflex. J Appl Physiol 1985; 59(1):56–63.
74. Morganroth ML, Young EW, Sparks HV. Prostaglandin and histaminergic mediation of prolonged vasodilation after exercise. Am J Physiol 1977; 233(1):H27–H33.
75. Zambraski EJ, Dodelson D, Guidotti SM, Harnett CA. Renal prostaglandin E2 and F2 alpha synthesis during exercise: effects of indomethacin and sulindac. Med Sci Sports Exerc 1986; 18(6):678–684.
76. Mitten LA, Hinchcliff KW, Pate JL. Phenylbutazone increases right atrial pressure and heart rate of running horses. J Appl Physiol 1996; 81:312–317.
77. Walch L, Labat C, Gascard JP, et al. Prostanoid receptors involved in the relaxation of human pulmonary vessels. Br J Pharmacol 1999; 126:859–866.
78. Koller A, Dornyei G, Kaley G. Flow-induced responses in skeletal muscle venules: modulation by nitric oxide and prostaglandins. Am J Physiol 1998; 275:H831–H836.
79. Cowley AJ, Stainer K, Rowley JM, Wilcox RG. Effect of aspirin and indomethacin on exercise-induced changes in blood pressure and limb blood flow in normal volunteers. Cardiovasc Res 1985; 19:177–180.
80. Kallings P, Persson SDG. Effects of theophylline and non-steroidal anti-inflammatory drugs on pulse and blood lactate responses to exercise in the horse – a preliminary report. In: Snow DH, Persson SDG, Rose RJ, eds. Equine exercise physiology. Cambridge; MA: Burlington Press, 1983:538–542.
81. Kallings P, Persson SDG, Essen-Gustavsson B. Effects of flunixin on cardiorespiratory, plasma lactate and stride length responses to treadmill exercise in standardbred trotters. Department of Large Animal Clinical Sciences. Uppsala: Swedish University of Agricultural Sciences, 1998:1–14.
82. Kallings P, Appelgren L, Wiese B, et al. Effects of phenylbutazone on exercising horses: studies of cardiorespiratory and metabolic parameters, plasma concentrations, and inhibition of prostaglandin synthesis. 6th International Conference of Racing Analysts and Chemists. Hong Kong, 1985. London: Macmillan; 1985.
83. Manohar M, Goetz TE, Griffin R, Sullivan E. Pulmonary vascular pressures of strenuously exercising thoroughbreds after administration of phenylbutazone. Am J Vet Res 1996; 57:1354–1358.
84. Hinchcliff KW, McKeever KH, Muir WW. Effect of phenylbutazone on the hemodynamic, acid–base and eicosanoid responses of horses to sustained submaximal exertion. Res Vet Sci 1994; 56:352–362.
85. Johansson IM, Kallings P, Hammarlund-Udenaes M. Studies of meclofenamic acid and two metabolites in horses – pharmacokinetics and effects on exercise tolerance. J Vet Pharmacol Ther 1991; 14:235–242.
86. Kallings P, Johnston C, Drevemo S. Effects of flunixin on movement and performance of standardbred trotters on the track. Eq Vet J 1999; Suppl. 30:270–273.
87. Drevemo S, Johnston C, Kallings P, Roepstorff L. Effects of phenylbutazone at low plasma concentrations on the locomotion pattern of lame horses. Proceedings of the 10th International Conference of Racing Analysts and Chemists. Stockholm, 1995. Newmarket, UK: R&W Publications; 1995.
88. Snow DH. Anabolic steroids. Vet Clin N Am Eq Pract 1993; 9:563–576.
89. Maher JM, Squires EL, Voss JL, Shideler RK. Effect of anabolic steroids on reproductive function of young mares. J Am Vet Med Assoc 1983; 183:519–524.
90. Snow DH, Munro CD, Nimmo MA. Effects of nandrolone phenylpropionate in the horse: (1) resting animal. Eq Vet J 1982; 14:219–223.
91. Heinlein CA, Chang C. Androgen receptor (AR) coregulators: an overview. Endocrine Rev 2002; 23:175–200.
92. Myhal M, Lamb DR. Hormones as performance-enhancing drugs. In: Warren MP, Constantini NW, eds. Contemporary endocrinology: sports endocrinology. Totowa, NJ: Humana Press, 2002:429–471.
93. Skelton KV, McMeniman NP, Dowsett KF. The effects of anabolic steroids on nitrogen metabolism in young horses. Proc 11th Equine Nutr Physiol Symp 1989: 114–115.
94. Snow DH, Munro CD, Nimmo MA. Effects of nandrolone phenylpropionate in the horse: (2) general effects in animals undergoing training. Eq Vet J 1982; 14:224–228.
95. Thornton JR, Dowsett KF, Mann R, Bodero DAV. Infuence of anabolic steroids on the response to training of 2 year old horses. In: Persson GB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: Granta Editions, 1991:503–508.
96. Hyyppa S, Karvonen U, Rasanen LA, et al. Androgen receptors and skeletal muscle composition in trotters treated with nandrolone laurate. J Vet Med Assoc 1997; 44:481–491.
97. Hyyppa S, Rasanen LA, Persson GB, Poso AR. Exercise performance indices in normal and anabolic steroid treated trotters. Eq Vet J 1995; Suppl. 18:443–447.
98. Hyyppa S. Effects of nandrolone treatment on recovery of horses after strenuous physical exercise. J Vet Med Assoc 2001; 48:343–352.
99. Bhasin S, Storer TW, Berman N, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. N Engl J Med 1996; 335:1–7.
100. Alway SE. Characteristics of elbow flexors in women body builders using androgenic-anabolic steroids. J Strength Cond Res 1994; 8:161–169.
101. Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. Clin Chem 1997; 43:1262–1279.
102. Squires EL, Voss JL, Maher JM. Fertility of young mares after long term anabolic steroid treatment. J Am Vet Med Assoc 1986; 186:583–587.
103. Squires EL, Todter GE, Berndtson WE. Effects of anabolic steroids on reproductive function in young stallions. J Anim Sci 1982; 54:576–582.
104. Squires EL, Berndtson WE, Hoyer JH. Restoration of reproductive capacity of stallions after suppression with exogenous testosterone. J Anim Sci 1981; 53:1351–1359.
105. Dowling PM, Williams MA, Clark TP. Adrenal insufficiency associated with long-term anabolic-steroid administration in a horse. J Am Vet Med Assoc 1993; 203:1166–1169.
106. Beech J. Evaluation of thyroid, adrenal, and pituitary function. Vet Clin N Am: Eq Pract 1987; 3:649–660.
107. Ishak KG, Zimmerman HJ. Hepatotoxic effects of the anabolic/androgenic steroids. Semin Liver Dis 1987; 7:230–236.
108. Erslev A. Erythropoietin. New Engl J Med 1991; 324:1339–1344.
109. McKeever K, Kirby K, Hinchcliff KW. Effects of erythropoietin on plasma and red cell volume, VO2max and hemodynamics in exercising horses. Med Sci Sports Exer 1993; 25:S23.

110. Jaussaud P, Audran M, Gareau R, Souillard A, Chavanet I. Kinetics and haematological effects of erythropoietin in horses. Vet Res 1994; 25:568–573.
111. Souillard A, Audran M, Bressolle F, et al. Pharmacokinetics and hematological parameters of recombinant-human-erythropoietin after subcutaneous administrations in horses. Biopharm Drug Dispos 1996; 17:805–815.
112. McKeever K, Agans J, Geiser S. Effect of recombinant human erythropoietin administration on red cell volume, aerobic capacity, and performance in standardbred horses. Raleigh, NC: 12th Equine Nutrition and Physiology Society 1999.
113. Kearns CF, Lenhart JA, McKeever KH. Cross-reactivity between human erythropoietin antibody and horse erythropoietin. Electrophoresis 2000; 21:1454–1457.
114. Piercy RJ, Swardson CJ, Hinchcliff KW. Erythroid hypoplasia and anemia following administration of recombinant-human-erythropoietin to 2 horses. J Am Vet Med Assoc 1998; 212:244.
115. Woods PR, Campbell G, Cowell RL. Nonregenerative anemia associated with administration of recombinant-human-erythropoietin to a Thoroughbred racehorse. Eq Vet J 1997; 29:326–328.
116. McKeever K. Erythropoietin: a new form of blood doping of horses. 11th International Conference of Racing Analysts and Veterinarians, 1996. Newmarket, UK: R&W Press; 1996.
117. Strobil J, Thomas M. Human growth hormone. J Am Soc Pharm Exp Ther 1994; 46:1–34.
118. Yarasheski K, Zachwieja J, Bier D. Short-term growth hormone treatment does not increase muscle protein synthesis in experienced weight lifters. J Appl Physiol 1993; 74:3073–3076.
119. Deyssig R, Frisch H, Blum W, Waldhor T. Effect of growth hormone treatment on hormonal parameters, body composition and strength in athletes. Acta Endocrinol 1993; 128:313–318.
120. Dart AJ, Strong M, Rose R, Hodgson DR. Effects of two large doses of equine recombinant growth hormone on clinical, haematological and serum biochemical variables in adult horses. Aust Vet J 1998; 76:339–342.
121. Guirnalda P, Malinowski K, Roegner V, Horohov D. Effects of age and recombinant equine somatotrophin (eST) administration on immune function in female horses. J Anim Sci 2001; 79:2651–2658.
122. Thomson K, Potter GD, Terrell K, et al. Bone density in the juvenile racehorse treated with exogenous somatotropin (eST). J Eq Vet Sci 2000; 20:511–515.
123. Capshaw E, Thompson DL, Kulinski K, et al. Daily treatment of horses with equine somatotropin from 4 to 16 months of age. J Anim Sci 2001; 79:3137–3147.
124. McKeever K, Malinowski K, Christensen RA, Hafs HD. Chronic recombinant equine somatotropin (eST) administration does not affect aerobic capacity or exercise performance in geriatric mares. Vet J 1998; 155:19–25.
125. Gerard MP, Hodgson DR, Lambeth R, et al. Effects of somatotropin and training on indices of exercise capacity in Standardbreds. Eq Vet J 2002; Suppl. 34:496–501.
126. Popot MA, Bobin S, Bonnaire Y, et al. IGF-1 plasma concentrations in non-treated horses and horses administered with methionyl equine somatotropin. Res Vet Sci 2001; 71:167–173.
127. de Kock S, Rodgers J, Swanepoel B. Growth hormone abuse in the horse: preliminary assessment of a mass spectrometric procedure for IGF-1 identification and quantitation. Rapid Comm Mass Spec 2001; 15:1191–1197.
128. Champion ZJ, Breier BH, Ewen W, et al. Blood plasma concentrations of insulin-like growth factor-I in resting standardbred horses. Vet J 2002; 163:45–50.
129. Jimenez M, Hinchcliff KW, Farris JW. Catecholamine and cortisol responses of horses to incremental exertion. Vet Res Commun 1998; 22:107–118.
130. Snow DH. Metabolic and physiological effects of adrenoceptor agonists and antagonists in the horse. Res Vet Sci 1979; 27:372–378.
131. Anderson MG, Aitken MM. Biochemical and physiological effects of catecholamine administration in the horse. Res Vet Sci 1977; 22:357–361.
132. Torneke MK, Ingvas Larsson JC, Johansson JM, Appelgren LE. Pharmacokinetics and pharmacodynamics of terbutaline in healthy horses. Am J Vet Res 2000; 61:761–765.
133. Erichsen DF, Aviad AD, Schultz RH, Kennedy TJ. Clinical efficacy and safety of clenbuterol HCl when administered to effect in horses with chronic obstructive pulmonary disease (COPD). Eq Vet J 1994; 26:331–336.
134. Harkins JD, Woods WE, Lehner AF, et al. Clenbuterol in the horse: urinary concentrations determined by ELISA and GC/MS after clinical doses. J Vet Pharmacol Ther 2001; 24:7–14.
135. Kallings P, Ingvast LC, Persson GB, et al. Clebuterol plasma concentrations after repeated oral administration and its effects on cardiorespiratory and blood lactate responses to exercise in healthy Standardbred horses. J Vet Pharmacol Ther 1991; 14:243–249.
136. Shapland JE, Garner HE, Hatfield DG. Cardiopulmonary effects of clenbuterol in the horse. J Vet Pharmacol Ther 1981; 4:43–50.
137. Torneke K, Ingvast LC, Appelgren L. Relaxation of equine tracheal smooth muscle in vitro by different adrenoreceptor drugs. J Vet Pharmacol Ther 1997; 20:216–219.
138. Torneke K, Ingvast LC, Appelgren LE. A comparison between clenbuterol, salbutamol and terbutaline in relation to receptor binding and in vitro relaxation of equine tracheal muscle. J Vet Pharmacol Ther 1998; 21:388–392.
139. Rose RJ, Allen JR, Brock KA, et al. Effects of clenbuterol hydrochloride on certain respiratory and cardiovascular parameters in horses performing treadmill exercise. Res Vet Sci 1983; 35:301–305.
140. Rose RJ, Evans DL. Cardiorespiratory effects of clenbuterol in fit thoroughbred horses during a maximal exercise test. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications, 1987:117–131.
141. Slocombe RF, Covelli G, Bayly WM. Respiratory mechanics of horses during stepwise treadmill exercise tests, and the effect of clenbuterol pretreatment on them. Aust Vet J 1992; 69:221–225.
142. Manohar M, Goetz TE, Rothenbaum P, Humphrey S. Clenbuterol administration does not attenuate the exercise-induced pulmonary arterial, capillary or venous hypertension in strenuously exercising Thoroughbred horses. Eq Vet J 2000; 32:546–550.
143. Manohar M, Goetz TE, Rothenbaum P, Humphrey S. Clenbuterol administration does not enhance the efficacy of furosemide in attenuating the exercise-induced pulmonary capillary hypertension in Thoroughbred horses. J Vet Pharmacol Ther 2000; 23:389–395.
144. Sleeper MM, Kearns CF, McKeever KH. Chronic clenbuterol administration negatively alters cardiac function. Med Sci Sports Exer 2002; 34:643–650.
145. Duncan ND, Williams DA, Lynch GS. Deleterious effects of chronic clenbuterol treatment on endurance and sprint exercise performance in rats. Clin Sci 2000; 98:339–347.

146. Burniston JG, Ng Y, Clark WA, et al. Myotoxic effects of clenbuterol in the rat heart and soleus muscle. J Appl Physiol 2002; 93:1824–1832.
147. Kearns CF, McKeever KH, Malinowski K, et al. Chronic administration of therapeutic levels of clenbuterol acts as a repartitioning agent. J Appl Physiol 2001; 91:2064–2070.
148. Prather ID, Brown DE, North P, Wilson JR. Clebuterol: a substitute for anabolic steroids? Med Sci Sports Exer 1995; 27:1118–1121.
149. Spann C, Winter ME. Effect of clenbuterol on athletic performance. Annals Pharmacother 1995; 29:75–77.
150. Derksen FJ, Olszewski MA, Robinson NE, et al. Aerosolized albuterol sulfate used as a bronchodilator in horses with recurrent airway obstruction. Am J Vet Res 1999; 60:689–693.
151. Dirikolu L, Mollett BA, Troppmann A, et al. Apparent ELISA detection times for albuterol after administration with the Torprex equine inhaler device. Vet Therapeutics 2002; 3:297–307.
152. Bayly WM, Slocombe RF, Schott HC, et al. Effects of inhalation of albuterol sulphate, ipratropium bromide, and frusemide on breathing mechanics and gas exchange in healthy exercising horses. Eq Vet J 2001; 33:302–310.
153. Mazan MR, Hoffman AM. Effects of aerosolized albuterol on physiologic responses to exercise in Standardbreds. Am J Vet Res 2001; 62:1812–1817.
154. Bailey J, Colahan P, Kubilis P, Pablo L. Effect of inhaled B2 adrenoceptor agonist, albuterol sulphate, on performance of horses. Eq Vet J 1999; Suppl. 30:575–580.
155. Weiner N. Norepinephrine, epinephrine, and the sympathomimetic drugs. In: Gilman AG, Goodman LS, Rall TW, Murad F, eds. The pharmacological basis of therapeutics. New York: Macmillan Publishing; 1985:145–180.
156. Conlee RK. Amphetamine, caffeine, and cocaine. In: Lamb DR, Williams MH, eds. Perspectives in exercise science and sports medicine: ergogenics: enhancement of athletic performance. Vol 4. Ann Arbor: Brown-Benchmark, 1991:285–310.
157. Chandler JV, Blair SN. The effect of amphetamines on selected physiological components related to athletic success. Med Sci Sports Exerc 1980; 12(1):65–69.
158. Stewart GA. Drugs, performance and responses to exercise in the racehorse. 2. Observations on amphetamine, promazine, and thiamine. Aust Vet J 1972; 48:544–547.
159. Smetzer DL, Senta T, Hensel JD. Cardiovascular effects of amphetamine in the horse. Can J Comp Med 1972; 36:185–194.
160. Gabel AA, Milne DW, Ray RS, et al. A double-blind study of the effects of amphetamine and methylphenidate on physiological parameters in standardbred horses performing submaximal exercise tests. In: Rose RJ, ed. Equine exercise physiology. Cambridge, UK: Granta Editions, 1983:521–530.
161. Gabel AA, Milne DW, Ray RS, et al. A study of the effects of methylprednisolone, promazine, amphetamine, and furosemide on the physiological parameters in standardbred horses performing a submaximal exercise test. In: Snow DH, Persson SDG, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions, 1983:531–537.
162. Lombardo JA. Stimulants. In: Strauss RH, ed. Drugs and performance in sports. Philadelphia: WB Saunders; 1987:69–86.
163. Sanford J, Aitken MM. Effects of some drugs on the physiological changes during exercise in the horse. Eq Vet J 1975; 7(4):198–202.
164. Aitken MM, Sanford J, Mackenzie G. Factors influencing deceleration of the heart and respiratory rates after exercise in the horse. Eq Vet J 1973; 5(1):8–14.
165. Harkins JD, Mundy GD, Stanley S, et al. Determination of highest no effect dose (HNED) for local anaesthetic responses to procaine, cocaine, bupivacaine and benzocaine. Eq Vet J 1996; 28:30–37.
166. Ritchie JM, Greene NM. Local anesthetics. In: Gilman AG, Rall TW, Nies AS, Taylor P, eds. The pharmacological basis of therapeutics. New York: McGraw Hill, 1990:311–313.
167. McKeever KH, Hinchcliff KW, Gerken DF, Sams RA. Effects of cocaine on incremental treadmill exercise in horses. J Appl Physiol 1993; 75:2727–2733.
168. Spielvogel H, Caceres E, Koubi H, et al. Effects of coca chewing on metabolic and hormonal changes during graded incremental exercise to maximum. J Appl Physiol 1996; 80:643–649.
169. Queiroz-Neto A, Zamur G, Lacerda-Neto JC, Tobin T. Determination of the highest no-effect dose (HNED) and of the elimination pattern for cocaine in horses. J Appl Toxicol 2002; 22:117–121.
170. Anderson RL, Wilmore JH, Joyner MJ, et al. Effects of cardioselective and nonselective beta-adrenergic blockade on the performance of highly trained runners. Am J Cardiol 1985; 55:149d–154d.
171. Cain SM. Exercise O_2 debts of dogs at ground level and at altitude with and without β-block. J Appl Physiol 1971; 30(6):838–843.
172. Kaiser P. Running performance as a function of the dose–response relationship to β-adrenoceptor blockade. Int J Sports Med 1982; 3:29–32.
173. Snow DH, Summers RJ, Guy PS. The actions of the β-adrenoreceptor blocking agents propranolol and metoprolol in the maximally exercised horse. Res Vet Sci 1979; 27:22–29.
174. Plummer C, Knight PK, Ray SP, Rose RJ. Cardiorespiratory and metabolic effects of propranolol during maximal exercise. In: Persson GB, Lindholm A, Jeffcott LB, eds. Equine exercise physiology 3. Davis, CA: ICEEP Publications, 1991:465–474.
175. Sexton WL, Erickson HH. Effects of propranolol on cardiopulmonary function in the pony during submaximal exercise. Eq Vet J 1986; 18(6):485–489.
176. Geor RJ, Hinchcliff KW, Sams RA. Beta-adrenergic blockade augments glucose utilization in horses during graded exercise. J Appl Physiol 2000; 89:1086–1098.
177. Bijman J, Quinton P. Predominantly β-adrenergic control of equine sweating. Am J Physiol 1984; 246:R349–R353.
178. Sexton WL, Erickson HH. Effects of propranolol on cardiopulmonary function in the pony during submaximal exercise. Eq Vet J 1986; 18:485–489.
179. Epstein SE, Robinson BF, Kahler RL, Braunwald E. Effects of beta-adrenergic blockade on the cardiac response to maximal and sub-maximal exercise in man. J Clin Invest 1965; 44(11):1745–1753.
180. Kaiser P. Physical performance and muscle metabolism during β-adrenergic blockade in man. Acta Physiol Scand 1984; 536:1–53.
181. Dyke TM. Sedative, tranquillizers, and stimulants. Vet Clin N Am: Eq Pract 1993; 9:621–634.
182. Ballard S, Shults T, Kownacki AA, et al. The pharmacokinetics, pharmacological responses and behavioral effects of acepromazine in the horse. J Vet Pharmacol Ther 1982; 5:21–31.
183. Parry BW, Anderson GA, Gay CC. Hypotension in the horse induced by acepromazine maleate. Aust Vet J 1982; 59:148–152.
184. Muir WW, Skarda RT, Sheehan W. Hemodynamic and respiratory effects of xylazine–acetylpromazine drug combination in horses. Am J Vet Res 1979; 40:1518–1522.

185. Booth NH. Drugs acting on the central nervous system. In: Booth NH, McDonald LE, eds. Veterinary pharmacology and therapeutics. Ames, IA: Iowa State University; 1988:153–406.
186. Keepers GA, Casey DE. Clinical management of acute neuroleptic-induced extrapyramidal syndromes. Curr Psychiatr Ther 1986; 23:139–157.
187. Brewer BD, Hines MT, Stewart JT, Langlois JF. Fluphenazine induced Parkinson-like syndrome in a horse. Eq Vet J 1990; 22:136–137.
188. Kauffman VG, Soma L, Divers TJ, Perkons SZ. Extrapyramidal side effects caused by fluphenazine decanoate in a horse. J Am Vet Med Assoc 1989; 195:1128–1130.
189. Marroum PJ, Webb AI, Aeschbacher G, Curry AH. Pharmacokinetics and pharmacodynamics of acepromazine in horses. Am J Vet Res 1994; 55:1428–1433.
190. Chou C, Chen CL, Atwood AC, et al. Development and use of an enzyme-linked immunosorbent assay to monitor serum and urine acepromazine concentrations in Thoroughbreds, and possible changes associated with exercise. Am J Vet Res 1998; 59:593–597.
191. Freestone JF, Wolfsheimer KJ, Kamerling SG, et al. Exercise induced hormonal and metabolic changes in Thoroughbred horses: effects of conditioning and acepromazine. Eq Vet J 1991; 23:219–223.
192. Fujii S, Yoshida S, Kusanagi C, et al. Pharmacological studies on doping drugs for race horses. IV. Chlorpromazine and phenobarbitol. Jpn J Vet Sci 1975; 37:133–139.
193. Daunt DA, Maze M. alpha-2 adrenergic agonist receptors, sites and mechanism of action. In: Short CE, Poznak AV, eds. Animal pain. New York: Churchill Livingstone, 1992:165–175.
194. Wagner A, Muir W, Hinchcliff K. Cardiovascular effects of xylazine and detomidine in horses. Am J Vet Res 1991; 52:651–657.
195. Moore RM, Trim CM. Effect of xylazine on cerebrospinal fluid pressure in conscious horses. Am J Vet Res 1992; 53:1558–1563.
196. Thurmon JC, Neff-Davis C, Davis LE. Xyalzine hydrochloride-induced hyperglycemia and hyperinsulinemia in Thoroughbred horses. J Vet Pharmacol Ther 1984; 5:214–246.
197. Thurmon JC, Steffey EP, Zinkl JG. Xylazine causes transient dose-related hyperglycemia and increased urine volumes in mares. Am J Vet Res 1984; 45:224–230.
198. Shults T, Combie J, Dougherty J, Tobin T. Variable-interval responding in the horse: a sensitive method of quantitating effects of centrally acting drugs. Am J Vet Res 1982; 43:1143–1146.
199. Chapman CB, Courage P, Huntington PJ. Detection of reserpine in horses by high-performance liquid chromatography. Aust Vet J 1991; 68:296–298.
200. White CC, Woods WE, Tobin T. The pharmacology of reserpine in the horse: II. Biochemical and behavioral effects of reserpine. J Eq Med Surg 1979; 3:446–456.
201. Lloyd KC, Harrison I, Tulleners E. Reserpine toxicosis in a horse. J Am Vet Med Assoc 1985; 186:980–981.
202. Fredholm BB, Persson C. Xanthine derivatives as adenosine receptor antagonists. Eur J Pharmacol 1982; 81:673–676.
203. Rall TW. Drugs used in the treatment of asthma. In: Gilman AG, Rall TW, Nies AS, Taylor P, eds. The pharmacological basis of therapeutics. New York: McGraw-Hill, 1990:618.
204. Casal DC, Leon AS. Failure of caffeine to affect substrate utilization during prolonged running. Med Sci Sports Exerc 1985; 17(1):174–179.
205. Dyke TM, Sams RA. Detection and determination of theobromine and caffeine in urine after administration of chocolate-coated peanuts to horses. J Anal Toxicol 1998; 22:112–116.
206. Greene EW, Woods WE, Tobin T. Pharmacology, pharmacokinetics, and behavioral effects of caffeine in horses. Am J Vet Res 1983; 44(1):57–63.
207. Queiroz-Neto A, Zamur G, Carregaro AB, et al. Effects of caffeine on locomotor activity of horses: determination of the no-effect threshold. J Appl Toxicol 2001; 21:229–234.
208. Fujii S, Yoshida S, Kusanagi C, et al. Pharmacological studies on doping drugs for race horses. II Caffeine. Jpn J Vet Sci 1972; 34:141–145.
209. Errecalde JO, Button C, Baggot JD, Mulders MSG. Pharmacokinetics and bioavailability of theophylline in horses. J Vet Pharmacol Ther 1984; 7:255–263.
210. Errecalde JO, Button C, Mulders MSG. Some dynamic and toxic effects of theophylline in horses. J Vet Pharmacol Ther 1985; 8:320–327.
211. Ingvast LC, Kallings P, Persson SDG, et al. Pharmacokinetics and cardiorespiratory effects of oral theophylline in exercised horses. J Vet Pharmacol Ther 1989; 12:189–199.
212. Elliot CG, Nietrzeba RM, Adams TD, et al. Effect of intravenous aminophylline upon the incremental exercise performance of healthy men. Respiration 1985; 47:260–266.
213. Vine J. Plasma total carbon dioxide concentrations in racehores: challenges to test results. Proc 12th Int Conf Racing Analysts and Veterinarians; 1998:32–36.
214. Frey L, Kline K, Brady A, Cooper S. Effects of warming-up, racing and sodium bicarbonate in Standardbred horses. Eq Vet J 1995; Suppl. 18:310–313.
215. Slocombe RF, Huntington PJ, Lind K, Vine J. Plasma total CO_2 and electrolytes: diurnal changes and effects of adrenaline, doxapram, rebreathing and transport. Eq Vet J 1995; Suppl. 18:331–336.
216. Frey LP, Kline KH, Foreman JH. Effects of prerace exercise, frusemide, sex and ambient temperature on blood sodium, bicarbonate and pH values in Standardbred horses. Eq Vet J 1995; 27:170–173.
217. Lloyd DR, Rose RJ. Effects of sodium bicarbonate on fluid, electrolyte and acid:base balance in racehorses. Br Vet J 1995; 151:523–545.
218. Lloyd DR, Rose RJ. Effects of sodium bicarbonate on acid–base status and exercise capacity. Eq Vet J 1995; Suppl 18:323–325.
219. Rivas LJ, Hinchcliff KW, Kohn CW, et al. Effect of sodium bicarbonate administration on blood constituents of horses. Am J Vet Res 1997; 58:658–663.
220. Greenhaff P, Snow DH, Harris R. Bicarbonate loading in the Thoroughbred horse: dose, method of administration and acid:base changes. Eq Vet J 1990; Suppl. 9:83–85.
221. Harkins JD, Kamerling S. Effects of induced alkalosis on performance in Thoroughbreds during a 1600 m race. Eq Vet J 1992; 24:94–98.
222. Corn CD, Potter GD, Odom TW. Blood buffering in sedentary miniature horses after administration of sodium bicarbonate in single doses of varying amounts. J Eq Vet Sci 1993; 13:589–592.
223. Lawrence LM, Miller PA, Bechtel PJ, et al. The effect of sodium bicarbonate ingestion on blood parameters in exercising horses. In: Gillespie JR, Robinson NE, eds. Equine exercise physiology 2. Davis, CA: ICEEP Publications, 1987:448–455.
224. Greenhaff P, Hanak J, Harris R, et al. Metabolic alkalosis and exercise performance in the Thoroughbred horse. In: Persson SDG, Lindholm A, Jeffcott LB, eds. Equine exercise physiology. Davis, CA: ICEEP Publications, 1991:353–360.
225. Hanson CM, Kline KH, Foreman JH, Frey LP. The effects of sodium bicarbonate administered nasogastrically on plasma

volume, electrolytes and blood gases in resting Quarterhorses. J Eq Vet Sci 1993; 13:593–596.
226. Kelso T, Hodgson DR, Witt E, et al. Bicarbonate administration and muscle metabolism during high intensity exercise. In: Gillespie JR, Robinson N, eds. Equine exercise physiology. Davis, CA: ICEEP Publications, 1987: 448–455.
227. Beard LA, Hinchcliff KW. Effect of NaCl and $NaHCO_3$ on serum ionized calcium and blood gas status during sprinting. Eq Vet J 2002; Suppl 34:519–523.
228. Rivas LJ, Hinchcliff KW, Kohn CW, et al. Effect of sodium bicarbonate administration on renal function of horses. Am J Vet Res 1997; 58:664–671.
229. Lloyd DR, Evans DL, Hodgson DR, et al. Effects of sodium bicarbonate on cardiorespiratory measurements and exercise capacity in thoroughbred horses. Eq Vet J 1993; 25:125–129.
230. Lawrence LM, Kline KH, Miller-Graber P, et al. Effect of sodium bicarbonate on racing standardbreds. J Anim Sci 1990; 68:673–677.
231. Greenhaff P, Harris R, Snow DH, et al. The influence of metabolic alkalosis upon exercise metabolism in the Thoroughbred horse. Eur J Appl Physiol 1991; 63:129–134.
232. Harkins JD, Lawrence LM, Hintz HF. Effect of supplemental sodium bicarbonate on equine performance. Compend Cont Educ Pract Vet 1994; 16:200–208.
233. Schuback K, Essen-Gustavsson B, Persson SDG. Effect of sodium bicarbonate administration on metabolic responses to maximal exercise. Eq Vet J 2002; Suppl. 34:539–544.
234. Heigenhauser G, Jones NL. Bicarbonate loading. In: Lamb DR, Williams M, eds. Perspectives in exercise science and sports medicine. Vol 4. Dubuque, IA: Brown and Benchmark, 1991:183–211.
235. Kirkendall D. Mechanisms of peripheral fatigue. Med Sci Sports Exerc 1990; 22:444–449.
236. Spriet L, Lindinger M, Heigenhauser G, et al. Effects of alkalosis on skeletal muscle metabolism and performance during exercise. Am J Physiol 1986; 251:R833–R837.
237. Matson L, Tran Z. Effects of sodium bicarbonate ingestion on anaerobic performance: a meta-analytic review. Int J Sports Nutr 1993; 2:2–28.
238. Freestone JF, Carlson GP, Harrold DR, Church G. Furosemide and sodium bicarbonate-induced alkalosis in the horse and response to oral KCl and NaCl therapy. Am J Vet Res 1989; 50:1334–1339.
239. Pedrick T, Moon P, Ludders J, et al. The effects of equivalent doses of tromethamine or sodium bicarbonate in healthy horses. Vet Surg 1998; 27:284–291.
240. Frey L, Kline KH, Foreman JH, Lyman J. Technical note: using calcium carbonate as an osmolar control treatment for acid–base studies. J Anim Sci 2001; 79:1858–1862.
241. Kallings P, Persson SDG. Effects of sodium bicarbonate on total carbon dioxide in blood and plasma lactate in the horse. 10th International Conference of Racing Analysts and Veterinarians, Stockholm, Sweden, 1994.

APPENDIX **1a**

Reference ranges for red cell variables in athletic horses

(Compiled by J. Kingston)

	RBC ($\times 10^{12}$/L)	Hb (g/L)	Hct L/L	MCV (fl)	MCH (pg)	MCHC (g/L)
Thoroughbreds						
Steel & Whitlock 1960[1]						
Mixed aged and sex	9.7 ± 1.3	134 ± 19	0.42 ± 0.05	43.8 ± 4.6	13.8 ± 1.8	315 ± 20
Lumsden et al 1979[2]						
Untrained mares	9.0 ± 1.3	148 ± 20	0.41 ± 0.06	45.3 ± 2.1	16.6 ± 0.8	361 ± 12
Revington 1983[3]						
At rest	9.5 ± 0.9	151 ± 12	0.42 ± 0.04	43.6 ± 2.2	15.7 ± 0.8	360 ± 13.4
1–3 h before racing	10.8 ± 1.2	166 ± 13	0.47 ± 0.03	45.2 ± 3.3	15.9 ± 1.1	353 ± 12.1
Snow et al 1983[4]						
Fit race horses	8.85 ± 0.57	159 ± 11.4	0.43 ± 0.03	48.5 ± 3.1	–	–
Allen 1986[5]						
Colt stayers	8.7–11.4	141–180	0.38–0.49	39.6–47.2	14.7–17.5	358–380
Colt sprinters	7.8–10.6	124–170	0.32–0.47	40.1–47.0	14.8–17.4	355–380
Filly stayers	8.2–11.4	135–174	0.36–0.47	39.5–46.6	14.5–17.1	355–379
Filly sprinters	7.8–10.5	126–168	0.34–0.46	39.4–47.0	14.5–17.3	358–378
Jablonska 1991[6]						
Jumpers						
1 month training	–	158 ± 26	0.44 ± 0.06	–	–	–
5 months training	–	131 ± 18	0.31 ± 0.05	–	–	–
7 months training	–	140 ± 20	0.37 ± 0.06	–	–	–
Standardbreds						
Steel & Whitlock 1960[1]						
Mixed age and sex	8.7 ± 1.4	124 ± 19	0.39 ± 0.04	45.5 ± 4.1	14.3 ± 1.3	314 ± 24
Lumsden et al 1979[2]						
In training	8.8 ± 1.0	146 ± 17	0.39 ± 0.04	45 ± 2.4	16.6 ± 0.9	372 ± 12
Rose et al 1983[7] (submaximal treadmill training)						
Untrained	7.8 ± 1.3	122 ± 1.5	0.35 ± 0.04	–	–	–
3 weeks training	7.2 ± 0.4	115 ± 5.1	0.32 ± 0.03	–	–	–
7 weeks training	7.2 ± 0.6	129 ± 8.9	0.33 ± 0.02	–	–	–
Robertson et al 1996[8]						
6 weeks light training	–	132 ± 3.2	0.36 ± 0.01	–	–	–
12 weeks full training	–	142 ± 3.9	0.38 ± 0.01	–	–	–
Tyler-McGowan et al 1999[9]						
7 weeks of training	6.8 ± 0.2	–	–	–	–	–
15 weeks of training	9.8 ± 0.4	–	–	–	–	–
28 weeks of training	9.0 ± 0.1	–	–	–	–	–
32 weeks of training	8.8 ± 0.3	–	–	–	–	–
Overtrained	8.2 ± 0.2	–	–	–	–	–
Quarter Horses						
Kästner et al 1999[10]						
Reining horses	7.71 ± 0.60	129 ± 8.6	0.36 ± 0.02	45.3 ± 1.7	16.7 ± 0.65	370 ± 7.1
Polo horses						
Craig et al 1984[11]						
5 months into season	–	149 ± 3.0	0.39 ± 0.9	–	–	–

	RBC ($\times 10^{12}$/L)	Hb (g/L)	Hct L/L	MCV (fl)	MCH (pg)	MCHC (g/L)
Endurance horses						
Carlson et al 1976[12]						
Competing horses	–	–	0.36 ± 0.03	–	–	–
Rose 1982[13]						
Competing horses	7.94 ± 0.19	132 ± 4.1	0.37 ± 0.01	46.6 ± 0.92	16.1 ± 0.26	356.3 ± 4.5
Grosskopf et al 1983[14]						
Competing horses	–	–	0.40 ± 0.04	–	–	–
Arabian						
Jain 1986[15]						
Mixed sexes	8.41 ± 1.2	138 ± 21	0.39 ± 0.05	46.9 ± 1.9	16.4 ± 0.9	349 ± 10
Rubio et al 1995[16]						
4-year-old males	7.1 ± 1.0	120 ± 7.0	0.43 ± 0.04	57 ± 8.0	17 ± 9.0	280 ± 40
Andalusian						
Rubio et al 1995[16]						
4-year-old males	8.1 ± 1.1	119 ± 8.0	0.42 ± 0.06	52 ± 5.0	14.9 ± 2.0	270 ± 50
Lipizzan						
Cebulj-Kadunc et al 2002[17]						
Stallions	8.16 ± 0.06	135 ± 13	0.43 ± 1.3	52.7 ± 0.3	16.6 ± 0.94	314.8 ± 0.94
Mares	7.53 ± 0.07	123 ± 12	0.43 ± 0.04	52 ± 0.39	16.4 ± 0.16	314.9 ± 0.86
Clydesdale						
Geiser et al 1984[18]						
70 geldings	6.23–9.03	107–14.6	0.28–0.39	44.6	–	38.1
American miniature horse						
Harvey & Hambright et al 1985[19]						
Mixed sex and age	7.1 ± 1.2	126 ± 19	0.34 ± 0.05	48.4 ± 5.7	–	–

Data are ranges or mean ± SD.

References

1. Steel JD, Whitlock LE. Observations of the haematology of Thoroughbred and Standardbred horses in training and racing. Aust Vet J 1960; 36:136–142.
2. Lumsden JH, Rowe R, Mullen K. Hematology and biochemistry reference values for the light horse. Can J Comp Med 1980; 44:32–42.
3. Revington M. Haematology of the racing Thoroughbred in Australia 1: reference values and the effect of excitement. Eq Vet J 1983; 15:141–144.
4. Snow DH, Ricketts SW, Mason DK. Haematological response to racing and training exercise in Thoroughbred horses, with particular reference to the leucocyte response. Eq Vet J 1983; 15:149–154.
5. Allen BV. Comparison of the haemogram between three-year-old Thoroughbred stayers and sprinters. Vet Record 1986; 118:555–556.
6. Jablonska EM, Ziolkowska SM, Gill J, et al. Changes in some haematological and metabolic indices in young horses during the first year of jump-training. Eq Vet J 1991; 23:309–311.
7. Rose RJ, Allen JR, Hodgson DR, et al. Responses to submaximal treadmill exercise and training in the horse: changes in haematology, arterial blood gas and acid base measurements, plasma biochemical values and heart rate. Vet Record 1983; 113:612–618.
8. Robertson ID, Bolton JR, Mercy AR, et al. Haematological and biochemical values in 12 Standardbred horses during training. Aust Eq Vet 1996; 14:72–76.
9. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Eq Vet J Suppl 1999; 30:621–625.
10. Kästner SBR, Feige K, Weishaupt MA, et al. Heart rate and hematological responses of Quarterhorses to a reining competition. J Eq Vet Sci 1999; 19:127–131.
11. Craig L, Hintz HF, Soderholm LV, et al. Changes in blood constituents accompanying exercise in polo horses. Cornell Vet 1985; 75:297–302.
12. Carlson GP, Ocen PO, Harrold D. Clinicopathologic alterations in normal and exhausted endurance horses. Theriogenology 1976; 6:93–104.
13. Rose RJ. Haematological changes associated with endurance exercise. Vet Record 1982; 110:175–177.
14. Grosskopf JFW, Van Rensburg JJ, J. BH. Haematology and blood biochemistry of horses during a 210 km endurance ride. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology. Cambridge: Granta Editions; 1983:416–424.
15. Jain NC. Schalm's Veterinary Hematology. Philadelphia, PA: Lea & Febiger, 1986.
16. Rubio MD, Munoz A, Santisteban R, et al. Comparative hematological study of two breeds of foals (Andalusian and Arab) subjected to exercise of progressive intensity. J Vet Med Sci 1995; 57:311–315.
17. Cebulj-Kadunc N, Bozic M, Kosec M, et al. The influence of age and gender on haematological parameters in Lipizzan horses. J Vet Med A 2002; 49:217–221.
18. Geiser DR, Goble DO, Held JP. Normal hematology and serology of the Clydesdale draft horse. Eq Pract 1984; 6:7–9.
19. Harvey RB, Hambright MB. Normal serum chemistry and hematology values of the American miniature horse. Eq Pract 1985; 7:6–8.

APPENDIX **1b**

Reference ranges for the leukogram of athletic horses

(Compiled by J. Kingston)

	WBC ($\times 10^9$/L)	Neutrophils ($\times 10^9$/L)	Lymphocytes ($\times 10^9$/L)	Monocytes ($\times 10^9$/L)	Eosinophils ($\times 10^9$/L)	Platelets ($\times 10^9$/L)
Thoroughbreds						
Steel & Whitlock 1960[1]						
Mixed aged and sex	6.35–20.0	1.0–15.4	1.0–16.0	0.02–2.8	0–1.4	–
Lumsden et al 1979[2]						
Untrained mares	8.1 ± 1.5	4.1 ± 1.0	3.4 ± 0.8	0.2 ± 0.1	–	239 ± 80
Bayly et al 1983[3]						
Six fit mature horses	–	–	–	–	–	220 ± 40
Revington 1983[4]						
At rest	8.8 ± 1.3	–	–	–	–	–
1–3 h before racing	10.2 ± 1.7	–	–	–	–	–
Snow et al 1983[5]						
Fit race horses	8.5 ± 1.9	5.3 ± 1.6	2.95 ± 0.98	–	–	–
Allen et al 1984[6]						
2-year-old in training	6.8–11.1	3.2–6.5	2.3–5.0	0.21–0.90	0.08–0.46	–
3-year-old in training	6.6–11.0	3.3–6.4	2.1–4.8	0.32–0.97	0.07–0.36	–
4-year-old in training	5.8–10.4	3.2–6.3	1.9–3.7	0.30–0.98	0.03–0.34	–
Allen 1986[7]						
Colt stayers	6.0–10.6	2.7–6.1	2.0–4.2	0.22–0.98	0.05–0.34	–
Colt sprinters	5.8–10.4	2.4–6.3	2.1–3.9	0.20–1.04	0.06–0.20	–
Filly stayers	6.4–10.6	2.9–6.3	2.1–4.6	0.21–1.01	0.04–0.32	–
Filly sprinters	6.7–10.8	2.6–6.7	2.1–4.5	0.24–0.96	0.06–0.22	–
Standardbreds						
Steel & Whitlock 1960[1]						
Mixed age and sex	5.0–17.5	1.6–14.3	0.3–10.8	0.05–1.6	0.02–1.6	–
Lumsden et al 1979[2]						
In training	7.5 ± 1.3	3.8 ± 0.9	3.1 ± 0.7	0.2 ± 0.1	0.2 ± 0.2	139 ± 44
Rose et al 1983[8] (submaximal treadmill training)						
Untrained	7.0 ± 1.3	–	–	–	–	–
3 weeks training	6.5 ± 0.7	–	–	–	–	–
7 weeks training	7.0 ± 0.7	–	–	–	–	–
Johnstone et al 1991[9]						
Mature racing horses	–	–	–	–	–	157 ± 42
Tyler-McGowan et al 1999[10]						
7 weeks of training	–	3.8 ± 0.4	2.8 ± 0.1	0.37 ± 0.02	0.18 ± 0.03	–
15 weeks of training	–	4.7 ± 0.4	2.5 ± 0.2	0.43 ± 0.06	0.17 ± 0.03	–
28 weeks of training	–	4.8 ± 0.3	2.5 ± 0.2	0.45 ± 0.06	0.12 ± 0.01	–
32 weeks of training	–	5.0 ± 0.4	2.3 ± 0.2	0.43 ± 0.04	0.12 ± 0.02	–
Overtrained	–	4.7 ± 0.3	2.7 ± 0.2	0.49 ± 0.04	0.09 ± 0.01	–
Quarter Horses						
Kästner et al 1999[11]						
Reining horses	7.53 ± 1.03	4.38 ± 0.51	2.89 ± 0.56	0.14 ± 0.17	0.10 ± 0.13	–

	WBC ($\times 10^9$/L)	Neutrophils ($\times 10^9$/L)	Lymphocytes ($\times 10^9$/L)	Monocytes ($\times 10^9$/L)	Eosinophils ($\times 10^9$/L)	Platelets ($\times 10^9$/L)
Endurance horses						
Carlson et al 1976[12]						
Competing horses	7.5 ± 1.2	4.5 ± 0.9	2.3 ± 0.6	0.33 ± 0.12	0.31 ± 0.2	–
Rose 1982[13]						
Competing horses	8.73 ± 0.61	5.42 ± 0.78	2.82 ± 0.20	0.30 ± 0.06	0.46 ± 0.14	–
Arabian						
Jain 1986[14]						
Mixed sexes	9.53 ± 2.35	4.75 ± 1.5	4.0 ± 1.3	0.42 ± 0.15	0.27 ± 0.11	–
Lipizzan						
Cebulj-Kadunc et al 2002[15]						
Stallions	7.56 ± 0.13	–	–	–	–	–
Mares	7.48 ± 0.18	–	–	–	–	–
Clydesdale						
Geiser et al 1984[16]						
70 geldings	3.9–12.4	2.6–7.2	0.89–3.6	0–0.62	0–0.62	–
American miniature horse						
Harvey & Hambright 1985[17]						
Mixed sex and age	10.0 ± 2.5	3.7 ± 0.8	5.9 ± 0.9	0.04 ± 0.08	0.3 ± 0.2	–

Data are ranges or mean ± SD.

References

1. Steel JD, Whitlock LE. Observations of the haematology of Thoroughbred and Standardbred horses in training and racing. Aust Vet J 1960; 36:136–142.
2. Lumsden JH, Rowe R, Mullen K. Hematology and biochemistry reference values for the light horse. Can J Comp Med 1980; 44:32–42.
3. Bayly WM, Meyers KM, Keck MT, et al. Exercise-induced alterations in haemostasis in Thoroughbred horses. In: Snow DH, Persson SGD, Rose RJ, eds. Equine exercise physiology. Cambridge, UK: Granta Editions; 1983:336–342.
4. Revington M. Haematology of the racing Thoroughbred in Australia 1: reference values and the effect of excitement. Eq Vet J 1983; 15:141–144.
5. Snow DH, Ricketts SW, Mason DK. Haematological response to racing and training exercise in Thoroughbred horses, with particular reference to the leucocyte response. Eq Vet J 1983; 15:149–154.
6. Allen BV, Kane CE, Powell DG. Leucocyte counts in the healthy English Thoroughbred in training. Eq Vet J 1984; 16:207–209.
7. Allen BV. Comparison of the haemogram between three-year-old Thoroughbred stayers and sprinters. Vet Record 1986; 118:555–556.
8. Rose RJ, Allen JR, Hodgson DR, et al. Responses to submaximal treadmill exercise and training in the horse: changes in haematology, arterial blood gas and acid base measurements, plasma biochemical values and heart rate. Vet Record 1983; 113:612–618.
9. Johnstone IB, Viel L, Crane S, et al. Hemostatic studies in racing Standardbred horses with exercise-induced pulmonary hemorrhage. Hemostatic parameters at rest and after moderate exercise. Can J Vet Res 1991; 55:101–106.
10. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Eq Vet J Suppl 1999; 30:621–625.
11. Kästner SBR, Feige K, Weishaupt MA, et al. Heart rate and hematological responses of Quarterhorses to a reining competition. J Eq Vet Sci 1999; 19:127–131.
12. Carlson GP, Ocen PO, Harrold D. Clinicopathologic alterations in normal and exhausted endurance horses. Theriogenology 1976; 6:93–104.
13. Rose RJ. Haematological changes associated with endurance exercise. Vet Record 1982; 110:175–177.
14. Jain NC. Schalm's veterinary hematology. Philadelphia, PA: Lea and Febiger, 1986.
15. Cebulj-Kadunc N, Bozic M, Kosec M, et al. The influence of age and gender on haematological parameters in Lipizzan horses. J Vet Med A 2002; 49:217–221.
16. Geiser DR, Goble DO, Held JP. Normal hematology and serology of the Clydesdale draft horse. Eq Pract 1984; 6:7–9.
17. Harvey RB, Hambright MB. Normal serum chemistry and hematology values of the American miniature horse. Eq Pract 1985; 7:6–8.

APPENDIX 2

References ranges for serum biochemical variables in athletic horses

(Compiled by J. Kingston)

Breed and/or use	Analyte								
	Na mEq/L or mmol/L	K mEq/L or mmol/L	Cl mEq/L or mmol/L	HCO_3^- mEq/L or mmol/L	Total protein g/dL (g/L)	Albumin g/dL (g/L)	Globulin g/dL (g/L)	Fibrinogen mg/dL (g/L)	AST U/L
Thoroughbreds									
Untrained mares[1]	138 ± 2.2	3.5 ± 0.5	99.5 ± 3.1	–	6.8 ± 0.4 (68 ± 4)	3.2 ± 0.2 (32 ± 2)	3.3 ± 0.4 (33 ± 4)	–	165 ± 33.6
Standardbreds									
Racing[1]	140 ± 1.5	3.6 ± 0.4	99 ± 1.0	–	6.4 ± 0.5 (64 ± 5)	3.1 ± 0.2 (31 ± 2)	3.3 ± 0.5 (33 ± 5)	–	217 ± 140
6 weeks light training[2]	140 ± 1.39	3.3 ± 0.3	–	–	–	–	–	–	336 ± 83
12 weeks full training[2]	140 ± 1.73	3.2 ± 0.24	–	–	–	–	–	–	443 ± 280
7 weeks of training[3]	–	–	–	–	6.7 ± 1.32 (67 ± 13.2)	3.2 ± 0.29 (32 ± 2.94)	–	–	299 ± 92
15 weeks of training[3]	–	–	–	–	6.3 ± 0.8 (63 ± 8)	3.3 ± 0.17 (33 ± 1.7)	–	–	337 ± 140
28 weeks of training[3]	–	–	–	–	6.7 ± 0.88 (67 ± 8.8)	3.4 ± 0.17 (34 ± 1.7)	–	–	401 ± 148
32 weeks of training[3]	–	–	–	–	6.9 ± 0.88 (69 ± 8.8)	3.7 ± 0.17 (37 ± 1.7)	–	–	425 ± 144
Overtrained[3]	–	–	–	–	6.7 ± 0.48 (67 ± 4.8)	3.7 ± 0.07) (37 ± 0.7)	–	–	645 ± 396
Performance horses									
Mixed breeds[4]	134–144	3.2–4.2	94–104	–	5.5–7.5 (55–75)	2.6–3.8 (26–38)	2.0–3.5 (20–35)	< 400 < 4	150–400
Endurance horses									
North America[5]	139.1 ± 2.5	3.6 ± 0.4	101.1 ± 2.4	29.5 ± 2.4	7.0 ± 0.4 (70 ± 4.0)	–	–	–	–
Australia[6]	134 ± 2.8	3.5 ± 0.3	–	26.9 ± 1.5	6.0 ± 0.7 (60 ± 7.0)	3.0 ± 0.4 (30 ± 4.0)	–	–	204 ± 107
South Africa[7]	139 ± 3.4	3.3 ± 0.6	–	–	6.8 ± 0.3 (67.5 ± 3.3)	–	–	–	–
Quarter Horses									
Reining horses[8]	143 ± 1.7	3.4 ± 0.8	100 ± 1.6	–	–	–	–	–	–
Three-day event horses									
Australia[9]	136.8 ± 2.7	3.4 ± 0.4	99.5 ± 2.7	–	6.8 ± 0.5 (68 ± 4.7)	4.7 ± 0.3 (47.1 ± 2.7)	–	–	174–401
North America[10]	137.6 ± 4.4	3.6 ± 0.3	105 ± 5.3	–	6.5 ± 0.4 (65 ± 4.0)	4.0 ± 0.2 (40.1 ± 2.2)	–	–	333 ± 85
Showjumpers									
In competition	138 ± 0.7	4.0 ± 0.1	105.7 ± 0.6	22.5 ± 0.9	6.7 ± 0.2 (67 ± 2.0)	–	–	–	105 ± 10
Hunter/Thoroughbreds									
In training[11]	–	–	–	–	–	–	–	–	285 ± 42
Heavy breeds									
English shire horses	–	–	–	–	7.2 ± 0.6 (72 ± 6.0)	2.8 ± 0.3 (28 ± 3.0)	–	–	172 ± 28
Clydesdales	137.1 ± 5.2	3.6 ± 0.5	101.9 ± 4.6	–	7.2 ± 0.1 (72 ± 0.8)	3.6 ± 0.5 (36 ± 5.0)	–	–	234 ± 163
Polo horses									
In competition[12]	136 ± 3.4	4.3 ± 0.8	98 ± 2.5	30.7 ± 1.7	7.3 ± 0.6 (73 ± 5.9)	–	–	–	–
Driving horses and ponies									
Mixed breeds[13]	137 ± 2.0	3.4 ± 0.5	100 ± 2.0	–	6.5 ± 0.4 (64.5 ± 4.0)	–	–	–	179 ± 61
American miniature horses									
Mixed sexes[14]	136 ± 2.2	4.3 ± 0.3	–	–	6.6 ± 0.6 (66 ± 6.0)	–	–	–	189 ± 33

Analyte									
CK U/L	LDH U/L	Glucose mg/dL (mmol/L)	GGT U/L	SDH U/L	AP U/L	Blood urea nitrogen mg/dL (mmol/L)	Creatinine mg/dL (mmol/L)	Total calcium mg/dL (mmol/L)	Ionized calcium mg/dL (mmol/L)
44.5 ± 22.3	153 ± 36.7	94.9 ± 27.7 (5.27 ± 1.54)	–	1.8 ± 1.2	59 ± 16.7	49.6 ± 9.2 (17.7 ± 3.3)	1.3 ± 0.2 (115 ± 18)	11.9 ± 0.4 (2.89 ± 0.1)	–
38.5 ± 40	140 ± 33.5	81.9 ± 9.36 (4.55 ± 0.52)	–	–	45.6 ± 10.8	31.1 ± 4.8 (11.1 ± 1.7)	1.3 ± 0.2 (115 ± 18)	11.9 ± 0.52 (2.98 ± 0.13)	–
301 ± 177 (301 ± 177)	–	–	16 ± 5.9 (16 ± 5.9)	–	–	–	–	–	–
231 ± 104 (231 ± 104)	–	–	24 ± 12.5 (24 ± 12.5)	–	–	–	–	–	–
282 ± 216	–	–	20 ± 13.6	–	–	–	–	–	–
194 ± 40	–	–	40 ± 31.2	–	–	–	–	–	–
210 ± 69	–	–	35 ± 28.4	–	–	–	–	–	–
223 ± 64	–	–	51 ± 36.8	–	–	–	–	–	–
396 ± 524	–	–	70 ± 48	–	–	–	–	–	–
100–300	< 250	70–140 (4–8)	10–40	–	70–210	11–22 (4–8)	1.1–1.8 (108–132)	10.8–13.2 (2.7–3.3)	–
–	–	–	–	–	–	–	–	12.2 ± 0.6 (3.04 ± 0.15)	–
80 ± 102	365 ± 140	98.2 ± 9.5 (5.45 ± 0.53)	–	–	159 ± 54	–	1.2 ± 0.2 (106 ± 17.7)	12.7 ± 0.7 3.17 ± 0.17	–
–	–	68.4 ± 12.6 (3.8 ± 0.7)	–	–	–	15 ± 3 (5.5 ± 1.0)	–	12.4 ± 0.4 (3.1 ± 0.1)	–
–	–	–	–	–	–	–	–	11.99 ± 0.64 (2.99 ± 0.16)	–
117–311	–	117 ± 12.6 (6.5 ± 0.7)	–	–	138–251	17 ± 3 (5.9 ± 1.1)	1.48 ± 0.19 (131 ± 16.4)	11.9 ± 0.64 (2.98 ± 0.16)	–
218 ± 149	–	100.8 ± 7.2 (5.6 ± 0.4)	–	–	–	16.5 ± 1.4 (5.9 ± 0.5)	1.38 ± 0.25 (121 ± 21.7)	12.8 ± 0.8 (3.2 ± 0.2)	6.82 ± 0.4 (1.7 ± 0.1)
48 ± 4.0	375 ± 30	–	–	–	–	–	–	12.8 ± 0.28 (3.3 ± 0.1)	–
115 ± 39	645 ± 168	–	–	–	–	–	–	–	–
58 ± 16	–	–	24.2 ± 6.0	0.8 ± 0.2	54 ± 11	–	–	–	–
56 ± 22	–	75.9 ± 19.2 (4.21 ± 1.1)	–	–	91 ± 36	14.5 ± 3.2 (5.2 ± 1.14)	1.7 ± 0.3 (151 ± 26.5)	11.9 ± 1.1 (2.97 ± 0.27)	–
–	–	–	–	–	–	–	–	12.9 ± 0.24 (3.21 ± 0.06)	–
35 ± 9	–	97.2 ± 9.0 (5.4 ± 0.5)	–	–	–	15 ± 3 (5.5 ± 1.1)	–	12.0 ± 0.4 (3.0 ± 0.1)	–
273 ± 136	–	91 ± 12.4 (5.1 ± 0.7)	11 ± 4.4	–	181 ± 53	23.7 ± 3.8 (8.5 ± 1.4)	1.0 ± 0.2 (88.4 ± 17.7)	11.6 ± 0.4 (2.9 ± 0.1)	–

References

1. Lumsden JH, Rowe R, Mullen K. Hematology and biochemistry reference values for the light horse. Can J Comp Med 1980; 44:32–42.
2. Robertson ID, Bolton JR, Mercy AR, et al. Haematological and biochemical values in 12 Standardbred horses during training. Aust Eq Vet 1996; 14:72–76.
3. Tyler-McGowan CM, Golland LC, Evans DL, et al. Haematological and biochemical responses to training and overtraining. Eq Vet J Suppl 1999; 30:621–625.
4. Rose RJ, Hodgson DR. Hematology and biochemistry. In: Hodgson DR, Rose EJ, eds. The athletic horse. Philadelphia, PA: WB Saunders; 1994;64–78.
5. Carlson GP, Ocen PO, Harrold D. Clinicopathologic alterations in normal and exhausted endurance horses. Theriogenology 1976; 6:93–104.
6. Rose RJ, Purdue RA, Hensley W. Plasma biochemistry alterations in horses during an endurance ride. Eq Vet J 1977; 9:122–126.
7. Grosskopf JFW, Van Rensburg JJ, J. BH. Haematology and blood biochemistry of horses during a 210 km endurance ride. In: Snow DH, Persson SGB, Rose RJ, eds. Equine exercise physiology, Cambridge, UK: Granta Editions, 1983;416–424.
8. Kästner SBR, Feige K, Weishaupt MA, et al. Heart rate and hematological responses of Quarterhorses to a reining competition. J Eq Vet Sci 1999; 19:127–131.
9. Rose RJ, Ilkiw JE, Arnold KS, et al. Plasma biochemistry in the horse during 3-day event competition. Eq Vet J 1980; 12:132–136.
10. Andrews FM, Geiser DR, White SL, et al. Haematological and biochemical changes in horses competing in a 3 Star horse trial and 3-day-event. Eq Vet J Suppl 1995: 57–63.
11. Anderson MG. The influence of exercise on serum enzyme levels in the horse. Eq Vet J 1975;7:160–165.
12. Craig L, Hintz HF, Soderholm LV, et al. Changes in blood constituents accompanying exercise in polo horses. Cornell Vet 1985; 75:297–302.
13. Snow DH. Haematological, biochemical and physiological changes in horses and ponies during the cross country stage of driving trial competitions. Vet Record 1990; 126:233–239.
14. Harvey RB, Hambright MB. Normal serum chemistry and hematology values of the American miniature horse. Eq Pract 1985;7:6–8.

INDEX

Notes
Page numbers in *italics* refer to figures: those in **bold** refer to tables or boxed materials.
To save space in the index the following abbreviations have been used:
EIPH - exercise-induced pulmonary hemorrhage
EPM - equine protozoal myeloencephalitis
HYPP - hyperkalemic periodic paralysis
IAD - inflammatory airway disease
NSAIDs - non-steroidal anti-inflammatory drugs
RAO - recurrent airway obstruction
As the subject of this book refers to horses, this has not been used as a main entry. Readers are advised to seek more precise terms. Please note *vs.* indicates a comparison.

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